Case Report

Hereditary Hemorrhagic Telangiectasia in association with Generalised Juvenile Polyposis

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CASE REPORT

A 22-year-old lady was referred to the respirology department of a tertiary referral hospital for further assessment of newly diagnosed pulmonary arteriovenous; malformations (AVMs) She had initially presented to a paediatric department at the age of 8 years for investigation of recurrent epistaxis and iron deficiency anaemia. Her stool was identified as being positive for faecal occult blood and following further gastrointestinal investigation, multiple polyps were discovered throughout her gastrointestinal tract (Fig. 1). Histological examination determined the polyps to be hamartomas and she was diagnosed as having generalised juvenile polyposis. She had a subtotal colectomy aged 9 years and a panproctocolectomy with subsequent fashioning of an ileal pouch anastomosis aged 19 years. During this period of time she continued to suffer from recurrent epistaxis and had numerous embolisation and surgical procedures carried out in an attempt to alleviate this problem. Within the last 2 years, multiple telangiectasias were identified on the vermillion border of her lips and underlying Hereditary Haemorrhagic Telangiectasia (HHT) or Osler-Weber-Rendu Syndrome was suspected. She had no documented family history of this or juvenile polyposis, however her father had been rejected several times from being a blood donor because of anaernia. A magnetic resonance imaging (MRI) scan of the brain did not show any evidence of an intracranial AVM. Computed tomography (CT) scan of her chest did however identify multiple pulmonary AVMs, thus prompting her referral to respirology.

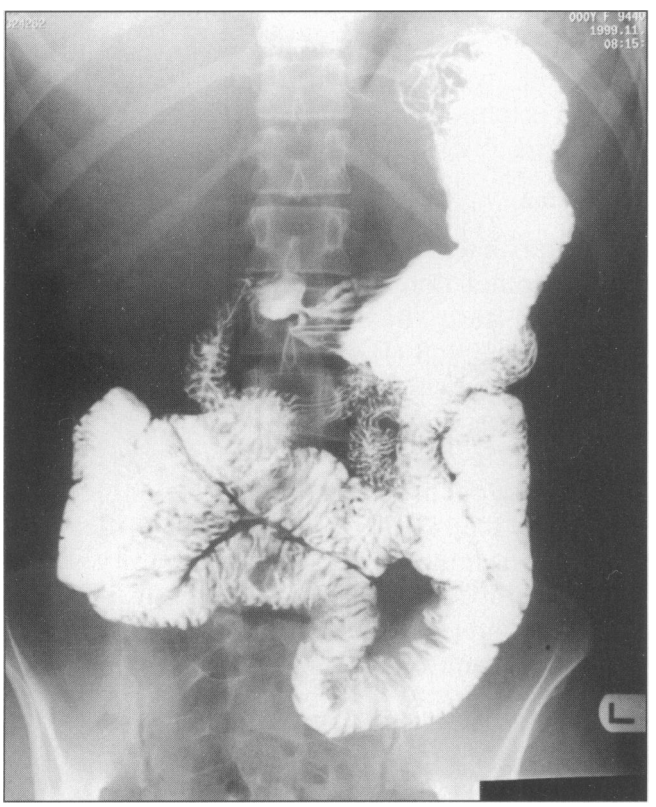

Fig 1. Small bowel series demonstrating several filling defects consistent with polyps in the jejunum. The patient was post colectomy at this stage.

At this presentation there was no history of dyspnoea, cough, haemoptysis or blackouts. On physical examination she had facial telangiectasia, which was most marked adjacent to her bottom lip. There was no evidence of anaernia or central cyanosis. Respiratory rate was normal and there was no finger clubbing. Apart from scars from her previous abdominal surgery, physical examination was otherwise unremarkable.

Haematological investigations revealed a haemoglobin of 122 g/L and normal electrolytes. Oxygen saturation was 86% on room air. An arterial blood gas revealed pH 7.40, pCO_2 40

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mmHg, pO2 52 mmHg, HC03 25 mmol/L and BE 0. Pulmonary function tests showed mildly impaired diffusion capacity at 71% predicted, but was otherwise within normal limits. A repeat spiral CT scan of chest (Fig.2) using a high resolution protocol was performed to accurately

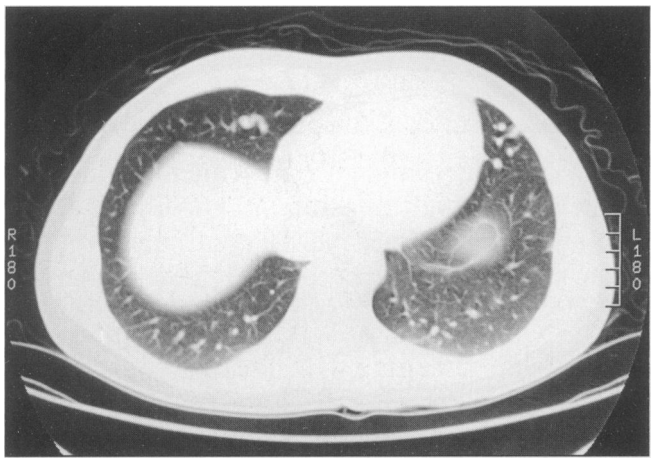

Fig 2. CT scan of chest showing the typical serpiginous characteristic of AVMs within the lingula and right middle lobe.

determine the size and distribution of the pulmonary AVMs. This identified multiple pulmonary AVMs in the right middle lobe, lingula and left lower lobe. These were later confirmed by a pulmonary angiogram (Fig.3). Coil

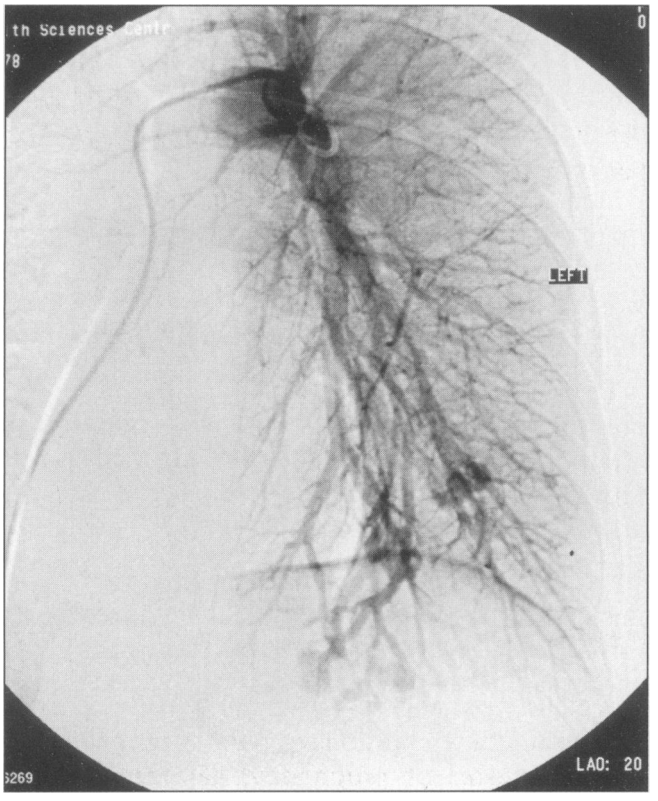

Fig 3. Pulmonary arteriogram confirming the nature of the AVM in the lingula prior to embolisation.

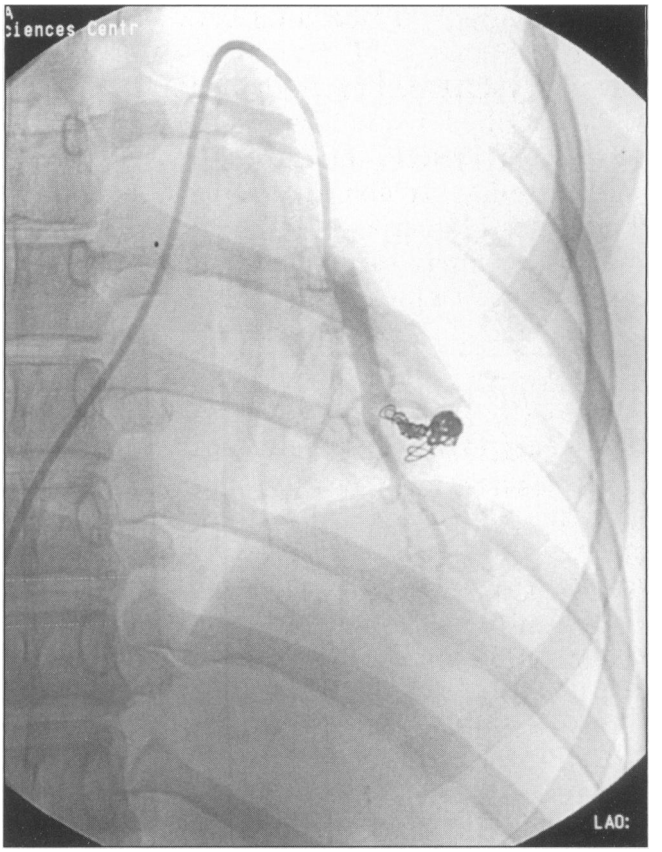

Fig 4. Post successful coil embolisation of the lingular AVM.

embolisation of the AVMs was attempted and the largest AVM in the lingula was successfully occluded, without complication (Fig.4). The patient is to return for further embolisation of her remaining AVMs.

Discussion

Hereditary haemorrhagic telangiectasia is a group of autosomal dominant disorders with genetic linkages that have been established to chromosome 9q3 (HHT 1) and 12q 13 (HHT2), although it is possible that genes on other chromosomes may also be involved[1]. The clinical diagnosis is made with two or moreof the following: recurrent epistaxis, telangiectasis elsewhere than in the nasal mucosa, evidence of autosomal dominant inheritance or visceral involvement. Visceral involvement includes AVMs found in the pulmonary, gastrointestinal, hepatic or central nervous system circulations.

Juvenile polyposis is also an autosomal dominant condition featuring the development of multiple hamartomatous polyps, most commonly in the colon, but which can also occur in the stomach or small intestine[2]. It usually presents in the first or second decade with the onset of rectal bleeding

and anaemia. An association between juvenile polyposis and HHT has only rarely been previously documented. Initially in 1982, Cox et al[3] described a mother and daughter with generalised juvenile polyposis, pulmonary AVMs and severe digital clubbing. Both patients fulfilled the diagnostic criteria for HHT. Since then further cases have intermittently been identified[2],[4-8], culminating in a short series of cases by Ballauff and Koletzko in 1999[9].

In HHTI, the genetic mutation at chromosome 9q3 has been identified as involving endoglin. This encodes an integral membrane glycoprotein that binds transforming growth factor ß (TGFß). In HHT2, the abnormal gene on chromosome 12q13 encodes activin receptor-like kinase 1 (ALK-1), a cell surface receptor for the TGFß superfamily of ligands[8]. When undergoing investigation for HHT, our patient had normal endoglin levels, making it likely she had either HHT2 or a mutation in a previously unidentified gene.

In juvenile polyposis, although the exact genetic abnormality is not known, it ha been proposed that mutations in the tumour suppressor gene PTEN on chromosome 10q may be responsible in certain cases[2]. Juvenile polyposis has also been described in association with other genetic syndromes including Gorlin Syndrome and Bannayan-Riley-Ruvalcaba Syndrome, as well as HHT, suggesting a certain genetic heterogeneity in its aetiology[2]. It is likely that the genetic abnormality associating HHT and juvenil polyposis is linked, and although this link has not yet been identified, it is statistically more likely than both these rare diseases existing as a coincidence[3].

The importance of diagnosing juvenile polyposis is that although the polyps are hamartomas, there is an overall increased risk of gastrointestinal malignancy in these patients when compared to the general population[10]. Colectomy is often required with continued surveillance of the upper gastrointestinal tract.

It is important to highlight that an association can occur between these two conditions. Early recognition of this association allows the pertinent management problems of each syndrome to be addressed. With regard to HHT, pulmonary and intracranial AVMs are of particular concern, as they may be clinically silent lesions, which can result in sudden morbidity or death[1]. Patients with pulmonary AVMs are much more common and at risk of stroke or cerebral abscess secondary to the pulmonary systemic shunt, Antibiotic prophylaxis is thus mandatory in these patients undergoing dental procedures and during endoscopy. Endoscopy may be performed for the investigation of gastrointestinal haemorrhage, either secondary to mucosal telangiectasia or hamartomatous polyps.

Screening protocols for pulmonary AVMs have been suggested to identify persons whose risk of pulmonary AVMs is sufficient for diagnostic imaging to be warranted. It is most indicated in patients with a low $P0_2$ or family history of AVM, but should be considered in all patients with HHT. A recent report from a Canadian group showed that screening with chest radiograph and pulse oximetry was insufficient[11]. They reported that initial screening by clinical examination followed by measurement of PaO_2 while breathing 100% oxygen is warranted[11]. This same group recently showed the added advantage of agitated saline contrast echocardiography as a useful adjunctive test. In their prospective study it was the only positive screening test in 31 % of patients[12]. This group have also reported their experience with diffuse pulmonary AVMs and reported that transcatheter embolectomy reduced the risk of neurologic complications[13]. They reported that the patients can live for many years and lead productive lives but they do not recommend lung transplantation as survival with the disease is difficult to predict and they had a perioperative transplant death[13].

In our hands screening for pulmonary AVMs is easily performed with spiral computed tomography. Screening for intracranial AVM is achieved with magnetic resonance imaging, although the indication for this is less well defined in the absence of headache or a family history of intracranial AVM[1]. It is advised that persons affected by, or at risk for, HHT who have a family history of pulmonary or cerebral AVMs should undergo pulmonary screening at puberty, or sooner if the family history includes prepubertal AVMs, and again at the end of adolescence. For persons from families without such a history, pulmonary screening should be considered but is less clearly indicated. As there have been cases of life threatening pulmonary haemorrhage in the third trimester of pregnancy, affected women should have pulmonary screening before conception. Anyone in whom a pulmonary AVM

is found should undergo helical computer tomography every five years to rule out the possible growth of residual malformations in the intervening period.

Particular care maybe needed to ensure appropriate screening investigations are preformed as the need for these particularly arises at a time when transition is being made from paediatric to adult clinics.

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