As we celebrate 5 years of BMJ Case Reports, we present this special edition of the journal presenting new medical findings and new techniques in clinical medicine. We hope you will find this collection of cases to be of interest, and hope you will see how valuable they can be in your own teaching.

So often, case reports focus on the rare and unusual, but this collection reminds us of the relevance of case reports in documenting what practising clinicians need to know in our daily work and reaffirms the role of case reports in reporting important new findings, ways of thinking about clinical outcome and risk, dealing with complications and the limitations of clinical investigations and their interpretation.

The last two articles are a taste of our new Global Health case reports which we are launching in celebration of our 5th anniversary. They show how powerful medical writing is in telling our patients’ stories and reporting the determinants of health and disease.

Seema Biswas,
Editor, BMJ Case Reports
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A lethal cocktail: gastric perforation following liquid nitrogen ingestion

James Scott Pollard,1 Joanne Elizabeth Simpson,2 Moatasem Idris Bukhari1

1Department of Surgery, Royal Lancaster Infirmary, Lancaster, UK
2Department of Emergency Medicine, Royal Lancaster Infirmary, Lancaster, UK

Correspondence to James Scott Pollard, james.pollard@doctors.net.uk

SUMMARY
We report a case of gastric perforation in an 18-year-old girl as a result of ingesting an alcoholic drink containing liquid nitrogen. The drink was purchased in licensed premises. The extent of the injury necessitated total gastrectomy with Roux-en Y reconstruction. We review the literature, discuss the mechanism of injury and consider the implications for medical services. The authors believe this case is of educational interest to professionals working in emergency medicine, general surgery and public health fields. It raises awareness of a rare injury, but one that may be more commonly encountered because of developing social trends. It informs surgeons confronted with this type of injury that trauma to the gastrointestinal tract can be extensive and preoperative contact with oesophago-gastric colleagues is advisable. Public health bodies must be aware of, and monitor, the use of liquid nitrogen in this way and consider regulation to prevent further injuries.

BACKGROUND
Liquid nitrogen is being used as an additive to alcoholic drinks to create an aesthetic ‘smoking’ effect. Recipes are available on the internet and such drinks are increasingly sold in some licensed premises. Use in this way requires no training and sales are unregulated. We report this case to raise awareness among the public and medical services of the potential dangers of using liquid nitrogen in this way.

CASE PRESENTATION
An 18-year-old girl presented to the emergency department following ingestion of an alcoholic drink containing liquid nitrogen purchased in licensed premises. She complained of sudden onset of severe abdominal pain and shortness of breath immediately after ingestion. She had no medical history. On examination she was tachycardiac and tachypnoeic. Her abdomen was distended, tympanic and peritonitic.

INVESTIGATIONS
Her white cell count was raised at 30.7×10⁹/l and an erect chest x-ray (figure 1) showed a large volume pneumoperitoneum. A CT scan of her abdomen confirmed the presence of both a large volume pneumoperitoneum and free intrabdominal fluid but was unable to identify the site of perforation.

TREATMENT
After initial resuscitation and broad spectrum antibiotics, an emergency laparotomy with on table oesophagogastroduodenoscopy (OGD) was performed.

At operation a 4 cm linear perforation was identified in the anterior wall of the stomach overlying the lesser curve. Surrounding this was an area of necrosis and haemorrhage extending around the posterior wall of the stomach and superiorly towards the gastroesophageal junction (figure 2). There was also some erythema affecting the fundus of the stomach. The rest of the abdominal contents were normal. OGD did not show any oesophageal injury but identified extensive tearing of the mucosa along the lesser curve (figure 3), extending up to the gastroesophageal junction (figure 4). Owing to the extent of the injury advice from a specialist oesophago-gastric surgeon was sought. The perforation could not be safely closed primarily due to the extent of the necrotic area and hence a total gastrectomy with Roux-en Y reconstruction was undertaken. Proximal gastrectomy was rejected because of the risk of poor function of the remaining gastric remnant. A feeding jejunostomy was sited to provide nutrition during the postoperative period. The patient was transferred to the critical care unit, ventilated and requiring vasopressor support.

OUTCOME AND FOLLOW-UP
The patient was extubated the next day and enteral feeding commenced via jejunostomy. She was transferred to the surgical ward on the fourth day postoperatively. Oral intake was commenced on the sixth postoperative day. She was discharged 15 days postoperatively.
DISCUSSION

With a boiling point of −195°C liquid nitrogen can cause severe thermal burns to the skin and the mucosal membranes. It has an expansion ratio of 1:694 on vaporisation leading to a rapid increase in volume.

Cases of ingestion resulting in gastric perforation are reported in the literature.1–4 In all these cases the clinical presentation is similar to the case we report, namely a rapid onset of abdominal pain associated with shortness of breath. In three cases, the site of perforation was identified as being over the lesser curve of the stomach, the same site as in our case.1–3 In one case an OGD was performed which did not show any thermal injury to the oesophagus,5 again a finding similar to this case.

The absence of injury to the oesophagus does not seem to support thermal injury as the major cause of visceral perforation, although it may have contributed to the gastric mucosal injury and subsequent perforation. The consistent finding of a large volume of gas within the peritoneum, would suggest barotrauma to the stomach, resulting from rapid increase in volume on vaporisation of the liquid, as the primary mechanism of injury. The consistent site of perforation may indicate that this part of the stomach is the most susceptible to barotrauma. Evidence from compressed air diving accidents would seem to support this, with the lesser curve commonly identified as the site of gastric perforation.5

Learning points

▸ Staff working in emergency departments and acute surgical units need to be aware of the potential for such injuries to occur.
▸ Surgeons facing this type of injury need to be aware of the potential for major upper gastrointestinal trauma and consider preoperative involvement of specialist oesophago-gastric colleagues.
▸ Public health bodies must monitor the increasing use of liquid nitrogen in alcoholic drinks and alert the public to the potential dangers.
▸ We believe regulators must take action to end use of liquid nitrogen in this way and look at restricting its sale to only those properly trained in its use in order to prevent future incidents such as this.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

CASE REPORT

C reactive protein may not be reliable as a marker of severe bacterial infection in patients receiving tocilizumab

Syed Farhan Bari, Afsha Khan, Tom Lawson

SUMMARY
This is a case of a 65-year-old man with seropositive erosive rheumatoid arthritis (RA), well controlled on methotrexate, sulfasalazine, low-dose prednisolone and monthly infusions of tocilizumab. He presented with a 3-week history of pain and swelling in his left knee, gradually increasing in severity with an inability to bear weight. He was systemically well with normal vital signs. Examination confirmed an effusion and aspiration was turbid in appearance. C reactive protein (CRP) was normal. He was treated empirically with antibiotics. Synovial fluid and blood cultures confirmed Staphylococcus aureus infection. He completed a 6 weeks course of antibiotics with complete resolution of symptoms. Throughout the treatment his CRP remained normal which is likely to have been the result of prior treatment with tocilizumab.

BACKGROUND
This case illustrates that systemic symptoms and an elevated C reactive protein (CRP) may not be present in patients treated with tocilizumab even in the context of severe life-threatening sepsis. A high index of suspicion should be retained in all patients presenting with new symptoms or signs. It is well recognised that in patients receiving disease modifying antirheumatic drugs (DMARDs) the symptoms and signs of infection may be diminished. However, with these drugs CRP still usually increases in the context of acute infection and can therefore be used as a marker of response to treatment. In patients receiving tocilizumab, CRP may remain suppressed even in the context of severe infection and may therefore be less useful for diagnostic or monitoring purposes.

CASE PRESENTATION
We present a case of a 65-year-old man with seropositive erosive RA, well controlled on methotrexate, sulfasalazine, low-dose prednisolone and monthly infusions of tocilizumab. He presented with a 3-week history of gradually worsening pain and swelling in his left knee. There was no history of trauma and he denied any fever, rigours or recent infection.

On examination he was systemically well, no fever, rigours or recent infection. There was no synovitis in other joints. He was systemically well with normal vital signs.

INVESTIGATIONS
Investigations revealed a total white cell count of 11.8×10^9/L (normal 4–11×10^9/L) with normal neutrophil count, CRP 4 mg/dl (normal <10 mg/dl); renal and liver function tests were also normal. Synovial fluid aspirated from the knee was turbid in appearance. Microscopy demonstrated polymorphs, but no visible organisms on Gram stain. Blood and synovial fluid cultures subsequently confirmed infection with Staphylococcus aureus.

DIFFERENTIAL DIAGNOSIS
The differential diagnoses considered in this case prior to synovial and blood culture results were: ▶ Septic arthritis ▶ Crystal arthropathy ▶ Monoarticular flare of RA

TREATMENT
Despite the absence of fever and the normal CRP, the turbid appearance of the synovial fluid and prior immunosuppression led to empirical treatment with intravenous flucloxacillin 2 gm and oral fusidic acid 500 mg. Culture of synovial fluid and blood subsequently confirmed S aureus septic arthritis and septicaemia. The organism was sensitive to flucloxacillin and fusidic acid. Tocilizumab was discontinued. Arthroscopic washout of the knee was performed and a total of 2 weeks of intravenous and 4 weeks of oral antibiotics were administered with complete resolution of his symptoms and signs. The CRP remained normal throughout.

OUTCOME AND FOLLOW-UP
The patient made a full recovery following arthroscopic lavage and 6 weeks of antibiotic treatment. The British Society of Rheumatology guidelines recommend avoiding tocilizumab therapy for a year after an acute, severe infection such as septic arthritis. However, in this case the patient suffered a flare of RA and due to persistent disease activity, tocilizumab was restarted after 4 months. The patient was fully informed of reinfection risks. Six months later there has been no recurrence of infection and the patient remains well.

DISCUSSION
Tocilizumab is licensed for the treatment of RA. It can be used as a first-line biological agent after inadequate response to or intolerance of DMARDs, or after inadequate response or intolerance to other biologics such as TNF-α inhibitors and rituximab. It is a humanised monoclonal antibody targeting circulating Interleukin-6 (IL-6) receptors. It blocks the proinflammatory effects of IL-6, affecting the function of neutrophils, T cells, B cells, monocytes and osteoclasts.2

Reminder of important clinical lesson
To cite: Bari SF, Khan A, Lawson T. BMJ Case Rep Published online: [please include Day Month Year] doi:10.1136/bcr-2013-010423 casereports.bmj.com

Department of Rheumatology, Princess of Wales Hospital, Bridgend, UK
Correspondence to Dr Syed Farhan Bari, dr_farhan@hotmail.com
IL-6 is a key driver of the acute-phase response and has an important role in the production of CRP in the liver. CRP is used in clinical practice as a marker of inflammation and infection. Although it is well recognised that patients on immunosuppressants may not exhibit the usual symptoms and signs of sepsis such as fever, there is still usually an elevation of CRP levels in such cases. Three case reports have reported the absence or masking of symptoms of severe infections in patients treated with tocilizumab. The suppression of CRP in patients treated with tocilizumab could lead to delay in diagnosis of serious infection in patients on this treatment. Physicians must be aware of the potential for infection when patients treated with tocilizumab present with new symptoms. The rate of infection in patients with RA treated with tocilizumab in clinical practice is higher than in the clinical trial populations. Risk may be increased in patients with longer disease duration, previous exposure to multiple DMARDs and those receiving concomitant leflunomide, prednisolone or proton-pump inhibitor treatment.

Contributors SFB was involved in the initial assessment, management and follow-up of the patient and contributed towards the writing of the case report. AK was involved in the management and further follow-up of the patient and contributed towards the writing of the case report. TL was the supervising consultant and supervised the management of the patient and the writing of the case report.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES
1 NICE technology appraisal guidance (TA 247).
Findings that shed new light on the possible pathogenesis of a disease or an adverse effect

Three cases of severely disseminated *Staphylococcus aureus* infection in patients treated with tocilizumab

Mai TT Nguyen, Jan Pødenphant, Pernille Ravn

**SUMMARY**

We report three cases of severe disseminated *Staphylococcus aureus* infection in patients with rheumatoid arthritis (RA) treated with tocilizumab. Tocilizumab is a new drug, unknown to most internists, and injections given weeks before admission may not be considered by the patient as part of their 'current medical treatment', and the physician may not be aware that the patient is severely immunosuppressed. Severe infections in RA patients treated with tocilizumab may present with mild symptoms despite severe and disseminated infection and, as these patients are severely immunodeficient-intensive diagnostic work-up and early treatment should be performed. Systematic postmarketing studies are needed to clarify if there is a true increased risk of disseminated *S aureus* infections. We suggest caution when prescribing tocilizumab to patients with prosthetic joints and/or prior invasive *S aureus* infections and that patients are taught to inform health staff about their medication history and their increased risk of infection.

**BACKGROUND**

Severe infections in rheumatoid arthritis (RA) patients treated with tocilizumab may present with mild symptoms despite severe and disseminated infection and intensive diagnostic work-up, and early treatment should be performed. The patients and the physician may not be aware of the severity of immunodeficiency.

We suggest caution when prescribing tocilizumab to patients with prosthetic joints and/or prior invasive *Staphylococcus aureus* infections. We argue for systematic postmarketing studies to clarify if there is a true increased risk of disseminated *S aureus* infection.

**CASE PRESENTATION**

**Background**

In 2008, the interleukin 6 (IL-6) inhibitor, tocilizumab, was introduced to treat patients with RA who do not respond to treatment with disease-modifying antirheumatic drugs (DMARDS) or other biological treatment. IL-6 plays a key role in eliciting an acute phase response by inducing production of C reactive protein (CRP), differentiation of B-cells to antibody-producing cells, differentiation of cytotoxic T cells, leucocytosis and thrombocytosis. A marginally increased risk of infection compared with DMARD has been observed.

Within the year 2011, we have seen three patients treated with tocilizumab who developed severe disseminated *S aureus* bacteremia in Denmark and we report the cases here.

**Case 1**

A 68-year-old woman, receiving tocilizumab and methotrexate (figure 1A) for her RA, was admitted with progressive global weakness, mild confusion, aphasia and neck stiffness, but no fever. She had a history of severe RA for 35 years with previous joint replacement of the right elbow, left hip and both knees. On suspicion of neurological infection, lumbar puncture was performed. The cerebrospinal fluid was purulent and grew *S aureus*. The blood culture was negative. MRI showed a massive epidural abscess from C2 to the sacrum and, in addition, a positron emission tomography (PET)-CT scan showed pathological activity around the prosthesis of the left hip. Immunosuppressive drugs were stopped and treatment was initiated with cefuroxime for a total of 6 weeks followed by oral dicloxacillin 1 g four times a day for 8 weeks and the infected hip prosthesis was removed. Despite this, she relapsed twice over the next 6 months and PET-CT was repeated which now revealed activity in the right elbow. She had clinical symptoms in both the knees and aspirate was performed from these joints which revealed *S aureus*. All three prostheses were removed and she is now receiving long-term antibiotic treatment and has not relapsed.

**Case 2**

A 63-year-old man with type 2 diabetes and RA, receiving azathioprine and tocilizumab (figure 1B) had a 1-day history of chest pain and increasing shortness of breath in his left ankle. He had prostheses in both knees inserted 3 years prior to admission. On admission he had fever and swelling of the ankle. On suspicion of septic arthritis from the ankle joint was performed and gentamicin and cefuroxime were initiated. Shortly after, the left elbow, both knees, the right wrist and the basal joint of the left thumb were tender with swelling. Multiple aspirations were conducted and *S aureus* was cultured from both knees, the left elbow joint and several blood cultures. Antibiotic treatment was changed to dicloxacillin and rifampicin after the growth of *S aureus*. He was admitted for a total of 7 months with a need for aggressive surgical debridement. He had a history of *S aureus* infection in the elbow >3 years prior to admission.

**Case 3**

A 59-year-old man with RA receiving methotrexate, prednisolone and tocilizumab (figure 1C) was admitted with 1 week of fever, cough and dyspnoea. Blood cultures were positive for *S aureus* and he was treated with intravenous dicloxacillin 1 g four times a day. A pleural effusion developed and *S aureus* was grown from a diagnostic aspirate.
despite 1 week of relevant treatment. The situation was complicated by respiratory failure, myocardial infarction and disseminated intravascular coagulation, and he died 11 days after admission. One year before, he had been treated for infection with \textit{S aureus} in his olecranon bursa. In all three cases, endocarditis was excluded by transoesophageal ECG.

**DISCUSSION**

We have reported three cases of severe \textit{S aureus} infection in RA patients treated with tocilizumab of whom one died and the other two were hospitalised for >4 months. All had advanced RA and a long treatment history and two patients had a history of prior invasive \textit{S aureus} infection and two had prosthetic joints.

All three cases had relevant symptoms for the doctor to suspect an infection and initiate early treatment and appropriate diagnostic investigations. The CRP was relatively low (table 1) and it was possible for the patients to make an inflammatory response, although the CRP seemed low compared with the extent and severity of infection.

It was not registered in any of the admissions file that the patients had received tocilizumab injections 1–4 weeks prior to admission. Tocilizumab is a new drug, unknown to most internists, and injections given weeks before admission may not be considered by the patient as part of the ‘current medical treatment’ and may not be registered properly by the physician.

Not removing prosthetic joints is a strong predictor for relapse. Whether immediate removal of all prosthetic joints in case 1 might have changed the duration of illness is unknown.

No information on \textit{S aureus} colonisation of the skin was available, and it is unknown whether de-colonisation would be able to prevent infection in these patients.

In Denmark, 158 patients received tocilizumab in 2011 (http://www.danbio.dk), and three cases of \textit{S aureus} infection

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<th>Table 1</th>
<th>Laboratory values on admission</th>
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<td></td>
<td>Case 1</td>
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<td>CRP</td>
<td>14</td>
</tr>
<tr>
<td>Total leucocyte count</td>
<td>20.3</td>
</tr>
<tr>
<td>Neutrophil leucocyte count</td>
<td>14.6</td>
</tr>
<tr>
<td>Lymphocyte count</td>
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</tr>
<tr>
<td>Haemoglobin</td>
<td>9.3</td>
</tr>
<tr>
<td>Albumin</td>
<td>44</td>
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<tr>
<td>Thrombocytes</td>
<td>152</td>
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CRP, C reactive protein.
reflect a high incidence, but systematic postmarketing studies should clarify if there is a true increased risk of *S aureus* infections.

We suggest caution when prescribing tocilizumab to patients with prosthetic joints and/or prior invasive *S aureus* infections. All patients should be aware that they should inform health staff about their medication history and their increased risk of infection.

**Learning points**

- Patients treated with biological antibodies should be considered severely immunocompromised and treated as such with intensive diagnostic work-up and immediate antibiotic treatment if infection is suspected, as severe infection may present in a less florid manner.
- Prior *Staphylococcus aureus* infections may be a risk factor for *S aureus* infection.
- Removal or debridement of infected prosthesis is essential if eradication of infection is to be achieved.
- Postmarketing surveillance is important to increase the level of evidence regarding an increased risk of severe or disseminated infections with *S aureus* following treatment with tocilizumab.

**Competing interests** None.

**Patient consent** Obtained.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**REFERENCES**

Unexpected outcome (positive or negative) including adverse drug reactions

Complications of facial fillers: resource implications for NHS hospitals

Nadine Hachach-Haram, Marco Gregori, Niall Kirkpatrick, Richard Young, Jonathan Collier

SUMMARY
Facial rejuvenation seeks to reverse the negative sequelae of multiple factors but most importantly of genetic predisposition, sun damage and smoking. With the advent of the so-called ‘non-surgical’ techniques, and perhaps fuelled by these austere times, volumetric facial augmentation using dermal fillers has soared in popularity among both patients and practitioners. However, legislation has yet to keep pace with the change in clinical practices leaving patients poorly informed and with no protection against unscrupulous suppliers and unregulated practitioners. When things go wrong, patients often turn to the National Health Service (NHS) to rectify both the acute and chronic sequelae resulting in potentially difficult ethical and resource implications. Here, we report one of an increasing number of cases presenting to our NHS craniofacial service with acute filler-related complications.

BACKGROUND
Volumetric ‘non-surgical’ facial augmentation has a long history spanning over two centuries. Following well-publicised disasters after facial injection with paraffin derivatives in the early 20th century, it was not until 1962 that the use of silicone for cheek augmentation was described. Since that time, a number of alternative materials have been developed and marketed and, most recently, hyaluronic acid (HA) fillers have massively increased their market share. The popularity of these HA-based fillers among patients and practitioners alike is probably due to their non-permanent nature and perceived improved safety profile, together with aggressive direct consumer marketing.

Patients seeking these ‘non-surgical’ procedures often fail to realise how poorly regulated this industry is, particularly outside the US. The US regards all dermal fillers as medicines and, consequently, requires them to be approved by the Federal Drug Administration. However, in Europe, fillers are regarded as medical devices requiring only Conformité Européenne (CE) certification. In the UK, a register of practitioners performing these treatments was introduced by the Independent Healthcare Advisory Service in 2011. However, this register remains voluntary and, in our experience, public awareness of the register remains poor.

Finally, even though regulation of these treatments remains poor (especially in the UK), access to unscrupulous suppliers via the internet is still available to individuals who wish to avoid the costs of professional treatment. Self-administration is fraught with dangers not least because there is usually no information provided regarding the type, composition and sterility of the material for injection actually supplied. We present the interesting case of a 31-year-old patient who presented to our hospital following the self-administration of an injectable filler material sourced from abroad on the internet. Issues regarding clinical management and potential resource implications will be discussed.

CASE PRESENTATION
A 31-year-old patient presented to our accident and emergency unit with a 24 h history of right facial pain and swelling with associated systemic malaise. The patient reported having self-injected approximately 10 ml of a filler material into the left and right nasolabial folds in two instalments over the previous 4 days. The patient had ordered this facial filler material (which the patient assumed to be HA-based) through the internet from a source in Brazil (figure 1). Previous, multiple-site, self-administered facial treatments from the same source had been performed during the last 12 months without complication. Sterile injection equipment had been purchased from Brazil and the patient denied needle sharing.

Hours after the second administration, the patient described a gradual increase in localised erythema, oedema and pain. Attempts to remove the material by gentle massage and expression through the injection site were unsuccessful.

The patient’s medical history included current hormone replacement therapy (oestrogen+anti-androgen). The patient had undergone breast augmentation and was awaiting male-to-female gender reassignment surgery. A background of poly-drug misuse was disclosed.

On examination, the patient was systemically well and all the observations were within normal range. A 4×3 cm swelling with associated induration was noted over the right cheek extending to the right lower eyelid. No discharge or punctum was visible. The swelling was fluctuant but did not transilluminate. Intraoral examination revealed a tense swelling distorting the buccal mucosa and associated systemic malaise. The patient was referred to the National Health Service (NHS) to rectify both the acute and chronic sequelae resulting in potentially difficult ethical and resource implications. Here, we report one of an increasing number of cases presenting to our NHS craniofacial service with acute filler-related complications.

INVESTIGATIONS
Blood tests were normal apart from a leucocytosis (12×10^3 cells/l) neutrophilia suggesting bacterial infection, and a mild elevation in the C reactive protein (27 mg/l). Microbiology swabs and trans-oral pus aspirates were taken and sent for microscopy, sensitivity and gram stain. The non-labelled
bottle containing the filler substance was sent for analysis. All the cultures were negative; no organisms were grown and only skin flora was found. Tests for acid fast-bacilli and HIV were also negative. Finally, the blood results also returned to within normal range 24 h after the commencement of intravenous antibiotic therapy.

Subsequent nuclear magnetic resonance spectroscopy and mass spectrometry of the unlabelled filler material was performed courtesy of the NMR Centre, Imperial College, University of London. The results confirmed that the sample was principally of silicone oil base (most likely a polydimethylsiloxane). Purity was estimated at 95% with trace contaminants.

DIFFERENTIAL DIAGNOSIS

- Concomitant skin-based pathology with supra-added infection
- Acute exacerbation of chronic granulomatous reaction secondary to multiple filler injections

TREATMENT

On presentation and after appropriate samples were obtained, treatment was commenced with intravenous antibiotics (benzylpenicillin and flucloxacillin). Conventional surgical management with percutaneous incision and drainage under general anaesthesia was advised but declined by the patient for fear of leaving a poor facial scar. The patient did consent to needle aspiration via an infra oral route and topical anaesthesia. This was performed daily for 4 consecutive days before the abscess did not clinically re-collect. On each occasion, 5–8 ml of frank pus was aspirated.

Since the patient stated that an HA-based filler was obtained, the intralesional injection of hyaluronidase was considered. Hyaluronidase degrades HA by lowering its viscosity and increasing its permeability within the tissues. However, given the ambiguous composition of the unlabelled filler, it was decided that administration of a biologically active substance into the wound was ill-advised. This decision was subsequently vindicated by chemical analysis (the results of which were only available after the patient had left hospital).

OUTCOME AND FOLLOW-UP

Once the patient’s clinical condition had settled and the abscess had been aspirated to dryness, the patient subsequently self-discharged. The inpatient length of stay was five nights. The patient failed to attend the outpatient review appointment that had been arranged.

Two months later, the patient re-presented with a similar erythematous fluctuant swelling in the contralateral nasolabial area. The patient denied any repeated self-administration of fillers. Again, the patient refused to consent to percutaneous incision and drainage, and a similar clinical course ensued with multiple needle aspirations of the acute abscess.

The total cost to the health service of these two clinical episodes was £2060 and £1968. The EBITDA for the hospital was +£624 and +£178, respectively. The EBITDA (earnings before interest, taxes, depreciation and amortisation) represents the money that the hospital retains after paying the costs of patient care.

DISCUSSION

Soft tissue augmentation is not a new phenomenon; it dates back to the beginning of the 20th century. Following well-publicised disasters after facial injection with paraffin derivatives in the early 20th century, it was not until 1962 that the use of silicone for cheek augmentation was described. Since that time, a number of alternative materials have been developed and marketed. The popularity of these fillers among patients and practitioners alike is probably due to their perceived improved safety profile, together with aggressive direct consumer marketing.

Volumetric ‘non-surgical’ facial augmentation has taken the industry by storm, and over the past 10 years, these non-invasive fillers have been easily available to the public. However, legislation has yet to keep pace with the change in clinical practices leaving patients poorly informed and with no protection against unscrupulous suppliers and unregulated practitioners. Parallel to this, the rate of globalisation has also been astounding, fuelling endless possibilities for ‘cosmetic tourism’ for those seeking cheaper aesthetic treatments abroad. Nonetheless, when things go wrong, patients often turn to the National Health Service (NHS) to rectify the acute and chronic situation resulting in potentially difficult ethical and resource implications and the case we present highlights this dilemma. We report this case to highlight one of an increasing number of cases presenting to our NHS craniofacial service with acute filler-related complications.

Outside the USA, the industry producing tools and applications of ‘non-surgical’ aesthetic procedures is very poorly regulated, with approvals only requiring a CE certification. The purchase of medications over the internet is entirely unregulated and this poses an even greater problem as this case highlights. Our patient erroneously assumed she had purchased a hyaluronic based filler when, in fact, subsequent chemical analysis showed this to be contaminated silicone oil (figure 2). This extends to the physician or beauticians administering the fillers with no way of assessing their techniques and complication rates.

The use of fillers is associated with normal sequelae that are not the same as complications. These sequelae include swelling, ecchymosis, postinjection pain and transient visibility of filler. Complications are often divided into three categories (table 1).

There is no ideal product on the market and fillers are generally categorised as temporary, semipermanent or permanent. The distinction is very important because although the permanent fillers last longer, they carry a much higher risk of complications that are challenging to treat.

Permanent filler complications can be present many years after injection with a high level of unpredictability deeming them a less predictable state than those fillers that are not permanent.
Unexpected outcome (positive or negative) including adverse drug reactions

Figure 2 Unlabelled filler material purchased over the internet and self-administered by the patient. Subsequent analysis showed it to be 95% silicone oil.

popular choice for the physician and the patient. Unfortunately, abnormal filler complications are not uncommon, forcing patients to seek help to improve their appearance. A survey among UK plastic surgeons, carried out by the British Association of Aesthetic Plastic Surgeons in 2009, revealed that approximately 40% of surgeons were seeing 1–3 patients/year with permanent facial filler complications.14

With patients presenting with the complications of fillers to their local NHS for help, advice and emergency treatment, the role of the NHS needs to be defined. Will it be considered on a case-by-case basis, or do guidelines and standards of treatment need to be outlined? Will the NHS limit its treatment to only the ‘acute’ cases? These are all unanswered questions that need to be addressed to help guide units such as ours on how to proceed.

Irrespective of the negative microbiology cultures, this case clearly demonstrates the risk of peri-prosthetic infections due to poor aseptic technique, contaminated instruments or nonsterile filler material as the patient experienced both early and late complications. More specifically, the unknown filler substance used by the patient was identified as polydimethylsiloxane, which can lead to chronic long-term sequelae including severe granulomatous reactions which are very difficult to treat.11 15

It also highlights the dilemma of maintaining aesthetic appearance in a patient disfigured by complications of fillers when trying to manage such cases where surgical incision and drainage is the gold standard. Patients’ refusal of further disfiguring incision and drainage, the advised course of treatment, results in prolonged hospital stay and considerable cost to the unit, which are not often reflected in the Healthcare Resource Group (HRG) codes. Treating complications of a procedure such as this is always more costly than the initial treatment.

In the modern health service, the financial and resource implications of treating patients with complications of cosmetic procedures cannot be ignored. Currently, the numbers are small; in the last 15 months, our unit saw 12 patients with infected facial fillers—the largest incidence in the reported literature. However, this is likely to increase as the popularity of facial fillers continues to increase.

The HRG code that each episode maps determines the hospital income for the treatment of these patients. Typically, this falls under ‘JC04C: intermediate skin procedures’. For the patient presented here, this totalled £40,028. The EBITDA represents the money that the hospital retains after paying the costs of patient care. For this patient, the total EBITDA was +£802. Interestingly, for the series of 12 patients treated by our unit in the last 15 months, the total cost and EBITDA were £38,454 and +£8,223, respectively.

These data demonstrate that, at present, the hospital does not incur a direct financial loss during the treatment of these patients. However, two factors suggest that this may not continue. Commissioning Groups may refuse to pay for such treatments reducing income and, for the reasons discussed above, the cost of treating these patients may increase due to additional resource requirements such as prolonged inpatient stays, multiple-imaging investigations and drainage procedures.

CONCLUSION

The literature is populated with case reports; literature reviews and editorials on facial fillers and referrals for management of the complications of dermal fillers are increasing. The British Association of Aesthetic Plastic Surgeons attributed this to the lack of information being provided to patients regarding the risks and side effects, the fact that unqualified practitioners are administering fillers with poor technique and that the lack of strict regulation in the UK has allowed unproven substances to be used.14

Therefore, it is vital that patients are assessed thoroughly and the contents used should be formally evaluated in order to tailor the management of the patient accordingly. Furthermore, raising patient awareness about the dangers of fillers is necessary to get a handle on this ever-growing market.

<table>
<thead>
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<th>Table 1 Fillar complications</th>
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<tr>
<td><strong>Immediate (0–2 days postprocedure)</strong></td>
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<tr>
<td>Under/over correction</td>
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<tr>
<td>Vascular compromise</td>
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<tr>
<td>Implant visibility (superficial injection)</td>
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Learning points

▸ Dermal filler complications presenting to the National Health Service are likely to increase in frequency owing to the unregulated nature of this industry both in the UK and abroad.

▸ Clinicians treating filler complications should remain sceptical about the real composition of the injected materials.

▸ Patients may decline conventional surgical techniques of abscess drainage for aesthetic reasons resulting in additional pressures on clinical provision and resource management.

▸ Prevention is better than cure: doctors and governments must raise patient awareness about the dangers and potential complications of ‘non-surgical’ facial rejuvenation.

▸ It is time that the UK followed the lead of the US and re-classified dermal fillers as medicines rather than medical devices.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES


CASE REPORT

Covered stents may provide extra protection during carotid artery stenting in high risk patients with an excessive thrombus burden

Ersan Tatli,1 Ahmet Barutcu,2 Emine Gazi,2 Yasemin Gunduz3

1Department of Cardiology, Ada Tip Hospital, Sakarya, Turkey
2Department of Cardiology, Onsekiz Mart University Hospital, Çanakkale, Turkey
3Department of Radiology, Sakarya University Hospital, Sakarya, Turkey

Correspondence to Professor Ersan Tatli, ersantatli@yahoo.com

To cite: Tatli E, Barutcu A, Gazi E, et al. BMJ Case Rep Published online: [please include Day Month Year] doi:10.1136/bcr-2013-010258

SUMMARY
Carotid artery disease is an important cause of mortality and morbidity related to atherosclerosis. Recently, percutaneous intervention procedures have been widely used to treat atherosclerotic carotid artery disease. We report the case of a 57-year-old male patient with a history of acute amaurosis fugax. Carotid angiography was performed as blood pressure differed between his left and right arms and there was a pan-systolic murmur on the left common carotid artery. Total occlusion of the proximal right brachiocephalic artery and a thrombus occluding 90–99% of the left internal carotid artery were detected by carotid angiogram. A self-expanding graft-covered stent was successfully implanted and there were no complications. This case shows that graft-covered stents may be a good alternative technique in special situations.

BACKGROUND
Atherosclerotic carotid artery disease is one of the most important causes of cerebrovascular adverse events and in developed countries is the most common cause of mortality and morbidity after coronary artery disease and malignancy. Carotid artery stenting (CAS) is the preferred therapy. As embolism formation is the most important complication of CAS, embolism protection techniques and devices are required during the procedure. In this case report, we described an alternative approach for reducing embolism formation through the use of covered stents in a patient with severe carotid artery disease.

CASE PRESENTATION
A 57-year-old male patient presented with a history of acute amaurosis fugax. He had a history of previous myocardial infarction, diabetes mellitus and hypertension. On physical examination, his blood pressure was 70/40 mm Hg in the right and 160/90 mm Hg in the left arm. There was a 3/6 pansystolic murmur on the left common carotid artery.

INVESTIGATIONS
Carotid angiography demonstrated total occlusion of the proximal right brachiocephalic artery. In addition, a thrombus occluded 90–99% of the left internal carotid artery (LICA). Cerebral perfusion was totally dependent on the left carotid artery system (figures 1 and 2). LICA stenting was the chosen therapy but brain perfusion needed to be protected. The right common carotid artery occlusion meant a proximal blocking-based protection system could not be used as there was a high probability of embolism formation from the thrombus on the blocking lesion.

TREATMENT
We decided to place a graft-covered stent through the lesion first, and contain the plaque and thrombus between the stent and the lumen. Therefore, a graft covered stent (5×13, Direct) was implanted with 12 atm pressure. After removing the distal blocking-based protection system, we opened the self-expanding stent (7×10×30, Cristallo) (figure 3) and dilated the stent using a post-dilatation balloon.
The procedure was completed successfully and there were no complications (figure 4).

OUTCOME AND FOLLOW-UP
Control Doppler ultrasonography examinations at 1 and 6 months after the procedure showed no evidence of restenosis nor were there any clinical sign of restenosis.

DISCUSSION
CAS is used frequently for the treatment of carotid artery stenosis. Most CAS-related complications occur as a result of embolism formation. The most embologenic phases of the CAS procedure are the pre-dilatation, stent deployment and post-dilatation stages. The use of protection devices has been associated with a reduced rate of neurological complications but may actually increase the number of emboli and cannot prevent post-procedural embolism formation.

An alternative approach to reducing embolisms may be through the use of covered stents. A covered stent, in which the stent mesh is coated with a thin membrane, may prevent the passage of atherosclerotic material through the stent grid. We have proposed that covered stents efficiently reduce embolism formation during stent deployment, post-dilatation and post-procedurally. Graft-covered stents contain the atherosclerotic and embolic materials between the vessel wall and the stent itself, thus

Figure 2 Left carotid angiogram shows a thrombus in the left internal carotid artery.

Figure 3 Stenting of the left internal carotid artery with a graft-covered stent.

Figure 4 Left carotid angiogram shows no residual stenosis after stenting.
reducing embolic events. Schillinger et al. followed 14 patients with carotid stenosis for 6 months. Graft-covered stents had been implanted in eight of these patients and bare stents in six. There were fewer embolic events during and after the procedure in the graft-covered than the bare stent group, but restenosis was observed in three of the patients in the graft-covered stent group. Cil et al. employed graft-covered stents in three patients with carotid artery stenosis without the use of protection devices; no restenosis was observed at 6-month follow-up. In contrast to the cases described in the literature, we used a self-expanding graft-covered stent.

Our experience indicates that graft-covered stents may be a good option when a proximal filter blocking system cannot be used due to the tortuous structure of the vessel.

Learning points

- Carotid artery stenting is the preferred treatment for atherosclerotic carotid artery disease but may result in embolism formation.
- The use of protection devices has been associated with a reduced rate of neurological complications but they do not prevent post-procedural embolism formation.
- Graft-covered stents may reduce embolic events and are a good alternative technique to prevent embolism formation.

Competing interests: None.
Patient consent: Obtained.
Provenance and peer review: Not commissioned; externally peer reviewed.

REFERENCES

CASE REPORT

Perioperative risk stratification for a patient with severe obstructive sleep apnoea undergoing laparoscopic banding surgery

Laurence Weinberg,1 Stan Tay,2 Chung Fei Lai,1 Maree Barnes3

SUMMARY

Despite the increasing prevalence of obstructive sleep apnoea (OSA), there is limited evidence to guide appropriate preoperative investigations, inpatient or outpatient surgery allocation, and the anticipated level of postoperative care. With reference to our institution’s perioperative risk stratification, we describe the case of a 46-year-old Caucasian male with a body mass index of 51 kg/m² admitted for laparoscopic band insertion. Management based on our guidelines involved a preoperative polysomnography where the patient was confirmed to have severe OSA. His postoperative care was then managed in the high dependency care unit. He was discharged home on day 2 with no further sequelae. We provide evidence that adoption of this model of care can simplify clinical decision making and resource allocation with favourable patient outcomes.

CASE PRESENTATION

A 46-year-old male with a body mass index (BMI) of 51 kg/m² (weight 150 kg, height 1.71 m) presented to our anaesthesia pre-admission clinic prior to an elective laparoscopic gastric band insertion. He had no other relevant medical history.

On presentation, his O₂ saturation in room air was 94%. He had no craniofacial abnormalities but had a neck circumference of 43 cm. He also had a history of snoring with witnessed apnoeas. Biochemical and haematological laboratory investigations were normal. A recent echocardiogram revealed normal biventricular function with mild biatrial enlargement.

Given his history, a polysomnography was arranged. A diagnosis of severe OSA was made with an apnoea hypopnoea index of 41 and an O₂ saturation nadir of 83%. Continuous positive airway pressure (CPAP) was recommended and a therapeutic polysomnography prescribed a pressure of 13 cm H₂O with effective sleep efficiency (87%). He remained compliant on this therapy up to the day of his surgery.

The plan for analgesia intraoperatively was multimodal using paracetamol 1 g, ketorolac 30 mg, tramadol 100 mg and local anaesthetic infiltration of the laparoscopic port wounds. Low dose opioids such as fentanyl were only to be used as rescue analgesia to minimise his sedation risk. However, the combination of his super-obesity (BMI>50 kg/m²) and severe OSA (compliant with CPAP) meant his perioperative clinical risk profile for airway complications was high. A HDU bed was therefore arranged for postoperative care.

OUTCOME AND FOLLOW-UP

The patient had an uneventful admission in HDU and was subsequently discharged home on the second post-operative day.

DISCUSSION

We report the use of a risk stratification algorithm for managing a patient with OSA undergoing a surgical procedure at our tertiary level hospital. Despite other published reviews discussing specific perioperative treatment strategies, this algorithm addresses for the first time the key issues of preoperative testing, patient care and resource allocation. As with all guidelines, the use of this risk stratification model cannot guarantee any specific outcomes. Therefore, this model may be adopted, modified or rejected according to each institution’s clinical needs and constraints.

To cite: Weinberg L, Tay S, Lai CF, et al. BMJ Case Reports Published online: [please include Day Month Year] doi:10.1136/bcr-2012-008336
We based our risk stratification model for perioperative life-threatening airway obstruction on three variables: clinical predictors, surgical factors and perioperative sedation risk (figure 1). We define the preoperative clinical predictors of OSA risk as major, intermediate or minor depending on the presence of obesity and/or the severity of OSA signs and symptoms. Major clinical predictors include severe OSA but poorly compliant with CPAP, super-obesity (BMI >50 kg/m²),4 and craniofacial abnormalities.5 Obesity itself profoundly alters pulmonary function and has adverse effects on respiratory mechanics.6–8 Intermediate clinical predictors include severe OSA based on sleep studies but compliant with CPAP, moderate OSA, morbid obesity (BMI >35 kg/m²), observed pauses in breathing, or awakening with a choking sensation.9 Minor clinical predictors are mild OSA, history of loud or frequent snoring,10,11 frequent arousals,12–14 and neuro-behavioural dysfunction.9,15

For patients with OSA, we consider major surgery involving the abdomen, thorax or airway to be ‘high-risk’ for OSA complications (figure 1). Intermediate-risk surgery includes peripheral surgery under general anaesthesia, non-major open abdominal surgery (eg, hernia repair), laparoscopic surgery, and airway surgery with sedation. Low-risk surgery includes peripheral surgery with regional anaesthesia or local anaesthesia, and all superficial surgery. High perioperative sedation risk includes patients who require high dose parenteral opioids, opioid infusions, neuraxial opioids or high dose oral opioids in the perioperative period.16 Intermediate sedation risk includes the use of low dose parenteral or oral opioids. Low sedation risk includes patients who will not require opioids in the perioperative period.

The patient described in this case report had super-obesity and severe OSA compliant with CPAP. This placed him in the major risk category for clinical predictors (figure 1). He was undergoing laparoscopic surgery, and therefore his surgical risk was considered intermediate. Our decision-making strategy then for preoperative polysomnography was based on the result of risk stratification of the three variables (figure 2).

Several screening tools have been developed and validated to identify potential surgical patients with OSA: the Berlin questionnaire,17 the American Society of Anesthesiologists checklist1 and the STOP-Bang questionnaire.18 While these questionnaires have been validated as screening tools for OSA in the surgical population,19 formal preoperative testing with polysomnography in patients with clinical risk factors for OSA is still...
useful. Although mandatory testing of all patients with OSA risk factors is recommended, limited facilities for testing in regional areas, long waiting periods in many sleep laboratories and the high cost of testing often limit the accessibility of this important diagnostic test as part of routine perioperative care.

If a diagnostic sleep study is recommended by our algorithm but cannot be obtained, we collaborate with the surgical team, intensive care and respiratory physicians to jointly decide whether to postpone surgery to obtain formal sleep studies or to pre-emptively initiate CPAP therapy. As outlined in figure 2, for patients with minor clinical predictors and for patients with intermediate clinical predictors undergoing low risk surgery, we do not advocate further preoperative testing. This is important in the key area of resource allocation. For patients with intermediate clinical predictors undergoing intermediate risk surgery and for patients with major clinical predictors undergoing low risk surgery, a low sedation risk also precludes further investigations.

We use a similar approach in deciding which patients should be offered a postoperative ICU, HDU or general ward bed (figure 3). This is important again from a resource allocation perspective. An ICU bed is reserved for all patients with major clinical predictors undergoing high-risk surgery. A HDU bed is reserved for patients with major clinical predictors undergoing intermediate-risk surgery. Bed allocation for patients with intermediate clinical predictors undergoing high- or intermediate-risk surgery depends upon sedation risk. Patients with an intermediate or low sedation risk are admitted to the post anaesthesia care unit for an extended period of 4 h, and in the absence of airway complications, are then transferred to the general ward. All patients with minor clinical predictors and all patients undergoing low-risk surgery are discharged to the ward or home if surgery allows.

Figure 3  Perioperative bed resource allocation for patients with obstructive sleep apnoea (OSA) at our tertiary centre institution. HDU, high dependency unit; ICU, intensive care unit; PACU, post anaesthesia care unit.

<table>
<thead>
<tr>
<th>CLINICAL PREDICTORS</th>
<th>Major</th>
<th>Intermediate</th>
<th>Minor</th>
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<tbody>
<tr>
<td>High</td>
<td>ICU</td>
<td>HDU or</td>
<td>Ward or Home</td>
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<td>Extended PACU</td>
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<td>Low</td>
<td>Ward or Home</td>
<td>Ward or Home</td>
<td>Ward or Home</td>
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High OSA risk: Requires ICU or HDU bed
High risk: HDU bed
Intermediate/Low sedation risk: Extended PACU then ward
Low OSA risk: General ward bed or home is surgery allows

ICU: Intensive Care unit; HDU: High Dependency Unit; PACU: Post Anaesthesia Care Unit

Competing interests  None.
Patient consent  Obtained.
Provenance and peer review  Not commissioned; externally peer reviewed.

REFERENCES
CASE REPORT

Think Hickam’s Dictum not Occam’s Razor in paediatric HIV

Felicity Goodyear-Smith,1 Mike Sharland,2 Simon Nadel3

SUMMARY

A 10-year-old girl with untreated congenital HIV developed acute sepsis to which she succumbed despite emergency treatment. Her red and dilated anal region with small areas of tissue breakdown due to advanced HIV destructive disease was misinterpreted as anal assault. Suffocation was then hypothesised to be the cause of her profound hypoxia and multi-organ failure. Criminal proceedings against her adoptive uncle ensued over a 5-year period at huge legal and social cost. Following the first acquittal, appellant hearings led to re-trial at which her uncle was acquitted for the second time. A shared idee fixe (anal assault and asphyxiation) resulted in the most likely clinical diagnosis (advanced HIV infection with subsequent overwhelming sepsis) being discarded. This was a case where the principle of parsimony (Occam’s Razor) led to exclusion of a diagnosis when in fact multiple diagnoses applied (Hickam’s Dictum), with devastating consequences for the family.

BACKGROUND

This case demonstrates how a shared idee fixe resulted in the most likely clinical diagnosis being discarded, with huge personal costs for a child’s family and financial costs for the state.

CASE PRESENTATION

In 2007, a 10-year-old girl, an immigrant to New Zealand from Zimbabwe, was found by her adoptive aunt in bed, deeply unconscious, gasping for breath and lying in a pool of diarrhoea. On transfer to accident and emergency at the local hospital, she was found to have a Glasgow Coma Score of 3, tachycardia (HR 183), no recordable blood pressure, pyrexia (40.3°C), tachypnoea (35), wide- spreads of pulmonary crepitations and mottled limbs. Her capillary re- sorption. Her blood pressure was maintained at around 70/40 once intravenous fluids and inotropic drugs were administered. Upon transfer to intensive care, a prolapsed and unusually inflamed rectal mucosa was interpreted as a 7 cm rectal tear. The clinical team diagnosed sepsis secondary to a perforated bowel secondary to rectal sexual assault. Her sepsis then was hypothesised as due to a perforated bowel from anal sexual assault. Proctoscopic examination by a paediatric surgeon revealed no rectal laceration, but multiple 1–3 mm mucosal splits were seen occurring radially around her anal margin. The clinicians in charge of her care continued to believe there was a large rectal wound, and speculated that her hypoxic state was the result of asphyxia in the context of anal rape.

INVESTIGATIONS

Arterial blood gas analysis

Transcutaneous oxygen saturation initially 91%, increased to 93% when oxygen was given by mask, and reached 100% following intubation. Initial venous pH 7.05, HCO3 8.6 (metabolic acidosis).

Haematology

INR 2.5 (0.8–1.2), APTT 58 s (26–36), thrombin clotting time 28 s (18–25), platelet count 140 (150–450), haemoglobin 94 (115–140), haematocrit 0.29 (0.34–0.44), white cell count 12.5, neutrophils 4.4, lymphocytes 7.6 (1.5–7), monocytes 0.37, myelocytes 0.03 (0). Neutrophils showed toxic granulation with Döhle bodies present, irregular shaped cells +, Rouleau ++.

Biochemistry

Sodium 142, potassium 3.5, urea 9.7 (3.5–5), creatinine 0.19 (0.03–0.09), bilirubin 5, ALP 123, GGT 91 (5–30), AST 227 (10–50), ALT 65 (<30), CRP 48 (<5).

Microbiology

HIV screening assay and Western blot positive. Vaginal swab grew Staphylococcus aureus. Single blood culture taken subsequent to administration of intravenous antibiotics was negative. No lumbar puncture was done.

Radiology

Chest X-ray showed consolidation in right lower lobe and both upper lobes. Abdominal X-ray normal (ruled out perforation). CT scan head showed diffuse decreased attenuation in the white matter of both frontal lobes and temporal lobes, basal ganglia and thalami bilaterally. Bilateral ostitis media and sinusitis. CT scan abdomen showed a ‘diffuse “shock bowel” appearance in the large and small bowel, consistent from changes from hypovolaemic septic shock’.

TREATMENT

Despite immediate resuscitation plus intravenous antibiotics, anti-viral and anti-fungal agents, the child failed to respond and died 19 h after first presenting.

DIFFERENTIAL DIAGNOSIS

Initially the girl was assumed to have an overwhelming sepsis in the context of advanced HIV disease. However, once the anal region was visualised, the hypoxia was diagnosed to be secondary to presumed asphyxiation with anal trauma from
Learning from errors

assault. The more common diagnosis of hypoxia secondary to acute respiratory distress syndrome and multi-organ failure due to septic/toxic shock was excluded. Her positive HIV status was considered not to be relevant by those involved in her care. It was claimed in court that her hypoxia could not be due to lung pathology because her oxygen saturation levels improved following administration of oxygen, and neither could it be due to hypovolaemic septic shock because she had failed to improve after being given a second bolus of intravenous fluid and remained anuric, and furthermore neither of these options explained the rectal trauma, hence the hypoxia could only be the result of suffocation.

Subsequent international expert review of the case and pathology indicates that this child had advanced AIDS with severe chronic HIV-destructive encephalitis, pneumonitis and pan-enteritis. It was considered most probable that the child succumbed to acute sepsis, possibly due to toxic shock from S. aureus infection. The child fulfilled the clinical criteria for toxic shock syndrome.

OUTCOME AND FOLLOW-UP

The child's parents had both died in Zimbabwe with 'immune deficiency' when she was a baby, and it became apparent she had congenital HIV infection which had never been treated.

Prior to her death the police and the forensic pathologist were notified that this was a case of rape and murder. The police attended the hospital and began interviewing family members (her aunt and uncle who were her adoptive parents and their biological children who were young adults). The child's biological sister aged 12 (who later tested negative for HIV) was immediately taken into care. Her uncle was arrested and charged with homicide and sexual violation. There followed a number of hearings: depositions (2007), a High Court trial (2008) resulting in acquittal, a Family Court hearing (2009) deciding that the older sister must remain in care, prosecution appeal to the Court of Appeal (2009) dismissed, prosecution appeal to the Supreme Court (2010) upheld and re-trial ordered.

The full story unfolded when the medical adviser for the defence (FG-S) pieced together chronologically the many facts pertaining to the case and obtained an overview of the events which had culminated in the girl’s demise.

For the retrial the defence called four experts from the UK: a paediatrician experienced in infectious diseases and HIV (MS), a paediatric intensivist (SN), a histopathologist with extensive HIV expertise (Professor Sebastian Lucas) and a Home Office forensic pathologist (Dr Nathaniel Cary). MS and SN explained how this case had all the hallmarks of overwhelming sepsis presenting in an immune-suppressed child. Having reviewed the case by preparing numerous additional slides using immunohistochemical stains, Professor Lucas concluded that this was the most severe case of tissue damage due to HIV that he had ever seen in a child. The High Court retrial (2012) resulted in a second acquittal.

Following the second acquittal, a Family Court judge lifted the restraining order preventing the deceased’s older sister (then 17) having contact with her adopted father.

DISCUSSION

The aetiological agent is often not identified in acute sepsis. Combination antiretroviral therapy has markedly reduced mortality in children with perinatally acquired HIV, and therefore few clinicians now have experience with this condition. In non-classical presentations, an underlying immune deficiency always should be considered. In this case, senior clinicians apparently developed an idée fixe with respect to the diagnosis (anal rape and asphyxia, mistakenly identifying rectal trauma and refusing to accept that even on histological examination a large tear was not present) and rejected the possibility that HIV might play an important part in the girl's presentation. This meant that it became increasingly difficult for more junior staff to consider alternative possibilities, possibly inadvertently colouring their perceptions and subsequent recall, and resulting in a team belief that the child had been a victim of assault. In a complex case where many people are involved in the acute care with prescribed roles, the story may subtly change when transmitted from one person to another. For example, the child presented with profuse strange-coloured watery diarrhoea, which drenched her clothes and bedding. A nurse inserting two suppositories of a paracetamol in the after-hours clinic had noted a smear of blood on her gloved finger. The hospital Record of Death stated that the child had been admitted with ‘rectal bleeding’, but there was no mention of diarrhoea or of her HIV status. Arranging for an external review of the whole case to be conducted may be very valuable so that the big picture can be seen.

Factors strongly suggesting infection (such as high pyrexia, profuse diarrhoea, haematological findings) were forced to fit with the rape and murder scenario. Sepsis was excluded as a possibility because it did not explain the presumed rectal injuries. This is an example of the inappropriate use of Occam’s Razor parsimony principle, which advocates reduction to a single hypothesis. In fact, this appeared to be more a case of Hickam’s Dictum, with a multifactorial pathogenesis combining direct HIV organ damage, immune deficiency and an overwhelming inflammatory response to sepsis.

Learning points

- Consider the possibility of immune deficiency in acute atypical presentations.
- Seek expert advice, internationally if necessary, when a case is outside one’s usual clinical experience, especially where there are serious ramifications.
- Consider all possible diagnoses and keep revisiting discarded ones if subsequent evidence fails to fit the assumed diagnosis.
- When senior clinicians present an idée fixe with respect to a diagnosis, it becomes increasingly difficult for more junior staff to consider alternative possibilities.
- The principle of parsimony (Occam’s Razor) may sometimes lead to exclusion of a diagnosis when in fact multiple diagnoses may apply (Hickam’s Dictum).

Acknowledgements To the family for the dignified way they conducted themselves throughout this 5-year ordeal.

Contributors All three authors have made individual contributions to the writing of the article in regard to its conception and design, drafting or revising it critically for important intellectual content and have given final approval of the version to be published.

Competing interests None.

Patient consent Obtained.

References


CASE REPORT

Exsanguinated uterus after massive atonic postpartum haemorrhage

Kalpana V Mahadik,1 M B Swami,1 Neha Pandey,1 Ashish Pathak2,3,4

SUMMARY
This article addresses issues related to pregnancy anaemia and late referral by a village birth attendant in resource poor setting in a central state of India. A young anaemic woman had labour onset at her village, a birth attendant tried to deliver her but failed. When she came to our hospital, had established sepsicaemia and absolutely non-reassurable uterine tone leading to intractable atonic postpartum haemorrhage. She died after 5 days because of coagulopathy and multiorgan failure. Huge budgets are being spent for the promotion of institutional deliveries but still the maternal mortality ratio has not reduced. The epidemiology of childbirth, social awareness for safe labour and administrative lethargy towards implementation of government programmes have not changed. The tertiary care—blood and components—multidisciplinary approach could not prevent the death of an anaemic woman. Unless there is a grassroot level change in the healthcare delivery system at the village level, the scenario might not change.

BACKGROUND
A 25-year-old woman was admitted to CR Gardi Hospital, a tertiary care institute located in Ujjain, India. The patient was in labour for more than 24 h. She landed in atonic postpartum haemorrhage (PPH) and succumbed to death despite blood and component transfusions and aggressive intensive care. Health facility at village and subsequent community health centre (CHC) had no emergency obstetric care (EmOC), forcing the patient to travel around 150 km to reach our hospital. The poor quality of woman reproductive healthcare in developing countries is a result of mishandled economy, corruption and illiteracy.1 Inadequacy of delivery care in remote areas in central state of India, Madhya Pradesh, is contextualised in this scenario. Those who do not have knowledge also do not have courage to accept it. The birth attendants in giving a trial of labour often waste precious time. In the present case not only 12-h period (of one night) was wasted in futile attempts to deliver but also, multiple internal examinations led to development of Gram-negative sepsicaemia superimposed on existing anaemia, resulting in massive atonic PPH and death. We aim to highlight epidemiological and health-system-related factors influencing maternal health in rural Madhya Pradesh, India.

CASE PRESENTATION AND TREATMENT
Presenting features
A 25-year-old woman was admitted to obstetrics and gynaecology department of a 650-bedded university hospital in Ujjain, India. She gave a history of 9 months amenorrhoea, strong pain in the abdomen since last 24 h, along with ‘feeling of sinking’ and dizziness. She was a primigravida and did not know the date of her last menstrual period. History revealed she had taken two injections of tetanus toxoid in the village and some iron and folic acid tablets. She did not receive any other obstetric care. She belonged to a village located in a neighbouring district, 150 km away from our hospital. The occupation of the family is farming. Income of her family is around 5000 rupees (approximately US$100) per month. There was no relevant feature in family history.

Health systems background and prereferral care
The village to which the patient belonged has a population of 950 and has no healthcare facility. There is a CHC, located 20 km away from her village. The village is connected to this CHC with a kachha (non-tar) road. At the CHC, two qualified primary care physicians are available for daytime outpatient care and two-auxilliary nurse midwives (ANM) stay round the clock for labour cases. However, CHC is not a facility, thus all complicated obstetric cases are referred out. Our patient revealed the history of having onset of abdominal pain since last morning and she stayed at home waiting for her delivery. In the night at 23:00 she was taken to the CHC, where the ANM gave her some intravenous fluids. Multiple vaginal examinations were carried out. In the morning as there was no progress of labour she was asked to go to our hospital and she reached at 12:15 the next day.

Clinical findings and treatment
On admission, that is, at zero hour, the young patient was dehydrated, with sunken eyes and in agony. Blood pressure (BP) was 106/80 mm Hg and pulse rate 100/min. The core temperature was 38.4°C but the peripheries were cold on touch. She looked pale and toxic. Uterus was full term with strong uterine contractions and head was engaged, fetal heart sound was absent. Vaginal examination revealed fully dilated cervix, 1 cm caput and head at plus one station. Examination of other systems revealed no abnormal signs. Her haemoglobin (Hb%) was 5 g/dL, total leucocyte count 20 000/mm3 and platelet 1 43 000/mm3. We decided to deliver the patient by low forceps under intravenous sedation. It was an easy outlet forceps delivery. A stillborn baby was delivered. There was no moulding of the head of stillborn baby. After placental delivery of the patient started bleeding.
per vagina and the uterus was found to be flabby and atonic. She was given intravenous crystalloids with 40 units oxytocin infusion, and manual uterine massage. However, she still continued to bleed; intravenous carboprost 250 μg and per rectal misoprostol 800 μg was also given. Simultaneously, the vagina and cervix was explored and no tear was found. By end of first hour, the patient lost about 600–800 mL blood and was started infusion of red blood cell concentrate (RBC) according to guidelines.2

By the second hour bleeding still continued profusely and we proceeded for obstetric hysterectomy. In our setting uterine artery embolisation is not routinely performed and we were not sure of immediate cessation of bleeding after ligation of internal iliac vessels. On opening the abdomen the uterus was absolutely pale, white and revealed no injury (figure 1). The patient was shifted to intensive care unit at end of 2.5 h of admission with systolic BP at 80 mm Hg and tachypnoea. The patient was put on ventilator support.

At the end of sixth hour central venous pressure (CVP) was 5 cm, platelet count 40 000/mm³ and the patient was in haemorrhagic shock. In view of her clinical condition RBC concentrates continued to be replaced and she was started on dopamine infusion. Her prothrombin time was 14 s and activated partial thromboplastin time 45 s. Coagulation profile and haematological parameters are shown in table 1 in consecutive order.

To summarise in the first 24 h of admission, the patient had lost about 3–4 L blood because of atonic PPH. Her CVP was going down, Hb was low and general condition was poor. Urine output was adequate throughout and remained proportionate to input till day 5. On day 1 the abdomen was mildly distended, with pelvic ultrasound showing about 400 mL collection. She was given blood and components, antibiotics–imipenem and metronidazole; intravenous tranexamic acid 2 g/day with high-dose hydrocortisone.

On day 2, abdominal and pelvic collection increased, basal effusions in lung appeared and pallor increased. With a suspicion of active bleeder, we carried out exploratory laparotomy. It revealed about 1000 mL clot on the vault of vagina and about 3 L free blood. Haematoma was drained and bilateral internal iliac artery ligation was carried out.

On day 3, the patient’s level of consciousness improved. She was given epsilon aminocaproic acid (200 mg intravenous). On day 4, tachypnoea was seen and basal crepitation in lung appeared. Her Hb was 9 g/dL. Considering fluid overload we treated her with intravenous frusemide-200 mg (divided doses), but without response. On day 5, she had a clinical picture of non-cardiogenic pulmonary oedema (figure 2). The ventilator tubing was repeatedly filled with pink coloured froth. The patient succumbed on the night of day 5.

INVESTIGATIONS
See table 1.

DIFFERENTIAL DIAGNOSIS
▸ Traumatic PPH
▸ Atonic PPH

OUTCOME AND FOLLOW-UP
The patient died of acute non-cardiogenic pulmonary oedema following multiorgan failure secondary to atonic PPH and subsequent coagulopathy causing haemorrhagic shock.

DISCUSSION
The major factors causing this death are antecedent anaemia and intractable atonic postpartum haemorrhage. Anaemia is directly or indirectly responsible for 40% maternal deaths. There is an 8–10-fold increase in maternal mortality ratio (MMR) when Hb falls below 5 g/dL.1 Anaemia, which was present in this

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Details of haematological and serological investigations along with transfusions given</th>
</tr>
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<tbody>
<tr>
<td>Day</td>
<td>Hour of day</td>
</tr>
<tr>
<td>---------</td>
<td>-------------</td>
</tr>
<tr>
<td>0</td>
<td>0–24</td>
</tr>
</tbody>
</table>
| 1       | 0–12        | 3.6     | 15 000  | 0.44        | 1 min 10 s | 2 min 30 s | 1.4 | 4 | 8 | 0
| 13–24   |             | 7.0     | 11 000  | 0.50        | 1 min 30 s | 2 min 60 s | 1.4 | 2 | 2 | 2
| 2       | 0–12        | 4.2     | 5210    | 0.36        | 14 s   | 34 s   | 2.1         | 6 | 6 | 4
| 13–24   |             | 7.0     | 6280    | 0.57        | 14 s   | 34 s   | 2.1         | 1 | 1 | 0
| 3       | 0–12        | 7.3     | 6940    | 0.66        | 17 s   | 34 s   | 2.1         | 2 | 2 | 2
| 13–24   |             | 6.0     | 6700    | 0.64        | 17 s   | 34 s   | 2.1         | 1 | 1 | 1
| 4       | 0–12        | 9.0     | 12 000  | 0.68        | 14 s   | 70 s   | 2.0         | 1 | 1 | 1
| 13–24   |             | 8.0     | 9900    | 0.68        | 14 s   | 70 s   | 2.0         | 1 | 1 | 1
| 5       | 0–12        | 12.0    | 16 200  | 0.47        | 14 s   | 34 s   | 2.3         | – | – | –
| 13–24   |             | 10.0    | 14 100  | 0.47        | 14 s   | 34 s   | 2.3         | – | – | –

aPTT, activated partial thromboplastin time; Day, day of admission; FFP, fresh frozen plasma; Hb, haemoglobin; PLT, Platelet count; PT, prothrombin time; S.cr, serum creatine; TLC, total leucocyte count.

Figure 1 Intraoperative photograph of a pale white uterus in massive atonic postpartum haemorrhage.

Figure 2 Clinical picture of non-cardiogenic pulmonary oedema.
Patient, caused a weak and non-reassuring uterine tone. \(^4\) Anemia causes rise in nitric oxide levels, which is responsible for hypotonic myometrium in atomic PPH. \(^4\) In the Indian context, haemorrhage is the chief cause of maternal deaths, that is, 31%. \(^5\) The present case was managed in a tertiary care hospital with the best of facilities. Ventilator support and massive blood transfusions could not save this patient; neither the timely administration of high concentration of oxytocin infusion nor carboprost and rectal misoprostol. \(^6\)–\(^8\)

The Government of India has started a cash incentive scheme—Janani Suraksha Yojna—to promote institutional deliveries with an aim to reduce MMR since year 2005. As such the rate of institutional deliveries has increased. \(^9\)–\(^11\) Still the question is why the MMR has not gone down? In another district in Madhya Pradesh, following local protests against a high number of maternal deaths in 2010, a study was carried out to find out causes of 27 maternal deaths. \(^12\) The study revealed absence of antenatal care despite high levels of anaemia, absence of skilled birth attendants, failure to carry out emergency obstetric care and referrals that never resulted in treatment contributing to maternal deaths. \(^12\) Most of the above causes are substantiated by our case as well. We do not have significant epidemiological data of outcome and complications of the women referred from rural areas to Ujjain district; however, a project is ongoing which will provide this much needed information in future. \(^11\)

A few studies suggest an increasing trend for this sudden, unpredictable, life-threatening condition, that is, atomic PPH. A recent study from Vancouver, Canada observed an increase in atomic PPH, from 4.8% in 2001 to 6.3% in 2009. \(^13\) This increase was not related to labour induction, augmentation or caesarean delivery. \(^13\) An Irish study \(^14\) also revealed a threefold increase of atomic PPH between 1999 and 2009. The study highlighted the pressing need for research and for clinical audit focusing on aetiological factors, preventative measures and quality of care, to guide current clinical practice. \(^14\) Biological differences may also play a role. Hispanic ethnicity and Asian/Pacific Islander race are significant risk factors for atomic PPH independent of measured potential mediators. \(^15\) Ethnicity may also play a role in the present case. In conclusion, we feel there is an unanswered question as to what was behind this sudden and massive PPH which killed a young woman. Of course, the prevailing anaemia and poor obstetric care prior to admission contributed to the outcome.

### Figure 2
X-ray chest showing fluffy white lung shadows involving whole of lungs in advanced pulmonary oedema.

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**Unusual presentation of more common disease/injury**

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**Learning points**

- Anticipate atomic uterus and septicaemia in anaemic patient referred from periphery with prolonged labour. \(^4\)
- Haemostatic resuscitation in form of tranexamic acid, blood components and early intensive care with ventilator support are components of good patient care.
- MSBOS (maximum surgical blood ordering schedule) \(^7\) should be followed for obstetric patients with haemoglobin (HB)<7 g, requiring general anaesthesia, in major blood letting surgery and symptomatic anaemia regardless of haemoglobin level.
- Minutes count in atomic postpartum haemorrhage; quick and aggressive decision-making is key to saving the patient’s life.
- Tertiary care alone will not reduce maternal mortality ratio but a social drive that respects the quality of care received at delivery is also needed.

**Acknowledgements**

The authors thank the medical director Dr VK Mahadik and Dean, Dr JK Sharma, RD Gardi Medical College, Ujjain for granting us permission to publish this case.

**Contributors**

KM, MBS and NP collected the clinical details and photographs of the patient’s report. KM performed the literature review and drafted the manuscript. KM verified the diagnosis and other scientific facts. KM, MBS, NP and AP revised the manuscript critically for substantial neurological content. All authors read and approved the final manuscript.

**Competing interests**

None.

**Patient consent**

Obtained.

**Provenance and peer review**

Not commissioned; externally peer reviewed.

**REFERENCES**

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