British Journal of Anaesthesia 1996; **76**: 464–466

CASE REPORTS

Myocardial ischaemia associated with Ehlers–Danlos syndrome

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Summary

A 38-yr-old man with an unusual type of Ehlers–Danlos syndrome presented for elective abdominal aortic aneurysm repair. During surgery he developed acute myocardial ischaemia, resulting in abandonment of the procedure. He was shown subsequently to have severe triple vessel coronary artery disease. Silent ischaemia associated with severe coronary artery disease, although rare, may be associated with the syndrome and is difficult to recognize as other cardiac abnormalities are frequently present. (*Br. J. Anaesth*. 1996; **76**: 464–466)

Key words

Ehlers–Danlos syndrome. Surgery, aneurysm. Heart, ischaemia. Complications, Ehlers–Danlos syndrome.

Ehlers–Danlos syndrome is a heterogeneous group of connective tissue disorders. It was described by Ehlers in 1899 and by Danlos in 1908. Its main features are articular hyperlaxicity, cutaneous hyperelasticity, vascular fragility and cutaneous fragility [1]. These features present the anaesthetist with potential problems and hazards. Many different types are classified on clinical criteria. However, the majority of patients do not fit neatly into any of the types. Recent developments in understanding the molecular structure of collagen have further confused the issue with the finding that similar abnormalities of the same type of collagen can produce varying phenotypes of Ehlers–Danlos syndrome or osteogenesis imperfecta. Although all Ehlers–Danlos syndrome types may present problems for the anaesthetist, it is type IV which poses the greatest problems and has been the subject of previous case reports [2–4]. Type IV is usually associated with abnormalities of type III collagen. Sufferers may have friable arteries which can rupture spontaneously causing sudden death.

We report a case of a young, apparently healthy man, who had an unspecified type of Ehlers–Danlos syndrome, with type 1 collagen abnormality. He developed acute, severe myocardial ischaemia during operation for elective aortic aneurysm repair. Emergency coronary artery bypass grafting was subsequently performed. To our knowledge this is the first case report of myocardial ischaemia occurring during anaesthesia that is specifically associated with Ehlers–Danlos syndrome.

Case report

A 38-yr-old man presented for elective abdominal aortic aneurysm repair. The aneurysm, measuring 7 cm, was discovered after x-ray of his lumbar spine. In the past he had undergone repair of a patent ductus arteriosus at 3 yr of age and was routinely followed-up by various cardiologists. When aged 13 yr he was found to have mild supravalvular pulmonary stenosis and was investigated for chest discomfort after cycling when aged 28 yr. An echocardiogram at that time revealed aortic regurgitation and mild left ventricular hypertrophy. He remained well and continued to have a yearly cardiology review, including an echocardiogram. Mild deterioration in left ventricular function was noted on echocardiogram 2 yr before this procedure for which he was commenced on enalapril. His exercise tolerance was good and he continued to cycle 5–10 miles a day until his aneurysm was discovered.

He was seen before operation by a cardiologist. On examination, he was noted to be of short stature with some dysmorphic features. His skin was velvety soft and he had absent earlobes. He had moderate kyphoscoliosis, flat feet and hypermobile joints, but no scarring. Para-umbilical and inguinal herniae were noted. Cardiovascular examination revealed murmur of aortic regurgitation, pulse in sinus rhythm with an arterial pressure of 120/60 mm Hg. Haematological and biochemical investigations, including clotting studies, were all normal. Chest x-ray was unremarkable. The electrocardiogram (ECG) showed prolonged QRS complexes, left ventricular hypertrophy and Q-waves in the inferolateral leads. These changes had all been present for the past decade and were thought to relate to his congenital heart defects and cardiac surgery. Echocardiographic findings were of moderate aortic regurgitation with an aortic root measurement of 4 cm, normal end-diastolic volume and mild impairment of systolic function. Ultrasound scan of his abdomen revealed a 7.2-cm infrarenal aneurysm extending to the bifurcation. The cardiologist also felt that he had

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dysmorphic features suggestive of Ehlers–Danlos syndrome and so referred him for a genetic examination. Although there was no family history of Ehlers–Danlos syndrome, his parents were noted to be first cousins. In the absence of any history of excessive bleeding, bruising or scarring, the provisional genetic opinion was that he had type VI Ehlers–Danlos syndrome, as opposed to the more common types I or IV.

Before operation it was felt that, in view of his congenital heart disease, he would benefit from pulmonary artery (PA) catheterization. He was therefore admitted to the intensive care unit. A PA catheter was inserted without difficulty. Measurements revealed cardiac output of a 4.7 litre min^{-1} with a pulmonary capillary wedge pressure of 12 mm Hg. In theatre a radial artery cannula was inserted, also without difficulty. Monitoring was then started and included an ECG in the CM5 configuration, pulse oximetry, direct arterial pressure and pulmonary artery pressure. His lungs were then preoxygenated and anaesthesia was induced with propofol 140 mg, fentanyl 150 μg and vecuronium 10 mg. Laryngoscopy revealed a grade 3 larynx necessitating intubation with the aid of a gum elastic bougie. An extradural catheter was inserted at L1–2. Sensation during insertion was found to be strange because of the abnormal feel of the ligaments. He was given Gelofusine 500 ml and a test dose of 0.5 % bupivacaine 3 ml without incident. This was followed by 0.5 % bupivacaine 7 ml and diamorphine 2.5 mg, given in incremental doses. His arterial pressure remained stable. The operation proceeded uneventfully until, during mobilization of the aneurysm, he developed marked ST segment elevation on the ECG which rapidly progressed to a supraventricular tachycardia, followed by ventricular tachycardia. His arterial pressure then decreased to 55/40 mm Hg. He required DC cardioversion of 50, 100 and then 200 J to restore sinus rhythm. Before this there was no episode of hypotension. However, after restoration of sinus rhythm he had an intermittent sinus tachycardia of 130 beat min^{-1} accompanied by hypotension and the procedure was therefore abandoned. These episodes were short-lived, not requiring further treatment. During the next 30 min, cardiovascular stability improved, ST segment on the ECG returned to normal and he did not require further treatment. He was transferred to the intensive care unit where a 12-lead ECG was performed. This showed no change from his previous ECG and an echocardiogram showed no deterioration from preoperative function.

He was sedated and his lungs ventilated overnight in intensive care and he remained stable. The following day attempts were therefore made to wean him, but this resulted in the return of marked tachycardia with accompanying ST segment elevation. Weaning was stopped and transfer to the regional cardiothoracic unit was arranged.

Cardiac catheterization revealed the presence of severe generalized triple vessel disease. He underwent coronary artery bypass grafting the following day without any further attempts to wean him. The aorta was noted to be extremely friable. He was stable throughout the procedure. He underwent an uneventful abdominal aneurysm repair 1 week later. Skin biopsy was taken for fibroblast culture and collagen studies.

Discussion

Ehlers–Danlos syndrome has a complicated, multifaceted presentation. Our patient was felt to have type VI Ehlers–Danlos syndrome, caused by lysyl oxidase deficiency on the basis of a likely recessive inheritance, the presence of scoliosis, scarring and the absence of bruising [5]. However, collagen studies did not confirm this and were more consistent with a type I collagen abnormality. This is associated more commonly with osteogenesis imperfecta although it has been reported in association with type VII Ehlers–Danlos syndrome [6]. Our patient did not fit neatly into any category. Indeed, the immense heterogeneity of the collagen diseases and improved detection of the genetic defects involved are likely to lead to re-classification of collagen disorders on the basis of the actual defective gene in the future.

Anaesthetic problems in Ehlers–Danlos syndrome were reviewed extensively by Dolan, Sisko and Riley [2]. Problems may occur in all types because of lax, unstable joints, abnormal skin elasticity and friable vessels. These lead to difficulty with tracheal intubation and insertion of cannulae or catheters. Abnormal vessel walls and platelet defects may lead to uncontrollable haemorrhage [7]. There may also be lung cysts present, increasing the risk of pneumothorax [9]. Dolan, Sisko and Riley did not recommend the use of extradural analgesia because of the risk of haematoma, but since then two authors have described its successful use in obstetric anaesthesia [3, 4]. We felt that extradural anaesthesia was appropriate in our patient. Extradural block is used routinely in many centres for aortic aneurysm repair as it provides excellent analgesia, reducing anaesthetic requirements during operation. After operation, pain may lead to increased oxygen requirement thus increasing the risk of myocardial ischaemia. Extradural analgesia reduces this risk compared with systemic opioids [9]. In aortic insufficiency an increase in afterload caused by pain may worsen regurgitation, with the risk of acute left ventricular volume overload [10]. Extradural analgesia may prevent this or actually decrease afterload. The extradural catheter was inserted under controlled conditions by an experienced operator with incremental doses of local anaesthetic accompanied by monitoring of pulmonary artery wedge pressure. Tachycardia, arrhythmia and hypotension occurred 1 h after the last dose of bupivacaine and we felt therefore that his problems were unrelated to the effects of the extradural.

Cardiac complications are a recognized feature of Ehlers–Danlos syndrome [11]. The main problems are: (a) valvular diseases—regurgitation or prolapse caused by abnormal valve structure; (b) congenital heart disease—atrioventricular septal defects, tetralogy of Fallot and dextrocardia; (c) conduction defects—atrioventricular block, incomplete right bundle branch block and extrasystoles.

Coronary artery disease occurring in association with Ehlers–Danlos syndrome has been reported [11]. Both cases were in type IV disease and led to myocardial infarction. All cases, including our own, had age ranges in their thirties. Neither of the cases reported had symptoms of angina pectoris before their myocardial infarction. It seems likely that fragility and friability of the coronary arteries leading to plaque formation may be implicated. In our patient ischaemia was related to handling of the aneurysm and later attempts to wean him. He did not develop myocardial infarction.

Because of the many cardiac defects seen in Ehlers–Danlos syndrome, ECG recordings are likely to be abnormal, making the detection of ischaemia more difficult. Cardiac catheterization has been described as hazardous in Ehlers–Danlos syndrome as the friable arteries make haemorrhage from the entry site likely [9]. Exercise or dipyridamole thallium scanning has been recommended for certain at risk candidates undergoing aortic aneurysm repair. It would perhaps be a suitable screening measure in Ehlers–Danlos syndrome sufferers before undertaking a major procedure.

In summary, the anaesthetic implications of Ehlers–Danlos syndrome are multiple. Before surgery, the help of a geneticist is useful to characterize the type of Ehlers–Danlos syndrome presenting so that a more accurate prediction can be made of the problems likely to occur. Myocardial ischaemia, although rare, can occur in young sufferers of Ehlers–Danlos syndrome without prior symptoms. This makes diagnosis difficult, especially if associated with other congenital abnormalities. This possibility should, however, be borne in mind and the appropriate investigations, such as thallium scanning, performed.

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