Headache and epistaxis in family history associated with ischemic stroke

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Introduction

Pulmonary arteriovenous malformation (PAVM) has direct connections between an artery and a vein in pulmonary circulation. Pulmonary arteriovenous fistulae (PAVF) are high-flow, low-pressure shunts that include a single feeding artery connected through an aneurysmal sac to a draining vein. PAVM may lead to the development of a brain abscess by letting easy bacterial access to systemic circulation through the right-to-left pulmonary vascular shunt, thus skipping the pulmonary capillaries filtering process. If they are not treated correctly, those may lead to critical neurological problems such as brain abscess and meningitis. Hereditary hemorrhagic telangiectasia (HHT), Rendu-Osler-Weber disease, is a genetic disease through autosomal dominant pattern to have a feature of vascular malformations

Case

A 34-year-old woman suffered from hemoptysis and headache with glittering visual complaint but checked into an emergency room with right arm weakness during 5 minutes. She has been suffered from a light headache and epistaxis since her middle school period. Also, her mother and aunts had been suffered from migraine and frequent nasal bleeding in their lives. (Fig.1) However, they did not get a diagnostic exam at all. During her military duty, she had gotten electro-coagulation therapy for the control of nose bleeding in a military hospital. Unfortunately, her epistaxis redeveloped even electro-coagulation therapy two times. And we met her in the ER complaining of weakness of right arm to go away soon. Thus, we tried to do the CAT scans and a MR scan for her including the chest X-ray. And she was transferred to the division of chest surgery to get video assisted thoracic surgery (VATs) with wedge resection for arteriovenous malformation in the right apex and right lower lung and underwent surgical removal of her cerebral AVM by a neurosurgeon. And then, her epistaxis and hemoptysis were dramatically controlled. From the pedigree of her family, we would get an idea for the gene study of hereditary hemorrhagic telangiectasia

Neurologic Exam & Lab, Genetics

She was alert and aware of time, place or people. She did not have pathologic reflexes on her extremities but disappeared left arm motor weakness with paresthesia. She was apyrexial (body temperature 36.5˚C), but her blood sampling showed normal liver function test but stable CRP level. Her chest PA indicated suspicious nodular opacities at RUL and RLL. (Fig.2) Thus, a radiologist recommended chest CT scan. T2 weighted MR brain image depicted irregular cystic cerebromalacia with peripheral dark hemosiderin deposit surrounding reactive gliotic change at the right frontal white matter area. Brain MRA revealed the nidus with tortuous, ectatic draining vein on the paramedian frontal region. (Fig. 3) Moreover, the axial CT scan of her chest demarcated a large (> 1 cm) AVM nidus in the right lower lung as well as a tiny lingular nodule, probably intrapulmonary lymph node. (Fig. 4) Transcranial doppler sonogram revealed that MES (microembolic signal) was detected during normal respiration, 170 embolic tracks and 250 embolic tracks when trying the Valsalva maneuver. It showed the existence of right-to-left shunt in her lung. (Fig. 5) Thus, she was transferred to the division of chest surgery to get VATs (video assisted thoracic surgery) wedge resection for AVM in the right apex and right lower lung and underwent surgical removal of her cerebral AVM. Furthermore, we tried to do gene test using whole blood for the patient and her mom and identified mutation such like transition and deletion involving exon 7 in ENG gene of them but did not find any ALK1 gene mutation. There was the first mutation on her gene in South Korea. To be details, the transition was of base change, c.859_858AC>G and deletion was of the frame shift, p. Asn286fs. (Fig. 6) She then regularly visited the clinic for outpatient to take an antiplatelet medication and some antiepileptic medications

Figure

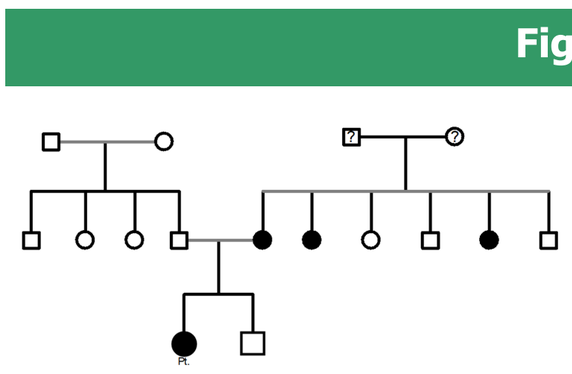

Figure 1. The pedigree: Her mother and aunts had been suffered from migraine and frequent nasal bleeding

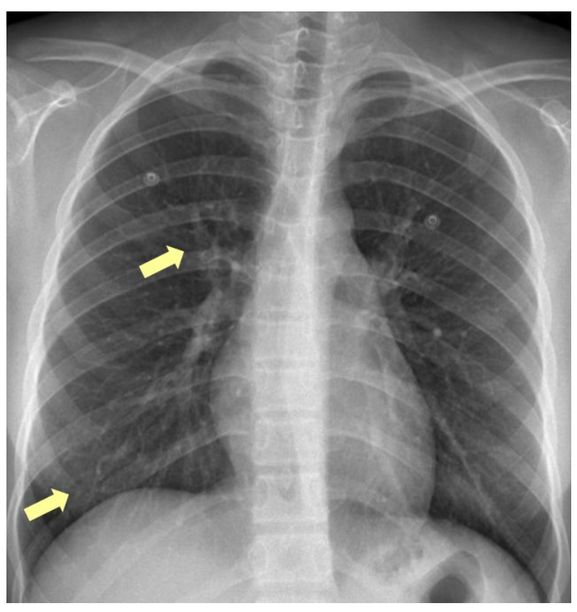

Figure 2. Chest X-ray showed suspicious nodular opacities at RUL and RLL

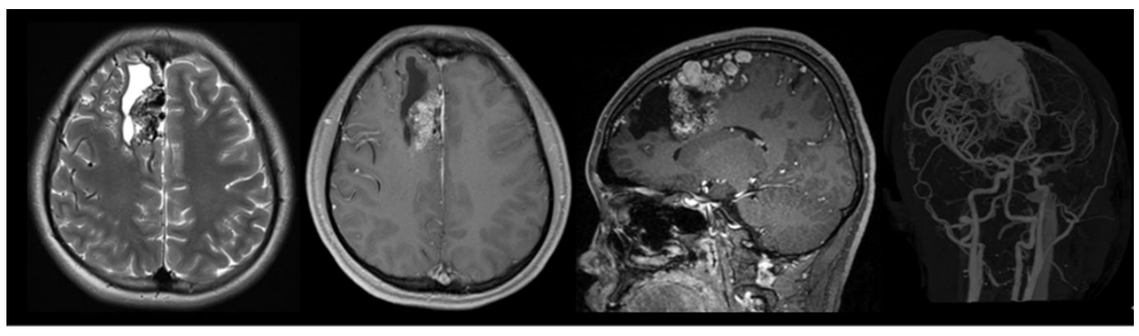

Figure 3. Brain MRI and MRA revealed the nidus with tortuous and ectatic draining vein on the paramedian frontal region

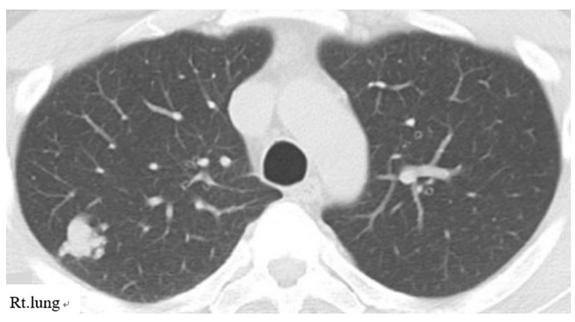

Figure 4. CT chest lung mediastinum (enhancement) showed a large (>1 cm) nodule in the right lower lung

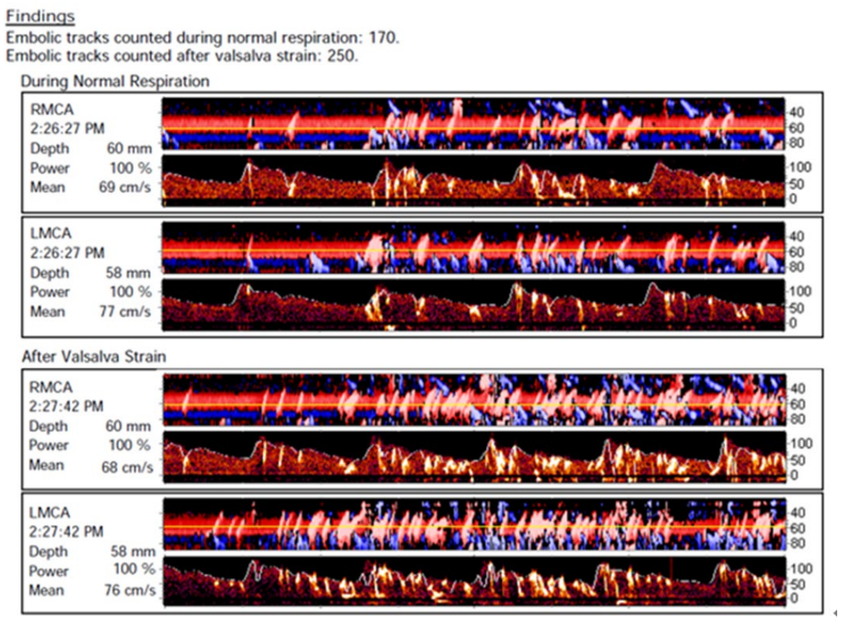

Figure 5. Transcranial doppler sonogram indicated that many microembolic signals were detected during Valsalva maneuver as well as normal respiration

Figure 6. Gene study clarified the ENG (ENDOGLIN on chromosome 9) mutation which would be proven the transition was of base change, c.859_858AC>G and deletion was of the frameshift, p. Asn286fs

Conclusion

Patients with HHT1 inclined to show a more severe disease progression such as more frequent recurrence associated with the complications of both pulmonary and cerebral arterio-venous malformations. Therefore, we will try to find out the genotype among them through genetic analysis

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