Uncommon presentation of a patient with hereditary haemorrhagic telangiectasia

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Abstract

Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant disorder. It is clinically characterised by telangiectasia, recurrent epistaxis, and visceral vascular lesions. We report a case of HHT without a significant family history. A 16-year-old girl presented with multiple episodes of bleeding, including uncommon sites, over a period of ten months. She denied a family history of bleeding. Her clinical examination was unremarkable. Investigations including basic and second-line coagulation tests were normal. Subsequently multiple telangiectasias in the right nasal septum and capillary dilatation in the bladder wall were detected. According to Curacao diagnostic criteria, a diagnosis of HHT was made. As her bleeding was self-limiting, follow up was arranged to monitor complications.

Keywords: hereditary hemorrhagic telangiectasia, haematuria, nipple bleeding

Introduction

Hereditary hemorrhagic telangiectasia (HHT) is a vascular disorder inherited as an autosomal dominant trait. Most patients with HHT have only epistaxis, mucocutaneous telangiectasia and iron deficiency anaemia secondary to blood loss. Urinary tract involvement occurs only in 3% of these cases. We report a case of HHT with uncommon bleeding manifestations without a significant family history.

Case presentation

A previously healthy 16-year-old girl presented with recurrent episodes of bleeding from multiple sites of the body over a period of 10 months. She had several episodes of epistaxis, bleeding from nipples and haematuria 4 months ago. She also had two episodes of bleeding manifestations from the right eye three months apart. Episodes were mild and self-limiting. There was no history of bleeding into muscles or joints, haemoptysis or bleeding from gastrointestinal tract. She denied excessive bleeding from cut injuries or menorrhagia. She denied recurrent infections or symptoms to suggest anaemia. She was a product of a non-consanguineous marriage and had no family history of bleeding disorders. She was not on any routine medications.

Her body mass index was 23.4 kg/m². She was not icteric or pale. Her clinical examination was unremarkable. Investigations showed a normal white cell count of 10.8 x 10⁹/L, Hb of 13.6 g/dL, platelet count of 274 x 10⁹/L, and normal liver and renal functions. Initial coagulation screening showed a bleeding time of 3 minutes, prothrombin time (PT) of 12.2 s, activated partial thromboplastin time (APTT) of 29 s, thrombin time (TT) of 16 s, fibrinogen of 358 mg/dL and negative D-dimers. Further coagulation studies revealed a factor XIII level of 97%, VWF antigen of 94% and normal VWF function of 96%. The peripheral blood smear showed normal neutrophil and platelet morphology, and early iron deficiency. A clot solubility study revealed a stable clot after 24
hours. Factor VIII assay excluded minor factor VIII deficiency with a factor VIII level of 98%. Platelet aggregation studies showed normal aggregation with ADP, collagen, arachidonic acid and ristocetin.

Nasal examination revealed a deviated nasal septum and multiple telangiectasias in the right septum. Ultrasound examination of breasts was normal. Serum ferritin, rheumatoid factor, P-ANCA, C-ANCA, C3, and C4 levels were normal. MRI brain was unremarkable.

Urine full report confirmed haematuria and ultrasound scan of the abdomen followed by CT urogram revealed no structural abnormality. Subsequent cystoscopy revealed capillary dilatation in the bladder wall. Upper gastrointestinal endoscopy, and fibre optic laryngoscopy were normal and ocular examination failed to show abnormal blood vessels.

With the given clinical history, normal coagulation tests, nasal telangiectasia, and capillary dilation of the bladder wall, a clinical diagnosis of hereditary hemorrhagic telangiectasia was made. As her bleeding episodes were recurrent and self-limiting, we prescribed oral tranexamic acid during episodes of bleeding. Iron deficiency anaemia was managed with hematinics.

**Discussion**

Majority of patients with HHT are unaware of their diagnosis and have not been diagnosed at the time of hospital admission.(4) Recurrent epistaxis is the most common and earliest clinical feature of HHT. Telangiectasias of the skin and buccal mucosa are typically present from about the third decade of life. HHT shows varying penetrance and expression. Pathogenic variants in multiple genes can cause HHT. Three major disease-associated genes that account for more than 80% of cases have been recognised. Absence of family history in the index case, can be due to the variable penetrance and expression of the disease. HHT presentation patterns are highly variable, even within the same family. Individuals with the same HHT pathogenic gene variant can have different clinical manifestations.

Our patient’s disease onset was around 15 years of age, and she had bleeding manifestations from unusual sites, including haematuria, bleeding from nipples and from the right eye. In HHT, coagulation tests are normal. Laboratory investigations usually demonstrate only iron deficiency. Diagnosis is based on the international consensus of the Curaçao diagnostic criteria.(3,5)

As our patient had normal PT, APTT, TT and fibrinogen assay, von Willebrand disease, factor XIII deficiency, platelet function defect, minor factor deficiency or vessel wall abnormalities were considered as differential diagnoses. Subsequent tests revealed normal factor VIII, XIII, VWF and normal platelet aggregation studies. Her nasal examination demonstrated deviated nasal septum and multiple telangiectasia in the right septum. Cystoscopy demonstrated dilated blood vessels in the bladder wall.

Our patient had three out of four Curaçao criteria and accordingly the diagnosis of HHT was made. Genetic testing was not available.

Ocular involvement can be seen in about 50% of cases of HHT.(6) But nipple bleeding has not been described in the literature. Breast pathologies were excluded with ultrasound examination. Patients diagnosed with HHT should be screened for asymptomatic arteriovenous malformations (AVM). Her Gastroscopy was normal and the MRI brain failed to show cerebral AVMs. Screening for pulmonary AVMs was planned with a CT Chest.

Iron deficiency anaemia in HHT is treated with iron replacement.(7) In our patient oral tranexamic acid was prescribed during her episodes of bleeding and iron deficiency was managed with hematinics. Annual follow-up was arranged.

**Conclusion**

Although rare, HHT should be kept in mind when patients presenting with spontaneous recurrent epistaxis and bleeding from uncommon sites when the coagulation studies are normal. Absence of family history does not exclude HHT.

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**References**

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