CASE REPORT

Spontaneous Rupture of the Renal Artery in a Patient with Ehlers–Danlos Syndrome Type IV

O. Øyen1, O. P. Clausen2, I. B. Brekke1, A. Bakka1 and F. M. Pope3

1Surgery Department B and 2Institute for Pathology, Rikshospitalet, 0027 Oslo, Norway and 3Strangeways Research Laboratory, Cambridge CB1 4RN, U.K.

Introduction

Spontaneous rupture of larger-sized arteries is often caused by inborn defects in genes encoding structural proteins (e.g. collagen/fibrillin/elastin). Recent advances in molecular biology have identified the causative genetic defect in several diseases with vascular fragility. The gene causing the Marfan syndrome2 encodes the elastin-associated glycoprotein Fibrillin I, whilst the Fibrillin II gene has been linked to a related condition called congenital contractural arachnodactyly.3 A major genetic component has also been demonstrated in the aetiology of “common” abdominal aortic aneurysms.4 Collagen type III (COL3A1), an important structural component of arterial walls, is linked to familial aortic aneurysms, and has been proposed as a candidate gene.5 It also causes Ehlers–Danlos syndrome type IV (EDS IV),6 which is one of the rarest of the 10 subtypes of Ehlers–Danlos syndrome (EDS).7 EDS IV has been estimated to cause 4% of EDS as a whole, with an incidence of 1:5 000 0007 (probably underestimated). It is clinically severe; causing spontaneous rupture of larger arteries as well as spontaneous intestinal perforations.9–12 During the past few years, the underlying mutations/deletions in the collagen type III gene have been characterised in detail in several patients.9,13,14 On this basis, structure–function relationships have been predicted.15

We report a patient presenting with spontaneous rupture of the renal artery. Histological examination showed remarkable and unique defects of the media layer. The diagnosis of EDS type IV was confirmed by clinical and biochemical criteria.

Case Report

A 12-year-old boy gave a 1 week history of abdominal pain and nausea with a falling Hb, but no history of trauma. An explorative laparotomy at his local hospital showed a large retroperitoneal haematoma. The midline incision was closed, and the patient was urgently transferred to our department. On admission he was severely hypovolaemic with gross abdominal distension. After massive transfusion, relaparotomy was performed. Bleeding into the abdomen from a retroperitoneal haematoma was primarily controlled by digital compression of aorta. We found that the right renal vessels had been detached from the aorta/vena cava. The loose kidney was removed, and the aortic and vena caval tears repaired with considerable difficulty. The vascular structures (as well as the intestines) were abnormally soft and friable – vessels were torn with minimal traction. Suturing the aortic wall gave the impression of “no hold”. Despite blood transfusion equivalent to 5–6 intravascular volumes, the postoperative course was uncomplicated. He was discharged uneventfully 21 days later and is currently healthy 3 years later.

Histological examination of the excised kidney showed remarkable defects of the arterial walls, even away from the rupture locus (Fig. 1). Here the intima and the adventitia were often directly apposed, without an intervening media. The renal vein showed similar changes (Fig. 2), with focal absence of the muscular wall. These distinct abnormalities were consistent in various sections of the renal vessels. Biochemical investigation of cultured fibroblasts from the patient showed virtual absence of collagen type III (Fig. 3). Bleeding and clotting parameters were normal.
The family history revealed no previous cases of acute vascular episodes or early death. Neither parent nor a younger sister expressed similar stigmata. The patient (Fig. 4) showed several unusual physical features. He had been born prematurely and had a lifetime history of easy bruising. Peculiar facial features included thin lips and nose, prominent eyes and a "high-arched" palate. The skin was thin and velvety with visible veins and "cigarette paper scars". Joint hypermobility was confined to the metacarpophalangeal finger joints. Ophthalmological investigation showed degeneration of Bruch’s membrane. Radiological examinations showed marked coxa valgus and thoracic scoliosis. As we considered invasive angiography to be contraindicated, a "vascular MRI" investigation was performed which showed no aneurysmal or other vascular malformations.

The family history revealed no previous cases of acute vascular episodes or early death. Neither parent nor a younger sister expressed similar stigmata. The patient (Fig. 4) showed several unusual physical features. He had been born prematurely and had a lifetime history of easy bruising. Peculiar facial features included thin lips and nose, prominent eyes and a "high-arched" palate. The skin was thin and velvety with visible veins and "cigarette paper scars". Joint hypermobility was confined to the metacarpophalangeal finger joints. Ophthalmological investigation showed degeneration of Bruch’s membrane. Radiological examinations showed marked coxa valgus and thoracic scoliosis. As we considered invasive angiography to be contraindicated, a "vascular MRI" investigation was performed which showed no aneurysmal or other vascular malformations.

The family history revealed no previous cases of acute vascular episodes or early death. Neither parent nor a younger sister expressed similar stigmata. The patient (Fig. 4) showed several unusual physical features. He had been born prematurely and had a lifetime history of easy bruising. Peculiar facial features included thin lips and nose, prominent eyes and a "high-arched" palate. The skin was thin and velvety with visible veins and "cigarette paper scars". Joint hypermobility was confined to the metacarpophalangeal finger joints. Ophthalmological investigation showed degeneration of Bruch’s membrane. Radiological examinations showed marked coxa valgus and thoracic scoliosis. As we considered invasive angiography to be contraindicated, a "vascular MRI" investigation was performed which showed no aneurysmal or other vascular malformations.

The family history revealed no previous cases of acute vascular episodes or early death. Neither parent nor a younger sister expressed similar stigmata. The patient (Fig. 4) showed several unusual physical features. He had been born prematurely and had a lifetime history of easy bruising. Peculiar facial features included thin lips and nose, prominent eyes and a "high-arched" palate. The skin was thin and velvety with visible veins and "cigarette paper scars". Joint hypermobility was confined to the metacarpophalangeal finger joints. Ophthalmological investigation showed degeneration of Bruch’s membrane. Radiological examinations showed marked coxa valgus and thoracic scoliosis. As we considered invasive angiography to be contraindicated, a "vascular MRI" investigation was performed which showed no aneurysmal or other vascular malformations.

Discussion

The phenotypical traits of this patient were entirely consistent with vascular EDS IV. Almost all of the reported stigmata were present. The clinical diagnosis was confirmed biochemically by the absence of collagen type III produced by cultured fibroblasts. The most remarkable feature of this patient is the general vessel wall defects that appeared in histopathological sections. These profound changes do not seem to have been described in previous reports.

The patient's clinical and biochemical features are consistent with a more severe form of EDS IV: the so-called acrogeric phenotype. The latter is commonly caused by glycine substitutions at the C-terminal end of the collagen III molecule. However, the patient has not suffered any further vascular episodes during the past 3 years and lives a near normal life, with minor physical restrictions. The negative family history suggests a new dominant mutation/deletion of the COL3A1 gene, arising in the germ cells of the mother or father. A single base mutation may produce a severe
vascular clamps frequently cut through the vessel wall. Minimizing vessel wall trauma is crucial.

In future, DNA analysis will help identify patients with predisposing vessel wall fragility. Investigation of the COL3A1 gene might not only detect the few classical EDS IV patients, but may point out "milder" mutations responsible for the development of abdominal aortic aneurysm or aortic dissection. However, there are other strong candidate genes for such abnormalities which include various other collagens, elastin, elastin associated proteins, fibrillins I/II and the modifying enzymes lysyl hydroxylase, lysyl oxidase and procollagen peptidase.

Acknowledgement
We are indebted to Mrs. Bjorg Badaro for excellent technical assistance.

References


Accepted 20 February 1996