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CASE REPORT

Vascular type of Ehlers-Danlos syndrome in a patient with a ruptured aneurysm of the splenic artery

P.W.B. Nanayakkara[1*], C.C. van Bunderen[1], S. Simsek[2], Y.M. Smulders[1], G. Pals[3]

Departments of [1]Internal Medicine, [2]Endocrinology and [3]Clinical Genetics, VU University Medical Centre, Amsterdam, the Netherlands, [*]corresponding author: tel.: +31 (0)20-444 44 44 (ext. 986791), fax: +31 (0)20-444 05 05, e-mail: p.nanayakkara@vumc.nl

ABSTRACT

A 39-year-old woman presented with a ruptured aneurysm of the splenic artery. The postoperative course was complicated by poor wound healing. This, in combination with a history of easy bruising and joint hypermobility, made us consider a connective tissue disease as underlying cause. The vascular type of Ehlers-Danlos syndrome was diagnosed by identifying collagen III deficiency and the corresponding gene mutation in cultured fibroblasts from a skin biopsy.

KEYWORDS

Aneurysm, Ehlers-Danlos syndrome, hypertension, splenic artery

INTRODUCTION

Ehlers-Danlos syndromes (EDS) are a group of heritable connective tissue disorders characterised by fragility of the skin and hypermobility of the joints. The Villefranche classification, introduced in 1997, differentiates six types of EDS.[1] The most severe form, the vascular type (type IV according to the old classification),[2] results from mutations in the gene for type III procollagen (*COL3A1*) and is life-threatening, often resulting in premature death because of arterial, bowel or uterine rupture.[3] We describe the case history of a young woman who presented with a ruptured aneurysm of the splenic artery that turned out to be the first complication of vascular type EDS.

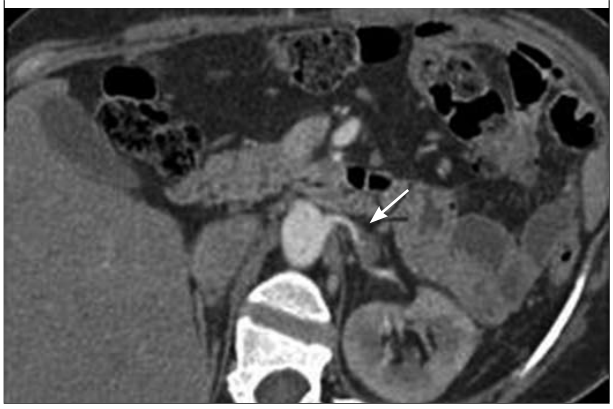
CASE REPORT

In July 2002, a 39-year-old woman presented to the emergency department of our hospital. She complained of mild upper abdominal discomfort during the previous 24 hours. One hour before presentation she had collapsed after sudden worsening of her abdominal pain. At presentation she was unconscious (Glasgow coma score: 5), blood pressure was 80/40 mmHg and the abdominal examination showed rigidity and guarding. Haemoglobin level was 3.1 mmol/l and ultrasound examination showed free fluid in the abdominal cavity. Immediate laparotomy revealed a ruptured aneurysm of the splenic artery. Splenectomy was performed and more than 2.5 litres of blood were drained from the abdominal cavity. The postoperative course was complicated by multiple pancreatic pseudocysts and intra-abdominal fluid collections. Abdominal wound recovery was slow. After four weeks, the patient was discharged. On discharge, the diagnosis of pregnancy-related aneurysm of the splenic artery was made.[4] Her medical history was uneventful, and included a normal pregnancy with vaginal delivery 18 months prior to the event.

An abdominal computed tomography angiography (CTA), performed in September 2002 to examine for aneurysms in other visceral arteries, was considered to show no abnormalities. A couple of days after the CTA, the patient developed progressive, severe headache and nausea. Physical examination showed a blood pressure of 180/120 mmHg with no neck stiffness, papilloedema or other neurological signs. Laboratory results and revision of the abdominal CTA made a couple of days before showed no abnormalities and CTA cerebrum revealed no cerebral aneurysms or signs of haemorrhage or reversible posterior leucoencephalopathy syndrome. Labetalol 200 mg three

times a day was administered and successfully lowered her blood pressure. Ten days later, she was admitted again with headache and a blood pressure of 210/130 mmHg. Long-acting nifedipine 60 mg/day was added to her medication with a good result. During the subsequent year her blood pressure medication was tapered and finally stopped altogether, and her blood pressure stabilised at 120/80 mmHg. Because we did not have a clear diagnosis, we decided to perform a full review of her medical history. In retrospect, her medical history also included repeated luxation of her patellae and easy bruising. In addition, re-examination of the abdominal CTA carried out in September 2002 showed two left renal arteries, one of which had a dissecting aneurysm with complete occlusion (*figure 1*), which was overlooked at first. This combined with her prolonged wound healing after surgery and aneurysm of the splenic artery made us consider a connective tissue disease as underlying cause. She had no dysmorphic features consistent with Marfan syndrome.[5] However, there were clear signs of joint hypermobility (according to Beighton's scoring system).[1] By means of skin biopsy and fibroblast culture, a collagen type III deficiency was found as a result of a mutation in the corresponding gene *COL3A1* (*figure 2*).[3] The vascular type of Ehlers-Danlos syndrome was diagnosed.

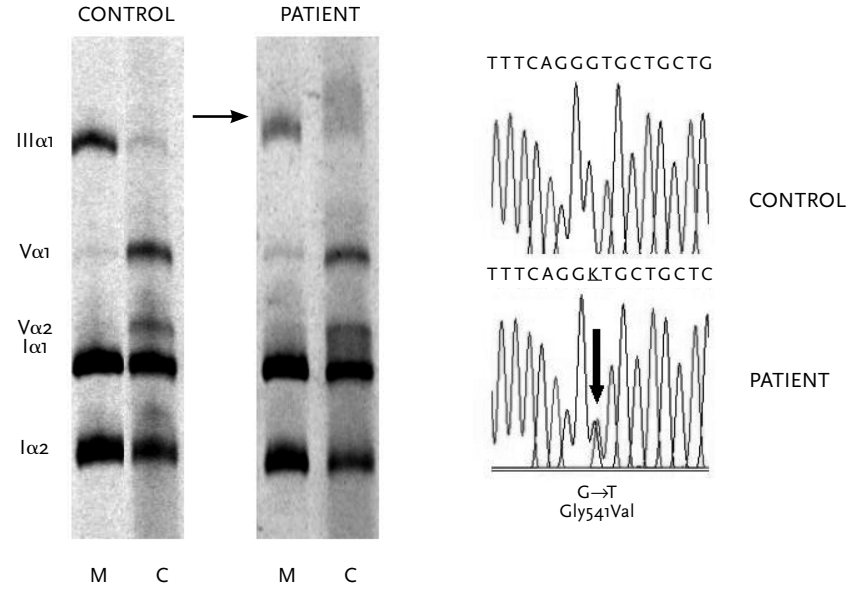
Figure 1. *CT scan showing a dissecting aneurysm of one of the left renal arteries*



DISCUSSION

The vascular type of Ehlers-Danlos syndrome is a rare connective tissue disorder caused by type III procollagen deficiency due to *COL3A1* gene mutation. The inheritance is autosomally dominant and in about half of the patients a *de-novo* mutation is found. The clinical diagnosis is established from two of four major clinical criteria: thin, translucent skin; extensive bruising; characteristic facial appearance

Figure 2. *Autoradiograph of SDS-PAGE electrophoresis of collagen from cultured fibroblasts (left), after metabolic labelling with ^{14}C-proline*



The types of collagen chains are indicated. M = media from tissue culture; C = cell contents. The excreted amount of collagen type III is reduced in the patient's fibroblasts and there is accumulation of overmodified material in the cells. This is caused by a glycine to valine substitution in the triple helix of collagen III due to a G to T base substitution at position 541 (right).

(large eyes, thin nose, lobeless ears, thin scalp hair and decrease in the subcutaneous adipose tissue) and arterial, bowel or uterine fragility or rupture. Hypermobility of large joints and hyperextensibility of the skin are unusual in the vascular type. However, our patient had clear features of hyperlaxity of the joints. The diagnosis can be confirmed by identification of the previously mentioned gene mutation. Vascular type EDS can be life-threatening due to weak arteries, bowel or uterus, which can lead to spontaneous ruptures. Most patients have the first complication by the age of 20 years. The mean life expectancy is 48 years.[3] The cause of death is usually due to vascular complications.[6] In our patient, a ruptured aneurysm of the splenic artery was the first complication. Dissection of one of the left renal arteries with total occlusion, which probably occurred after injection of contrast for CTA, could explain the hypertensive period. A CTA performed after normalisation of blood pressure showed a patent lumen in the previously occluded renal artery. Temporary renal hypoperfusion due to the dissecting aneurysm with transient occlusion of the left renal artery probably activated the renin-angiotensin-aldosterone system, resulting in the hypertensive period.[7] Despite of luxation of her patella, which was treated conservatively, no other complications had occurred following these events. The patient was advised to avoid pregnancy, avoid activities that put pressure on locked joints, minimise skin trauma risks and avoid forms of invasive diagnostic tests where possible. Genetic counselling was provided and the patient's mother and brother were tested, the results of which were negative. As for our patient's four-year-old daughter, the parents have postponed testing because of the minimal risk of complications at such a young age.

CONCLUSION

In young patients with unexplained ruptures of arteries, bowel or uterus, with or without a positive family history, the diagnosis of vascular type Ehlers-Danlos syndrome should be considered. Although no specific treatment is available, knowledge of the diagnosis may influence the management of surgery, pregnancy and major complications, and may have implications for genetic counselling.

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ERRATUM

In the photo quiz entitled 'The ECG in hypothermia: Osborn waves' by T.J. Olgers and F.L. Ubels (Neth J Med 2006;64(9):350,353) the top ECG (p. 350) should have been shown only. Furthermore on the page were the answer to this photo quiz is given (p. 353), only the top ECG of figure 1 and the bottom ECG of figure 2 should have been shown. We apologize for any inconvenience caused.