

Cerebral and spinal vascular involvement in Hereditary Hemorrhagic Telangiectasia: Report of two cases

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Abstract

Introduction—We present two cases of Hereditary Hemorrhagic Telangiectasia (HHT), one pediatric and the other adult, with a view to highlight the myriad cerebral and spinal vascular manifestations of this disease. The syndrome and its various findings will be reviewed including the utility of angiography in assessing the various vascular abnormalities of the cerebral and spinal vasculature.

Methods—A review of literature regarding various developmental abnormalities including brain and spinal cord arterio-venous malformations (AVMs), arterio-venous fistulae (AVFs), micro AVMs, micro-fistulae, aneurysms and cavernomas that occur in pediatric and adult population subsets of HHT. Both patients underwent thorough clinical and laboratory evaluation. The pediatric patient underwent a contrast enhanced computed tomography (CECT) of the chest; cerebral, Pulmonary & celiac angiography. The adult patient underwent cerebral and spinal angiography.

Conclusion—The spectrum of vascular malformations in Hereditary Hemorrhagic Telangiectasia (HHT) is varied. The incidence and manifestations of brain and spinal cord AVMs, AVFs, micro AVMs, micro-fistulae, aneurysms and cavernomas are different in the pediatric and adults affected by the disease. Cerebral and spinal angiography are necessary in characterising the various developmental vascular abnormalities in order to guide further management.

Keywords

Hereditary Hemorrhagic Telangiectasia; arterio-venous malformations; arterio-venous fistulae; micro-fistulae

Introduction

Hereditary Hemorrhagic Telangiectasia (HHT) is a rare, autosomal dominant disease with an estimated prevalence of 1 in 5000-8000 [1]. The disease is characterized by mucosal and visceral telangiectasias and manifests differently in the affected pediatric and adult population. We wish to highlight the various cerebrovascular abnormalities associated with this syndrome which include arteriovenous malformations (AVMs), micro AVMs, arteriovenous fistulae (AVFs), telangiectasias, cavernous malformations, and aneurysms.

Case Reports

Case 1

A 7 yr old girl, first of two siblings, presented with history of severe breathlessness on exertion and cyanotic spells which she had from infancy. The child had two episodes of generalized tonic clonic convulsions in the

past. There was no limb or facial weakness, hemoptysis, nasal, genital or GI bleeds. Family history for similar complaints was negative. Examination revealed: Ht=102 cms, Wt=17 Kgs, grade IV clubbing, cyanosis of lips, oral mucosa and nails. Neurological examination was normal. Chest auscultation revealed a harsh, continuous murmur in the right infra-mammary, left mammary & right axillary regions. Contrast enhanced computed tomography (CECT) of the chest showed multiple pulmonary arterio-venous fistulae (PAVF) in both upper & lower lobes [fig. 1a]. Pulmonary angiography confirmed the presence of bilateral high flow PAVFs [fig.1b,c]. Celiac angiogram revealed two slow flow hepato-portal shunts in the anterior segments of the right and left lobes [fig. 2].

CECT of the brain showed dilated and tortuous superficial veins in the right parietal region and a small AVM in

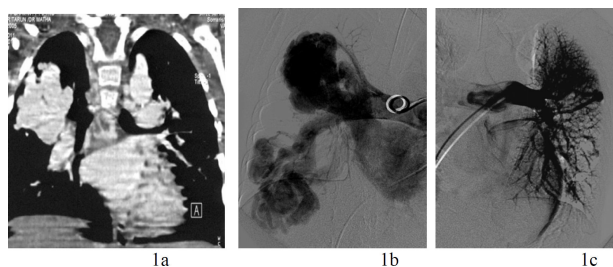


Fig. 1. (a). Coronal reformatted image of Ct pulmonary angiography shows a large pulmonary Avf in the right upper lobe (b,c) Right & left pulmonary angiograms show multiple high flow pulmonary Avfs bilaterally

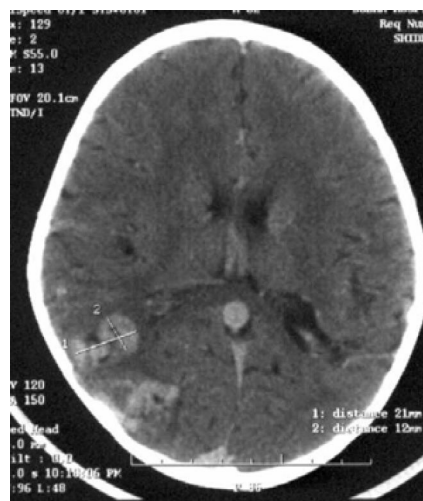


Fig. 2:Celiac angiogram shows slow flow hepato-portal fistulae in segments V & Ii of the liver (white arrows)

the right parasagittal frontal region [fig.3a,b]. Cerebral angiography showed multiple high flow micro-AVMs in right cerebral & cerebellar hemispheres; a pial AVF in the right parietal region [fig.4a, b, c] & multiple telangiectasias in the right frontal region and right cerebellar hemisphere [fig.5a, b].

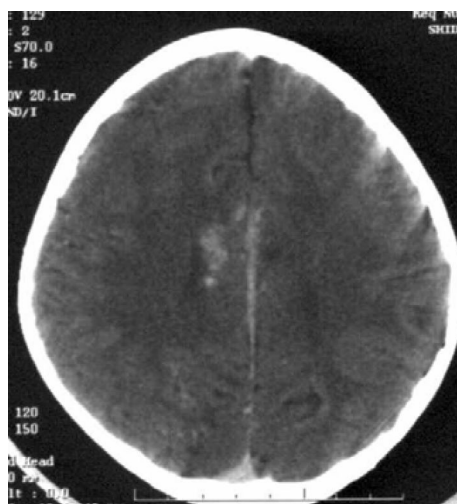
Case 2

A 52 yr old man presented with history of recurrent nasal bleeds since twenty five years. The bleeds were slight (10-15 mL/ episode), self limiting and had a frequency of 2-3 episodes/ week. He complained of severe pain at the nape of the neck radiating along the left arm since 2 yrs. There was no episode of GI bleed, seizures, hemoptysis or genital bleeds. There was history of similar episodes of nasal bleeds in his mother & first degree female relatives on the maternal side. Examination revealed a pale, thinly built and averagely nourished patient. Multiple muco-cutaneous telangiectasias were



3a

Fig. 3a:CECT brain shows multiple dilated pial veins in the right parietal region secondary to Pial AVF.



3b

Fig. 3b:A small AVM is seen in the para-sagittal aspect of the right frontal region.

present on the lower lip and finger tips. No icterus or cyanosis was present. CNS examination revealed 10% sensory loss to crude touch, pain & temperature involving the left D2-D4 dermatomes. Power was 5/5 in all four limbs. Rest of the systemic examination was normal. Blood investigations revealed microcytic hypochromic anemia with Hb= 6.4 gm%. MRI Cervical spine showed atrophy of the cord from the C1-C7 levels with anterior perimedullary and intramedullary flow voids.

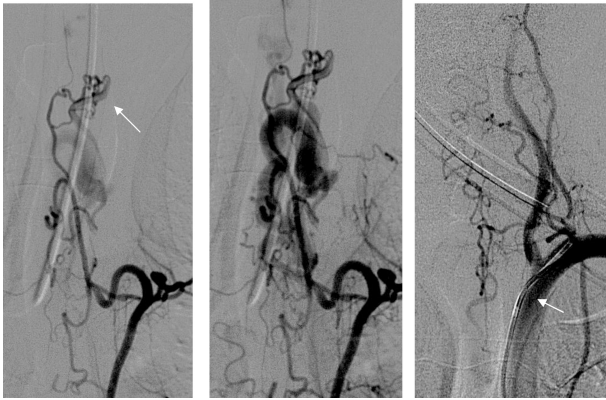


Fig. 6a,b,c:Left D6 & subclavian angiograms showing a moderate flow, complex peri-medullary Avf at the D2-D4 vertebral level supplied by radiculo-pial branches & left costocervical trunk. Note the common fistulous segment (white arrows) in both angiograms

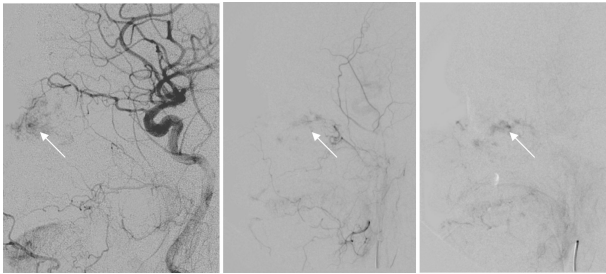


Fig.7a,b,c:Telangiectasias involving the septum & lateral nasal walls supplied by hypertrophied turbinate & septal branches of sphenopalatine branch of distal internal maxillary arteries, nasal branches of infraorbital arteries & anterior & posterior ethmoidal branches of both ophthalmic arteries

Spinal angiography revealed a moderate flow, complex, peri-medullary AVF at the D2-D4 vertebral level supplied by radiculo-pial branches of the D6, D7 intercostal arteries bilaterally and left costocervical trunk. The fistulous segment of the vein was between the D2-D4 vertebral levels & drained into a large ectatic anterior spinal vein which thereafter exited via the anterior ponto-mesencephalic and lateral mesencephalic systems [fig. 6a,b]. Bilateral ECA & ICA angiograms revealed telangiectasias involving the septum & lateral nasal walls supplied by hypertrophied turbinate & septal branches of sphenopalatine branch of distal internal maxillary arteries, nasal branches of infraorbital arteries & anterior & posterior ethmoidal branches of both ophthalmic arteries [fig.7a,b].

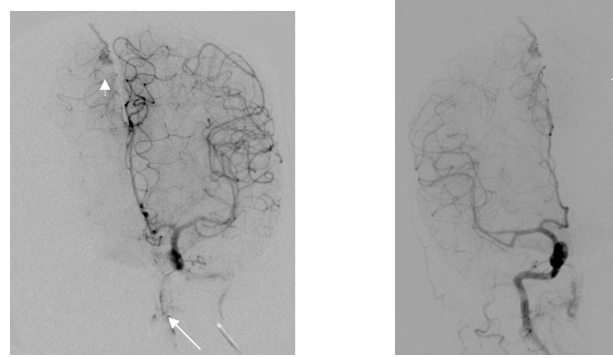


Fig. 8a,b:Bilateral Ica angiograms in Townes projection show a slow flow, micro-Avm (white arrowhead) in the para-sagittal aspect of the right parietal region supplied by internal parietal branches of the pericallosal artery & draining via a frontal cortical vein into the Sss. Long white arrow shows the lateral nasal and septal telangiectasias

Cerebral angiography showed a small, slow flow, micro-AVM in the para-sagittal aspect of the right parietal region supplied by internal parietal branches of the pericallosal artery. Venous drainage was via a cortical vein into the SSS [fig.8a,b].

Discussion

The term, hereditary hemorrhagic telangiectasia (HHT) was coined by the pathologist Hanes in 1909. Also known as Rendu-Osler-Weber syndrome, the disease is autosomal dominant (chromosome 9q33-q34) and requires inactivation of the normal allele as the initiating event in the formation of a vascular lesion. The mutations in the affected genes alter Endoglin synthesis (Endoglin is expressed on human endothelial cells) which leads the endothelial cells to respond poorly to Transforming growth factor- B1. TGF- B1 is a potent mediator of vascular remodeling and lack of its binding leads to dilatation of the post capillary venules, eventually leading to formation of tortuous veins and arteriovenous fistulae [2].

Clinical manifestations of the disease are different in pediatric and adult population. The commonest presentation in the affected adult population subset is recurrent epistaxis. Other manifestations in this group include hemoptysis, melena and genital bleeds. On the other hand, children with HHT usually present with cyanosis and breathlessness due to PAVF, seizures or bleed due to cerebral AVM [3].

Cerebrovascular abnormalities occur in 10-15 % of patients with HHT. These include brain AVMs

(BAVMs), AVFs, cavernous malformations, telangiectasias and aneurysms, of which BAVMs are the commonest [4]. Intracranial AVMs in HHT usually have a low Spetzler-Martin grade and have the same or even lower incidence of bleeding compared to non-HHT population [5]. In light of the significantly higher incidence of BAVMs in patients with Pulmonary AVMs many investigators have recommended screening patients for the same [6]. Pial AVFs were initial manifestations of the disease in 3.3% of Garcia-Monaco's series. All patients in his series had one or many single hole fistulae with large venous pouches. Additionally two of them also had small nidus type lesions. None of the patients had features of chronic venous congestion [7]. Pial AVFs commonly present with bleeds. Seizures and focal neurological deficits occur in patients who have spontaneous thrombosis of the venous pouches. Children may also complain of bruits or pulsatile tinnitus due to high flow AVFs. Spinal cord AVMs/ AVFs present with pain and motor weakness.

Pulmonary AVMs cause right-to-left pulmonary shunting and are a major cause of TIAs, septic emboli and strokes in HHT patients. Almost 10% mortality is caused by cerebral abscess and stroke in HHT, which emphasizes the importance of treating these lesions. Cyanosis and clubbing are particularly associated with an increased risk of cerebral abscess and stroke [8].

In summary, it is important to thoroughly angiographically evaluate the cerebral and spinal vasculature of patients with HHT so as to better understand the disease

process, plan for and offer a holistic management strategy & lower the risk of morbidity and mortality in these patients.

References

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