The patient was weaned off the ventilator, but died nine days after his second laparotomy of an extensive myocardial infarction.

Histology of the excised colon showed attenuation of the muscularis propria with no evidence of active colitis, confirming that the spontaneous perforation was due to Ehlers-Danlos syndrome and not the result of ulcerative colitis.

**Questions**

1. What is seen on the chest radiograph?
2. Comment on the history and computed tomogram.

Postgrad Med J 2002;78:501

**Authors’ affiliations**

Z Soonawalla, M Puntis, Department of Surgery, University Hospital of Wales, Cardiff, UK

F M Pope, Department of Dermatology, West Middlesex University Hospital, Isleworth and Institute of Medical Genetics, University Hospital of Wales, Cardiff, UK

Correspondence to: Mr Zahir Soonawalla, Hepatobiliary and Liver Transplant Unit, Queen Elizabeth Hospital, Edgbaston, Birmingham B15 2TH, UK; soonawalla@aol.com

Submitted 13 August 2001

Accepted 7 January 2002

16 year old girl was admitted because of low grade fever, headache, and nuchal rigidity. She complained of galactorrhoea during the preceding year and irregular menstruation since menarche at 13 years old.

Physical examination was unremarkable except for the galactorrhoea.

The diagnostic work-up for meningitis was negative. Cranial computed tomography and subsequent magnetic resonance imaging showed a large, possibly cystic, pituitary lesion (fig 1). The laboratory work-up showed a mild elevation of basal prolactin levels, 1.05 IU/l; evaluation of pituitary reserve showed normal thyrotrophin, luteinising hormone, and follicle stimulating hormone responses after stimulation. The α-subunit levels were 0.1 mIU/ml. Mild bilateral superior constriction was found on Goldman visual field examination. There were no findings suggestive of sarcoidosis (normal chest radiography, normal serum angiotensin converting enzyme levels).

**Questions**

1. What is the differential diagnosis for this patient?
2. Which specific work-up should the follow up include?

Postgrad Med J 2002;78:502

**Authors’ affiliations**

I Ilias, E Zapanti, G Philippou, M Alevizaki

1st Department of Endocrinology, “Alexandra” University Hospital, Athens, Greece

M Alevizaki, Endocrine Unit, Department of Clinical Therapeutics, University of Athens Medical School, “Alexandra” University Hospital, Athens, Greece

Correspondence to: Dr Maria Alevizaki, Department of Clinical Therapeutics, University of Athens Medical School, “Alexandra” University Hospital, 80 Vassilissis Sofias Avenue, Athens GR-11528, Greece; mani@otenet.gr

Submitted 17 September 2001

Accepted 21 May 2002
Type IV Ehlers-Danlos syndrome: a surgical emergency

Q1: What is seen on the chest radiograph?

The chest radiograph (see p 502) shows gas under the right hemidiaphragm. This is not free intraperitoneal gas, but is a loop of bowel interposed between the liver and the right hemidiaphragm, the Chilaiditi sign.¹

Q2: Comment on the history and computed tomogram

There was no evidence of perforative peritonitis. The computed tomogram (see p 502) shows a large retroperitoneal haematoma around the aorta, but no aortic aneurysm. Spontaneous retroperitoneal bleeding is often associated with type IV Ehlers-Danlos syndrome and is the commonest cause of death in this population.

Discussion

Ehlers-Danlos syndrome is an inherited disorder of collagen synthesis. Type IV, far less common than types I, II and III, is caused by a deficiency of type III collagen.² The causative mutations in the COL3A1 gene are very variable, and are usually inherited in an autosomal dominant pattern. Biochemical examination in the present case showed the secretion of an abnormal type III collagen protein.³ DNA sequencing of cDNA produced from cultured skin fibroblasts showed a glycine (GGA) to glutamic acid (GAA) substitution at position 847 of the COL3A1 gene (fig 1). In keeping with other helical glycine substitutions, this causes severe reduction of tissue type III collagen, resulting in severely weakened arteries, intestines, ligaments, and other organs. We also detected similar changes in his mother and brother, while his maternal grandmother was a clinically silent somatic/gonadal mosaic for the error.⁴

Type III collagen forms only 15% of normal skin and ligaments, and is absent in bones and joints. In contrast to the other Ehlers-Danlos syndrome subtypes, skin laxity and joint hypermobility are not prominent features of type IV Ehlers-Danlos syndrome. The walls of blood vessels, the gastrointestinal tract and uterus are the main depositories of type III collagen. These patients often suffer spontaneous rupture of arteries, commonly affecting main branches of the aorta, but not uncommonly involving intrathoracic and intracerebral vessels.⁵ Haemorrhage may even occur in the absence of aneurysmal dilatation of the vessel. Spontaneous retroperitoneal bleeds are the commonest cause of death in this population. They are also at risk of spontaneous perforations of the gastrointestinal tract, commonly the colon.⁶ During the third trimester of pregnancy, there is a 5%–15% risk of uterine rupture.⁷

The present case demonstrates most of the complications that are associated with this unfortunate condition. It is due to a high incidence of these catastrophic complications that the life expectancy of patients with type IV Ehlers-Danlos syndrome is markedly shortened. They usually die in the fourth decade of life and survival beyond the age of 50 is rare. This contrasts with other Ehlers-Danlos syndrome variants who have normal life expectancy.

Awareness and early recognition of these life-threatening complications are essential to the management of this unfortunate group of patients. Elective surgery should be undertaken with great caution, and only if absolutely necessary, as they tend to bleed uncontrollably and heal poorly after operations.

Final diagnosis

Spontaneous retroperitoneal bleeding associated with type IV Ehlers-Danlos syndrome.

References


Galactorrhoea in a 16 year old girl with a large sellar mass

Q1: What is the differential diagnosis for this patient?

Craniohypophysectomy: this is the most common tumour in the region of the hypothalamus and the pituitary in this age, presenting with headache, vision impairment, various degrees of hyperprolactinaemia, and pituitary insufficiency. Two thirds of craniohypophysecomas are suprasellar and one third extend into or are within the sella. The majority of craniohypophysecomas are cystic or mixed cystic/solid lesions. Califications of the rim of the tumour mass are a common feature.

Pituitar adenoma: this was probably non-functioning (NFPa) as no signs of growth hormone excess were present and there was only a mild increase in prolactin levels. These usually present as space occupying lesions. The clinical manifestations of NFPa include headaches, visual field defects, and extracocular nerve palsies. Pituitary insufficiency commonly results from destruction of the remaining normal pituitary tissue.

Primary hypophysitis: this is a rare disorder with about 140 cases reported...
Although the aetiology of lymphocytic hypophysitis includes suprasellar extension. Further radiological homogeneous pituitary mass and occasionally cases. In 95% of cases MRI shows a solid pituitarism is present in 60% to 70% of head. In 95% of cases MRI shows a solid pituitarism is present in 60% to 70% of head. In 95% of cases MRI shows a solid pituitarism is present in 60% to 70% of head. In 95% of cases MRI shows a solid pituitarism is present in 60% to 70% of head. In 95% of cases MRI shows a solid pituitarism is present in 60% to 70% of head. In 95% of cases MRI shows a solid pituitarism is present in 60% to 70% of head. In 95% of cases MRI shows a solid pituitarism is present in 60% to 70% of head. In 95% of cases MRI shows a solid pituitarism is present in 60% to 70% of head. In 95% of cases MRI shows a solid pituitarism is present in 60% to 70% of head. In 95% of cases MRI shows a solid pituitarism is present in 60% to 70% of head. 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