Pneumomediastinum complicating diabetic ketoacidosis

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SUMMARY
Pneumomediastinum is an uncommon finding in patients with diabetic ketoacidosis (DKA) and may occur spontaneously or secondary to an effort rupture of the oesophagus. Excluding oesophageal rupture is important, as delaying treatment increases the risk of mortality. We discuss a case of DKA complicated by vomiting, pneumomediastinum, pneumopericardium and air in the epidural space. Instead of fluoroscopic oesophagography, chest CT was used to investigate oesophageal rupture. We present an overview of case reports and retrospective studies illustrating the utility of chest CT in the investigation of oesophageal rupture over fluoroscopic oesophagography.

BACKGROUND
Pneumomediastinum is an uncommon finding in which air occupies the mediastinal space.1 Air may enter the mediastinum secondary to disruption of the skin, airway or oesophagus or may be produced by gas-forming bacteria spreading inferiorly from the oral cavity or neck.2 Alternatively, it may occur 'spontaneously', following alveolar rupture through straining, vomiting, coughing or an increased respiratory effort.1 2 Spontaneous pneumomediastinum is a diagnosis of exclusion and is made only after ruling out traumatic injury, oesophageal perforation and infection.2

Depending on its aetiology, pneumomediastinum can be a benign condition or life-threatening emergency. Its presence in Boerhaave syndrome, a transmural oesophageal rupture caused by severe straining or vomiting, is associated with a mortality risk of 15% to 43%.4 5 Death may result from an infectious mediastinitis or compression of the great vessels by an increased mediastinal pressure.2 6 7 Spontaneous pneumomediastinum, on the other hand, generally has a good prognosis and is self-limiting.7

Patients with diabetic ketoacidosis (DKA) often experience retching and vomiting, which can lead to both alveolar and oesophageal rupture, making differentiating between spontaneous and secondary pneumomediastinum a challenge.8 Although fluoroscopic oesophagography is considered the imaging study of choice for diagnosing oesophageal rupture, its use in emergencies is limited by the inability of critically ill patients to change positions and swallow contrast medium.9 Alternatively, upper endoscopy may be performed but could enlarge a perforation’s size and risks the need for surgery.8 10 Despite these difficulties, every effort has to be made to exclude oesophageal rupture because if surgery is required, its delay beyond 24 hours increases morbidity and mortality.10 Here, we present a case of DKA complicated by pneumomediastinum, in which fluoroscopic oesophagography was unavailable and feasible.

CASE PRESENTATION
A man in his 20s, with a body weight of 84 kg, presented late in the evening to the emergency department with vomiting and reduced consciousness. Four years prior, he was diagnosed with type 1 diabetes. According to his family, he had been ill for 3 days, complaining of nausea, abdominal pain and having diarrhoea. While feeling unwell, had not been using insulin therapy. Since 1 day, he had vomited repeatedly, developed laboured breathing and became increasingly lethargic. He had no other medical history or history of trauma.

INVESTIGATIONS
Physical examination revealed a Glasgow Coma Scale of 13 (E3M6V4). Kussmaul breathing pattern was present with a frequency of 35 bpm. He was tachycardic and had a systolic blood pressure of 79 mm Hg and a diastolic pressure of 60 mm Hg. In the chest and neck region, subcutaneous emphysema was felt. Thoracic excursions were symmetric and no tracheal deviation was detected. Breathing sounds were heard bilaterally with inspiratory crepitations on the right lower side of the chest. Heart sounds were normal and no distended jugular veins or Kussmaul’s sign were observed.

Laboratory analysis of his blood showed a glucose of 48 mmol/L (864 mg/dL), Na+ 117 mmol/L, K+ 6.0 mmol/L, Cl− 86 mmol/L, creatinine 196 umol/L, albumin 41.8 g/L, c-reactive protein 296 mg/L, white cell count of 37×10⁹/L and an arterial blood gas with a pH of 6.84, pO₂ of 8.1 kPa (61 mm Hg), pCO₂ of 2.2 kPa (17 mm Hg), HCO₃− of 2.9 mmol/L and lactate of 1.5 mmol/L. The effective osmolality was calculated to be 282 mOsm/L. The anion gap was 28 mEq/L, providing a delta anion gap/delta HCO₃− ratio approximating one. Urine analysis confirmed ketonuria. His ECG showed a sinus tachycardia without ST-segment deviations or T-wave alterations. Respiratory virus PCR testing of COVID-19 and influenza were negative.

A chest X-ray showed subcutaneous emphysema at the upper chest and radiolucent streaks outlining the heart and aortic arch, indicating a pneumomediastinum (figure 1). Additionally, there were consolidations in the right lower lobe and behind...
the heart. A CT scan without intravenous contrast material of his chest and neck was made to evaluate the extent of the pneumomediastinum and whether airway or oesophageal injury was present (figures 2 and 3). Pneumomediastinum and pneumopericardium were seen without evidence of rib fractures, tracheal or oesophageal injury. Air extended superiorly from between the clavicles to the cranial base and was also visible in the epidural space of the spinal canal. No pneumothorax was present. Aspiration pneumonia was suggested by the combined findings of gastric dilatation, stasis of gastric content in the lower half of the oesophagus and consolidations in the lower lobes of both lungs.

DIFFERENTIAL DIAGNOSIS

Our patient was diagnosed with DKA complicated by a pneumomediastinum and an aspiration pneumonia. The DKA may have been precipitated by a (viral) gastroenteritis or respiratory infection and worsened by discontinuation of insulin therapy.

The pneumomediastinum resulted from his laboured breathing, retching and vomiting, increasing alveolar pressure and causing alveolar rupture. Oesophageal rupture was unlikely as the patient did not experience fever, had no history of chest pain or pain when swallowing and had a CT-scan without oesophageal wall thickening, periesophageal fat stranding and effusions. Although the lower posterior mediastinum contained air, we regarded this to be of alveolar origin spreading diffusely into all mediastinal compartments, rather than originating from the oesophageal lumen.

Figure 1  Anteroposterior chest X-ray (upper image) with a corresponding coronal CT image (lower left image) and illustration (lower right image). Air demarcates the right cardiac border and surrounds the aortic arc. A pneumopericardium is visible, with air separating the left cardiac border from the pericardium and mediastinal parietal pleura.

We considered using fluoroscopic oesophagography to rule out oesophageal rupture, but at the time of presentation the fluoroscopy suite and qualified technologist were unavailable. Also, due to his reduced consciousness and gastroparesis, drinking contrast material would have risked further aspiration. CT oesophagography was not performed, as there were no standardised protocols in place.

TREATMENT

Treatment of his pneumomediastinum was supportive with antiemetics and close monitoring for complications. The DKA was treated according to national protocols. We initiated intravenous antibiotics for aspiration pneumonia and placed a nasogastric tube to resolve gastric retention. This tube was seen to be positioned correctly on X-ray imaging and no bloody gastric content was aspirated.

OUTCOME AND FOLLOW-UP

After 2 days of insulin therapy, the blood pH and anion gap had normalised. He remained haemodynamically stable without the use of vasopressors, seemingly confirming the absence of an oesophageal rupture.

Despite high-flow oxygen therapy, blood oxygen levels deteriorated and work of breathing increased. Intubation was
performed and mechanical ventilation was started. A chest CT with intravenous contrast material was repeated to evaluate the presence of mediastinal abscesses and the extent of the pneumo mediastinum. It showed a clear reduction of mediastinal air and subcutaneous emphysema (figure 4). New consolidations had developed in the apical segments. Our patient was later diagnosed with bronchopulmonary aspergillosis and treated with voriconazole. His stool culture was negative for bacterial, viral and parasitic pathogens.

He was discharged to a rehabilitation centre 2 months after admission to recover from ICU-acquired weakness. After 3 months, he returned to his daily routine. He currently attends the outpatient diabetic clinic every 2 weeks.

DISCUSSION
Coexistence of DKA and pneumomediastinum was first described in 1937 and has been reported in 90 cases since. We reviewed 40 case reports and series with 51 patients having DKA and pneumomediastinum (online supplemental material 1). Forty-five patients had spontaneous pneumomediastinum and were treated successfully with supportive management (table 1). Four patients were diagnosed with oesophageal rupture: two were treated surgically, one had conservative management and one was lost to follow-up. The one death was caused by a pneumonia. Our patient had spontaneous pneumomediastinum, confirmed by a chest CT negative for signs of oesophageal injury and absence of complications during follow-up.

Spontaneous pneumomediastinum in DKA is thought to result from the Kussmaul breathing pattern, vomiting and retching, increasing alveolar pressure or inducing hyperinflation. Hyperinflation of the alveoli lining pulmonary vessels may result in rupture of their base, with air entering the pulmonary interstitium in between the alveolar membrane and vessel wall. Concurrent hypotension with inadequate filling of pulmonary vessels exacerbates traction on the perivascular sheath and increases the risk of alveolar rupture.

Animal experiments show that the mediastinal pressure varies during the respiratory cycle. Similar to the intrapleural pressure, the normal mediastinal pressure is lower than or equal to the alveolar pressure. With inspiration lowering the mediastinal pressure and (forced) expiration, vomiting and retching increasing the alveolar pressure, a pressure difference is created. When alveolar rupture occurs, air follows these pressure differences and travels from the pulmonary interstitium towards the hilum to enter the mediastinum (figure 5). With ongoing mediastinal insufflation, air may disseminate into contiguous tissue. It can reach superiorly along the investing layer of the deep cervical fascia to the cranial base or may extend posteriorly through the neural foramen, along the sheath of the nerve root and into the epidural space. Rarely, it tracks along the pulmonary venous sheath to the pericardial space and causes a pneumopericardium.

The most common presenting symptom of pneumomediastinum is chest pain, occurring in 75% of patients. Half of patients experience mild dyspnoea and one-third have a cough or neck pain. Physical examination may be normal, but often subcutaneous emphysema is felt in the neck and upper chest. In 18%, Hamman’s sign is present: an audible crepitation on each heartbeat arising from air in the anterior mediastinum or pericardium. Hypotension is unlikely to be caused by pneumomediastinum but may indicate a serious underlying condition.
such as a severe pneumonia, oesophageal rupture or DKA. Rarely hypotension is caused by an increased mediastinal pressure compressing the heart and great vessels, known as a ‘tension pneumomediastinum.’

Different diagnostic modalities were used to evaluate oesophageal rupture in patients with DKA and pneumomediastinum (table 1). Among 51 patients, 33 had chest CT, 12 had fluoroscopic esophagography and 8 received both. Only six patients had upper endoscopy.

Contrary to fluoroscopic esophagography, CT is readily available in most hospitals and may, in the absence of oesophageal rupture, provide an alternative cause of pneumomediastinum. CT findings suggestive of oesophageal rupture are wall discontinuity and thickening, increased periesophageal fat stranding, mediastinal and pleural effusions and subdiaphragmatic air.

Two retrospective cohort studies showed that in the absence of these findings, chest CT had a 100% negative predictive value for oesophageal rupture. In patients with a negative chest CT, subsequent fluoroscopic esophagography would not show oesophageal contrast extravasation and they were managed without endoscopy or surgery. These findings should be interpreted with caution given the rare outcome, with only 24 out of 206 patients having a surgically, endoscopically or fluoroscopically proven oesophageal perforation.

When using chest CT for investigating oesophageal rupture, radiologists often use intravenous contrast material to enhance visualisation of the oesophageal wall, mediastinal and pleural abscesses. Addition of intravenous contrast did not improve diagnostic performance or interobserver agreement in the aforementioned studies. Our patient received chest CTs with and without intravenous contrast material, providing similar results. However, if no contraindications exist (eg, iodine allergy, renal failure), we suggest adding intravenous contrast material to increase the demarcation of the oesophageal wall and improve the detection of mediastinal pathology. In our institution, we use non-ionic contrast agents (80 mL of iomeron 300 mg/mL) with a 40 s scan delay. Similar CT protocols are used in other institutions.

CT esophagography combines the use of oral contrast with chest CT. The patient may lie supine while contrast is administered into the upper oesophagus through a tube inserted at the level of the cricopharyngeal sphincter. No fluoroscopy suite is needed. The addition of oral contrast material increases the positive predictive value of chest CT and provides the exact location of the oesophageal defect.

This case report illustrates the diagnostic challenge of investigating the presence of oesophageal rupture in patients with DKA and pneumomediastinum. Although data are limited, we consider chest CT with intravenous contrast as the diagnostic modality of choice. We think that fluoroscopic esophagography is impractical and, in case of a negative CT, of no added value. If doubt remains after negative CT, we recommend CT esophagography. In all cases of suspected oesophageal rupture, we advise that imaging is interpreted by an experienced radiologist, given the rarity of its occurrence.

Table 1: Review of case reports including patients with diabetic ketoacidosis complicated by pneumomediastinum, providing details on the aetiology, used diagnostic modalities, treatment and outcome (N=51).

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Patients with DKA and pneumomediastinum (N=51)</th>
</tr>
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<tbody>
<tr>
<td>Spontaneous pneumomediastinum</td>
<td>45</td>
</tr>
<tr>
<td>Secondary pneumomediastinum</td>
<td>6</td>
</tr>
<tr>
<td>Oesophageal rupture</td>
<td>4</td>
</tr>
<tr>
<td>Tracheal rupture</td>
<td>1</td>
</tr>
<tr>
<td>Retroperitoneal abscess</td>
<td>1</td>
</tr>
<tr>
<td>Diagnostic modalities</td>
<td></td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>51</td>
</tr>
<tr>
<td>Chest CT</td>
<td>33</td>
</tr>
<tr>
<td>Chest CT and FE</td>
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</tr>
<tr>
<td>Chest CT oesophagography</td>
<td>4</td>
</tr>
<tr>
<td>FE</td>
<td>12</td>
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<tr>
<td>Upper endoscopy</td>
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<tr>
<td>Treatment</td>
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<td>Conservative</td>
<td>48</td>
</tr>
<tr>
<td>Thoracotomy</td>
<td>3</td>
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<tr>
<td>Endoscopic intervention</td>
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<tr>
<td>Outcome</td>
<td></td>
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<tr>
<td>Uncomplicated</td>
<td>44</td>
</tr>
<tr>
<td>Morbidity*</td>
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</tr>
<tr>
<td>Mortality</td>
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</tbody>
</table>

*Morbidity included: Mallory-Weiss lesion (N=2), acute oesophageal necrosis (N=1), tracheal tear (N=1), Takotsubo cardiomyopathy (N=1), recurrent pneumomediastinum (N=1).

DKA, diabetic ketoacidosis; FE, fluoroscopic esophagography.
Patient’s perspective

The first author translated the patient’s perspective.

I was feeling ill 3 days prior to admission. It was the first time I experienced this kind of weakness. Like my organs were not functioning properly. I was vomiting continuously and was unsure whether to use my insulin. I cannot recall if I used it or not. The last thing I remember is trying to get to my general practitioner. I do not have any recollection of being in the ambulance, emergency department or intensive care unit.

Once I woke up, it was hard to tell my dreams apart from reality. My surroundings felt very surreal. I am glad my friends and family were present the first days after I was off the ventilator. They were the only thing familiar to me in this world of machines. Together with the doctors and nurses, they repeatedly explained to me what had happened. I had been in the intensive care unit for several weeks. I could not believe it at first, but my mother had taken pictures of my time there.

My physical recovery was expeditious. I trained daily with the physiotherapist in the hospital and only stayed shortly at the rehabilitation centre. However, the challenging part was the mental recovery. I would like to advise doctors and nurses in the intensive care unit to take special care of patients the moment they regain consciousness. In my case, the presence of my family members and friends made a huge difference and reduced my anxiety significantly.

My time in the hospital and the recovery afterwards made me more aware of my diabetes. I started to read on nutrition and use my glucose sensor regularly. Previously, I never expected that my diabetes could make me this sick. Sometimes I wonder whether the fungus in my lungs was with me all this time, even before I was put in the intensive care unit.

The patient was asked to comment on his chest computed tomography images showing a pneumomediastinum.

The doctor (SZ) tells me the amount of air in my chest, but outside of my lungs, was visually impressive, but I do not remember having any issues of chest pain, shortness of breath or feeling air bubbles underneath my skin. My mother told me she felt the air bubbles when I was in the intensive care unit. Currently I do not have chest pain or problems when eating or drinking.

Learning points

- Pneumomediastinum is an uncommon complication of diabetic ketoacidosis and may occur spontaneously and rarely secondary to oesophageal rupture.
- Mediastinal air may spread to adjacent tissue, resulting in pneumopericardium, subcutaneous emphysema in the upper chest and neck, and air in the spinal canal.
- Chest CT is the preferred diagnostic modality for investigating secondary causes of pneumomediastinum, as it is widely available, easy to perform and has a high sensitivity for oesophageal rupture.

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Contributors

SCZ, CB, MV and MG were responsible for drafting of the text, sourcing and editing of clinical images, investigation results, drawing original diagrams and algorithms, and critical revision for important intellectual content. SCZ, CB, MV and MG gave final approval of the manuscript. The patient is not one of the authors of the manuscript.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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REFERENCES

20. Ho AS, Ahmed A, Huang JS, et al. Multidetector computed tomography of spontaneous versus secondary pneumomediastinum in 89 patients: can multidetector...
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computed tomography be used to reliably distinguish between the 2 entities? *J Thorac Imaging* 2012;27:85–92.

