CASE REPORT

Testicular torsion in a patient with Ehlers-Danlos syndrome

Amy Lee Fowler,¹ David Bouchier Hayes,¹ Eszter Feher²

¹Department of Urology, Galway Clinic, Galway, Ireland
²Department of Anaesthetics, Galway Clinic, Galway, Ireland

Correspondence to
 Dr Amy Lee Fowler,
 amyleefowler@rcsi.ie

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SUMMARY

We present a 19-year-old man with a diagnosis of Ehlers-Danlos syndrome (EDS) and a delayed presentation of testicular torsion. EDS is a rare and heterogeneous condition affecting collagen synthesis and presents multiple difficulties in a surgical setting. Management of this case of testicular torsion was complicated by impaired cognition of the patient, difficulty with intubation, a contralateral undescended testis and postoperative bleeding. We discuss the specific challenges faced in this case of testicular torsion with longstanding ischaemia and perioperative considerations of EDS.

BACKGROUND

Rare conditions pose a clinical dilemma to the surgeon in emergency situations, where unfavourable conditions are exacerbated by the underlying illness.

We present the case of testicular torsion in the setting of Ehlers-Danlos syndrome kyphoscoliosis type (EDS). EDS comprises a range of heterogeneous connective tissue disorders characterised by skin hyperextensibility, atrophic scarring, joint hypermobility, generalised tissue and vascular fragility.¹ Six major subtypes exist with an incidence of around 1 in 5000 worldwide^{2,3} (table 1). In recent times, novel but overlapping types of EDS and syndromes with phenotypic similarities to EDS have been identified as genetic and molecular testing continues to expand.⁴

All subtypes of EDS have surgical and anaesthetic implications. Bleeding diathesis can be seen in forms of the disease irrespective of normal coagulation studies, bleeding time, platelet count and function.^{2,3} Joint issues and mucosal fragility can lead to difficulty with intubation, while scoliosis and scarred skin can also inhibit effectiveness of regional anaesthesia.⁵

Kyphoscoliosis type is a rare subtype of EDS and the first inborn error of human collagen metabolism identified.⁴ It consists of severe congenital scoliosis, joint laxity, muscle hypotonia and fragility of vessels and sclera.^{3,6} In ideal situations, it is recommended that such patients be treated in specialised centres due to anticipated mortality and morbidity associated with the condition. However, this is unavoidable in an emergency situation.⁵

This case documents complications of surgery in the setting of EDS as well as the practicalities faced by a surgeon when presented with an uncommon condition.

CASE PRESENTATION

A 19-year-old man presented with a 4-day history of constant, dull, aching pain in the right scrotum. He presented to his general practitioner with a swollen, erythematous and tender right hemiscrotum. He had a known diagnosis of Ehlers-Danlos, kyphoscoliotic type (type VIa) with associated aortic root dilatation, scoliosis, ocular fragility, asthma and sleep apnoea. He had undergone previous posterior spinal fusion for kyphoscoliosis, encountering difficulty with induction and bleeding during this procedure. He also had mild developmental delay. The picture was complicated from an anaesthetic point of view, as the patient had a full stomach. He was transferred urgently to our centre and seen immediately by the consultant urologist on-call.

Physical examination revealed an erythematous, severely oedematous right hemiscrotum, the right testis was descended in the scrotum but had a horizontal lie with an absent cremasteric reflex. No testis was palpable within the left hemiscrotum.

INVESTIGATIONS

Initial investigations demonstrated a high white cell count (WCC) of $19.7 \times 10^9/L$, a neutrophilia of $16.9 \times 10^9/L$ and a raised C reactive protein (CRP) of 107.4 mg/L. He was immediately started on intravenous ciprofloxacin as per local antibiotic guidelines.

Urgent testicular ultrasound demonstrated a right testis with heterogeneous thickened testicular tissue and internal reduced echogenicity consistent with liquefaction. No Doppler flow was present. No testis was visualised in the left hemiscrotum.

DIFFERENTIAL DIAGNOSIS

The clinical and radiological picture was highly suspicious for longstanding right-sided testicular torsion, although initial differential diagnosis included epididymo-orchitis. Inability to palpate or visualise the left testis on ultrasound was thought to be due to severe oedema of the scrotum and difficulty tolerating examination, but was of concern for a left undescended testis.

TREATMENT

The patient was transferred to theatre for urgent scrotal exploration. The patient was given midazolam sedation due to his level of distress and developmental delay. Anaesthetic assessment revealed limited mouth opening and a high-arched palate, which predicted difficult airway. A bougie, McCoy

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Table 1 Villefranche classification of EDS^{4 20 21}

Type	Genetic mutation	Clinical features
Classical	Autosomal dominant. COLVA1, COLVA2. Leads to arginine-to-cysteine substitutions. Pathogenesis not well understood.	Vascular fragility, cardiac valvular issues, skin hyperextensibility, atrophic scars, generalised joint hypermobility and pes planus.
Hypermobility	Autosomal dominant. No genetic defect identified. Related to tenascin X gene deficiency/haploinsufficiency.	Hyperextensible skin, chronic joint pain and abnormalities, muscle weakness and deformities of hands and feet.
Arthrochalasia	Autosomal dominant. COLIA1, COLIA2. Leads to structural abnormalities in pro- $\alpha 1$ (I) or $\alpha 2$ (I) chain and loss of procollagen N-proteinase cleavage site.	Craniofacial features (frontal bossing, hypertelorism and micrognathia), congenital hip dislocation, joint hypermobility, foot abnormalities, hypotonia and osteopenia.
Kyphoscoliosis	Autosomal recessive. Caused by mutations in PLOD 1/LH1. Leads to mutation in collagen modifying enzymes.	Congenital scoliosis, hypotonia, severe joint pain, delayed motor skills, osteopenia and microcornea.
Vascular	Autosomal dominant COL3A1	Characteristic appearance, rupture of medium-large sized vessels, AV fistulae and aneurysms.
Dermatosparaxis	Autosomal recessive. Caused by mutations in ADAMTS2 leading to defects in processing of type I procollagen to mature type I collagen.	Craniofacial features (prominent protuberant eyes and hypoplastic chin), excessive skin, extreme skin fragility and easy bruising.

EDS, Ehlers-Danlos syndrome; LH1, lysine hydroxylase 1; PLOD 1, procollagen-lysine 2-oxoglutarate 5-dioxygenase 1.

blade, glide scope and Airtraq were prepared and on standby. The patient was intubated without any major difficulty, but ideal awake fibre-optic intubation was precluded due to developmental delay. Modified rapid sequence induction was performed with fentanyl, propofol and rocuronium. Extreme caution was taken with patient positioning and padding due to the known risk of bruising and skin fragility.

Intraoperative findings demonstrated a tortorted right cord with black testicular tissue representing longstanding ischaemia. Tissues were dissected carefully and with minimal handling. The testis was detorted and left in warm saline packs. The left hemiscrotum and inguinal canal were examined under anaesthetic and found to be empty. No viability was seen in the right testis and after second opinion the surgeon proceeded to right orchidectomy. No intraoperative complications or excessive bleeding was encountered. Skin was closed loosely with 3–0 vicryl sutures.

Induction and the maintenance of the anaesthesia were performed with sevoflurane. At the end of surgery sugammadex was used to fully reverse the muscle paralysis. After extubation, the patient developed bronchospasm and laryngospasm. Following stabilisation, the patient was transferred to intensive care unit (ICU) for overnight observation due to the potential for complications, known sleep apnoea and continuous positive airway pressure ventilation (CPAP).

OUTCOME AND FOLLOW-UP

Postoperatively, the patient recovered with WCC and CRP within normal limits.

Haematological investigations, including a Rotem analysis, did not reveal any deviation from the normal values. CT scan of abdomen and pelvis was suggestive of testicular tissue in the left inguinal canal. This was confirmed as a 3.4×1.2 cm testis on ultrasound. He was discharged on day 2 with decision to perform elective left-sided orchidopexy at a later date. Histology results demonstrated a 'testis and epididymis showing marked vascular congestion between the testicular tubules and in the submucosa of the tubules of the epididymis', consistent with torsion effect. No evidence of malignancy was seen.

The patient re-presented 10 days postoperatively with a 12-hours history of swelling and pain in the postoperative site. Examination revealed an erythematous, tense right hemiscrotum with tachycardia (115 bpm) and a low-grade fever (37.5°C). Inflammatory markers were elevated. Ultrasound testis confirmed a partially organised infected haematoma. This spontaneously discharged and he was treated conservatively with intravenous gentamycin and metronidazole after input from microbiology results. He was discharged 1 day later on oral linezolid following culture and sensitivity results.

At 18 days postoperatively, the patient was readmitted again with a swollen right hemiscrotum and a discharging sinus consistent with an unresolved infected haematoma. Open exploration was planned for the following day. Necrotic tissue was removed from the right hemiscrotum and washed with saline and Betadine. Wound edges were loosely apposed with 3–0 vicryl sutures and a drain left in situ. Microbiology culture reports demonstrated growth of *Klebsiella pneumoniae*, *Enterococcus faecalis* and Gram-negative anaerobes. He was commenced on an intravenous cephalosporin and oral linezolid. He was discharged day 6 of readmission on a 10-day course of cephalexin and metronidazole due to linezolid-induced myelosuppression.

Six weeks postoperatively, the patient had complete healing of his scrotal wound. The patient was referred to a specialist unit with an interest in paediatric and adult orchidopexy for assessment, to maximise future viability of his remaining testicular tissue. He was put in touch with a specialist centre in the UK with expertise in hypermobility disorders to provide long-term input and management into his underlying condition.

DISCUSSION

As far as we are aware, this is the first reported case of testicular torsion in a patient with EDS. It presents many potential pitfalls, which are exacerbated by the time dependency of testicular torsion. EDS is a rare condition which presents many clinical challenges.³ Genetic mutations for collagen defects have been identified for most of the subtypes, however, phenotypic variability exists between them.^{1 6} Kyphoscoliotic type is rare, with an incidence of 1:100 000 births and presents with a wide clinical spectrum. Features include severe muscular hypotonia, progressive kyphoscoliosis, joint hypermobility and skin hyperelasticity. This occurs due to mutations in the gene encoding for the collagen-modifying enzyme, procollagen-lysine 2-oxoglutarate 5-dioxygenase 1 and lysine hydroxylase 1, which lead to impaired cross-linking of lysyl residues and underglycosylation of hydroxylysyl residues resulting in instability of collagen tissue.⁶

All elements of perioperative management must be handled with extreme care in EDS. Patient positioning and padding must be considered to prevent blunt injury, joint dislocation and excessive bruising.⁵ Prior difficulties with intubation and ventilation should be established before surgery.⁵ Difficult intubation arises from temporomandibular dysfunction, premature

spondylosis and atlantoaxial instability. These features are often subclinical with normal examination findings.⁷ Tissue fragility can lead to excessive bleeding with repeated intubation attempts and so elective fibre-optic intubation with smaller cuff endotracheal tubes may be preferred to prevent mucosal damage.^{5,7} In this case, the patient was intubated without any major difficulty and ideal awake fibre-optic intubation would have been difficult because of developmental delay. Our patient was admitted to the ICU postoperatively due to known sleep apnoea and high likelihood for postoperative complications.

No recommendations for general or regional anaesthesia exist in patient with EDS. The alternative to general anaesthesia in those with multiple comorbidities would be use of regional techniques. The risk of bleeding, nerve injury and perforation when using spinal anaesthesia make it unsuitable for use in patients with EDS.^{5,7} Specific to kyphoscoliosis type, tissue fragility and meningeal involvement in the form of Tarlov cysts can lead to higher rates of postdural headache. Scoliosis can prevent epidural spread or the ability to perform spinal anaesthesia.⁵

Intraoperative surgical considerations include minimal surgical dissection and minimal force during incision, retracting and suturing. Clamping of blood vessels should be avoided.⁸ Wound rupture and postoperative bleeding can occur weeks after initial surgery, as experienced in our case. Technical measures can be taken to minimise excessive bleeding and postoperative wound issues. Skin closure should be performed with tension free, non-absorbable cutaneous stitches and should be left in situ for double the recommended length of time.^{8,9}

Currently, no consensus on the management of bleeding exists in these patients. Studies report elongated bleeding time in 94.7% of patients with EDS despite normal coagulation studies.¹⁰⁻¹³ The underlying pathophysiology is thought to be due to abnormalities in the structure and function of vessel walls.¹¹ The use of prophylactic desmopressin acetate (DDVAP) may be of benefit in patients with EDS and has been proven in those with normal coagulation studies and a prolonged bleeding time. DDVAP acts by causing release of von Willebrand factor and factor VIII from vascular endothelial cells.^{9,11,13} It has been reported that adding conjugated oestrogens can act to simultaneously prolong the action of DDVAP.¹²

Our patient re-presented multiple times for recurrence of an infected haematoma. We feel that readmission was unavoidable in this case. Complications in EDS are often delayed and invasive procedures should generally be avoided at all costs due to the risk of excessive bleeding and poor ability to close wounds directly.⁸

Intellect has historically been shown to be normal in patients with EDS. Our patient exhibited mild developmental delay adding further clinical complexity. In a study by Rohrbach *et al*, 5 of 12 EDS kyphoscoliotic type sufferers exhibited developmental delay, although whether this is directly attributable to the underlying condition remains unclear.⁶ Developmental delay may contribute to poor communication of pain by the individual, delaying diagnosis in a time critical conditions.¹⁰

Testicular torsion remains a common condition and affects 1 in 4000 males under age 25 years, with the majority of younger patients presenting after the critical 6-hour window.^{14,15} The condition can mimic epididymo-orchitis, especially when long-standing.¹⁰ There should be a high degree of clinical suspicion, particularly in connective tissue disorders where integrity of fascial layers is poor, leading to poor intravaginal fixation of the testis. Testicular salvage is directly linked to time from onset of symptoms, with delay in operation beyond 12 hours uniformly resulting in orchidectomy.¹⁶⁻¹⁹ This justifies our decision to

remove the affected testicle even in light of a contralateral undescended testis.

CONCLUSION

Rare conditions such as EDS can present a clinical conundrum to the treating surgeon particularly in an emergency situation. Knowledge of basic implications of the condition can minimise morbidity and mortality of the patient without a need for in-depth knowledge of the condition.

Learning points

- ▶ Testicular torsion remains a common surgical emergency and clinicians should exercise a high index of suspicion, particularly where patients present with communication difficulties.
- ▶ Conservative management options should be considered in Ehlers-Danlos syndrome (EDS), due to high incidence of immediate and delayed complication. If surgery is indicated, precautions must be taken as detailed in this report.
- ▶ Patients with EDS should be followed closely in the perioperative and postoperative periods to allow early recognition of complications.
- ▶ Rare clinical syndromes present difficulties to the surgeon. Perioperative preparation and questioning regarding previous surgical procedures are key to avoiding complications.

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