Acute ischaemia of the glans penis post-circumcision managed with pentoxifylline, topical nitroglycerin and epidural

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SUMMARY
Acute ischaemia of the glans penis is a rare and serious complication following circumcision. We report the case of a teenage boy with glanular ischaemia shortly after circumcision with dorsal penile nerve block. This was successfully treated with total 11 days of topical 2% nitroglycerin ointment, 14 days of oral pentoxifylline 400 mg three times a day and 3 days of epidural (0.2% ropivocaine). There was marked clinical improvement at 4 days with a few patches of cyanosis remaining. Surgical intervention was not required, and the patient was discharged with follow-up review. At 12 days, there was complete resolution of ischaemia and the glans penis appeared normal. We suggest that oral, topical and epidural regimen of vasodilators and anti-sympathomimetic agents can be used in combination for acute ischaemia of the glans penis.

BACKGROUND
Circumcision is a common paediatric surgical procedure that is associated with a 0%–10% rate of complications, commonly bleeding, swelling, cosmetic deformities and wound infection.1 More severe outcomes are rare, such as penile amputation, urethrocutaneous fistulas, meatal stenosis and especially ischaemia and/or necrosis of the glans penis.2

Glanular ischaemia has been reported as a result of compressive wound dressings, circumferentially constricting sutures and the use of monopolary diathermy. The use of dorsal penile nerve block (DPNB) or local anaesthesia with vasoconstrictors such as epinephrine should be avoided.3 Ischaemia of the glans has however also been reported in a boy in early childhood without the use of local anaesthesia.4

The exact aetiology of the ischaemia may be unclear and there is no standardised guideline for managing ischaemia of the glans penis. Limited case reports suggest the therapeutic success of methods to induce vasodilation locally with topical 2% nitroglycerin or 10% testosterone, epidural or caudal infusion of bupivacaine, systemically using vasoactive drugs pentoxifylline and epoprostenol, or anticoagulants such as enoxaparin. The use of corticosteroids and hyperbaric oxygen therapy has also been reported.3,4

We report the case of a teenage boy who developed acute glans penis ischaemia after circumcision done under DPNB, which was successfully treated with oral pentoxifylline, topical 2% nitroglycerin and epidural (0.2% ropivacaine).

CASE PRESENTATION
A teenage boy was admitted to our hospital with a congested, swollen and dark purple glans penis 7 hours after an elective circumcision performed under general anaesthesia at the same hospital (Figure 1). The indication for the procedure was persistent difficulty retracting the foreskin despite two courses of topical steroid therapy. Preoperatively, DPNB was undertaken with 10 mL of 0.5% bupivacaine without epinephrine. Circumcision was uneventful and meticulous haemostasis was achieved with bipolar diathermy. The skin was closed with interrupted 5-0 catgut sutures. A Jelonet dressing with loose combine was applied. There were no intraoperative issues of concern.

The glans appeared normally perfused at the end of the procedure. At 4 hours after surgery, the glans penis appeared congested, although well perfused with normal sensation. Shortly after discharge, the patient noted further swelling and darkening of colour of the glans, and the surgical consultant advised for urgent presentation to the emergency department.

Physical examination revealed that the glans penis was swollen and deep purple in colour and was hypersensitive to touch. There was no evident haematoma, the operative wound was clean and the penile shaft was unremarkable. The patient was otherwise afebrile, haemodynamically stable and pain free.

INVESTIGATIONS
Doppler ultrasound of the penis demonstrated good flow in the proximal dorsal penile vessels with no evidence of haematoma.

DIFFERENTIAL DIAGNOSIS
The diagnosis was ischaemia of the glans penis secondary to venous congestion based on initial distension of the glans and subsequent normal Doppler flow on ultrasound. The patient’s only medical history was asthma, Chiari malformation and a previous adenoidectomy. He had a previous episode of superficial thrombophlebitis of a tributary of the left basilic vein. Haematology tests (coagulation studies, antithrombin III level, protein C/S studies) were normal. There was no significant family history.

TREATMENT
Immediate application of a glyceryl trinitrate 25 mg patch to the glans was carried out while closely
monitoring blood pressure and performing two hourly reviews of the glans vascularity. Two hours later, the patch was removed, and the patient was commenced on regular topical nitroglycerin 2% ointment two times per day. The following morning, an epidural infusion of 0.2% ropivocaine was commenced and continued for 3 days to reduce sympathetic vascular tone and optimise vasodilation to the glans penis. An indwelling urinary catheter (IDC) was inserted after the epidural due to failure to void. Oral pentoxifylline 400 mg three times a day was commenced.

OUTCOME AND FOLLOW-UP
Over the next 4 days, there was marked clinical improvement. The glans penis appeared more pink and significantly less congested. There were some sparse and small patches of cyanosis. The glans penis had progressively normal sensation. On day 4, the IDC and epidural catheter were successfully removed without complication. The patient was deemed well for discharge with a 7-day course of topical nitroglycerin 2% ointment two times per day and 11 days of oral pentoxifylline 400 mg three times a day.

The patient was reviewed the following day and the glans penis appeared better with improving patches of cyanosis. The patient was again followed up at 8 days after discharge and the glans penis was completely normal, totally pink in colour with brisk capillary refill. Normal function of the penis was also restored, including preserved sensation over the glans, ability to have morning erection and erection upon urination. There was no phimosis resulting from this ischaemic episode. The nitroglycerin ointment was ceased and the pentoxifylline weaned off over 3 days.

DISCUSSION
Post-circumcision, ischaemia of the glans penis is a rare and serious complication, in which the aetiology may be unclear. Venous/vasospasm of dorsal penile vessels may result from needle-associated endothelial microtrauma from DPNB. The literature suggests this is the most commonly described cause of glans ischaemia following circumcision. For DPNB, a dose of 0.5% bupivacaine 1 mL plus 0.1 mL/kg is recommended, although it is important to have adequate volume to pass posteriorly ensuring the ventral branch supplying the frenulum is blocked. Larger volumes of local anaesthetic can cause pressure on dorsal penile vessels causing temporary obstruction/congestion. The 0.5% bupivacaine acts as a vasodilator, whereas subclinical doses have shown a vasoconstrictive effect. It has been suggested that DPNB may be associated with penile vascular thrombosis as demonstrated by either elevated D-dimer levels or compromised flow on Doppler ultrasound. Although D-dimer levels were not measured in our patient, his ultrasound findings were normal.

There is no standardised pharmacological management protocol for glanular ischaemia; however, a consensus from available case reports indicates the importance of improving blood flow and oxygen supply to the glans. Aminsharifi et al reported the success of topical 10% testosterone in improving foreskin vascular density. Zvizdic et al further demonstrated the success of a 5-day course of topical 2.5% dihydrotestosterone and low molecular weight heparin (LMWH) in completely resolving glans ischaemia at 43 hours. Mittino et al reported the efficacy of LMWH with acetylic acid 100 mg/day. Hyperbaric oxygen therapy has been demonstrated to be effective alone in treating glans ischaemia or at 2.5 atm of pressure for 90 min with intravenous pentoxifylline 10 mg/kg. Burke et al treated temporary ischaemia of glans after DPNB (0.75% ropivacaine) with infusion of iloprost 0.52 µg/µl/hour. Studies have shown complete resolution of severe glans ischaemia with oral 10 mg/kg/day pentoxifylline for 5 days’ or 8 days.

The mechanism of action of pentoxifylline is not completely understood. It is a non-selective phosphodiesterase inhibitor that augments cAMP synthesis and stimulates prostaglandin production thus is an effective peripheral vasodilator and reduces whole blood viscosity. It is used to treat peripheral vascular and cerebrovascular disease. Topical nitroglycerin also allows for localised vasodilation of penile vessels. Epidural or caudal block acts to reduce sympathetic tone and further improve arterial supply and venous drainage. Kaplanian et al revealed that caudal block (0.25% bupivacaine) can improve perfusion of the glans in a few minutes.

Dennison, Garrido-Abad and Suárez-Fonseca described the successful management of glans superficial necrosis with 7-day treatment with topical nitroglycerin and gentamicin, oral pentoxifylline 60 mg three times a day and epidural with bupivacaine 0.25% 1 mL/kg. Our treatment was most similar to this regimen and resulted in complete resolution of glans ischaemia.

Learning points
- We report a case of glanular ischaemia, a rare and serious complication following a routine, elective circumcision procedure.
- Ischaemia of the glans penis may result in urethral stricture, meatal stenosis and rarely, irreversible necrosis requiring amputations of the glans.
- There is no standardised protocol for managing glans penis ischaemia; however, evidence suggests the importance of topical, oral and intravenous vasodilators and anti-sympathomimetic agents to improve vascular flow and oxygen delivery to the glans.
- We suggest that ischaemia of the glans penis after circumcision can be managed with topical nitroglycerin 2%, oral pentoxifylline and epidural with 0.2% ropivacaine.
- Frequent monitoring of the ischaemic glans penis and regular follow-up post-discharge are mandatory to evaluate therapeutic success, especially in this rare instance supported by limited literature. Assessing such ischaemic changes/progress is mainly dependent on clinical judgement.

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