HEREDITARY HEMORRHAGIC TELANGIECTASIA:
CONSEQUENCES OF DELAYED DIAGNOSIS

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INTRODUCTION

- Hereditary Hemorrhagic Telangiectasia (HHT) often underdiagnosed
- Also known as Osler-Weber-Rendu Disease
- Rare autosomal dominant disorder
- Estimated prevalence is 1 in 500
- Presenting symptom commonly spontaneous, recurrent nose bleeds
- Followed by the development of mucocutaneous telangiectasias
- May develop arteriovenous malformations (AVMs)
  - Locations in the spine, lung, brain, and liver
- Less than 25% of patients with HHT develop cerebral AVMs
  - Annual bleed risk is thought to be less than 1 percent

CASE PRESENTATION

36-year-old male presented to the longitudinal Bedlam free clinic to establish care

Past Medical History

- Left frontal Intraparenchymal hemorrhage occurred 8 months prior resulting in
  - residual neurologic and cognitive deficits
  - seizure disorder managed on lamotrigine 100mg
- Recurrent and spontaneous epistaxis 2 to 3x per week beginning in middle school
- Life-threatening gastrointestinal (GI) bleed with a hemoglobin 3.0 seven years prior
- Alcoholic liver cirrhosis, drank a tall boy a night
  - Quit drinking a tall boy a night diagnosis
- Smoked cigarettes ½ pack per day for 10 years; quit after stroke
- Denied family history of stroke, telangiectasia, HHT, or known AVMs

Physical Exam

- Telangiectasias on chest, back, fingers, and multiple on roof of mouth
- Jaundice skin with scleral icterus
- Splenomegaly
- Emotionally liable, laughs at inappropriate times
- Slurred speech
- Right-sided weakness, unsteady gait

Imaging

- Multiple intracerebral AVMs, initially seen 8 months prior on cerebral arteriogram
  - High flow AVMs of pons and left occipital region
- No changes on MRI brain angiogram 2 months prior to initial bedlam visit
- Hepatic AVM on Doppler abdominal ultrasound as well as cholelithiasis
- Positive pulmonary AVM screen on transthoracic echo with agitated saline

Additional Work-up

- Unenhanced multidetector thoracic CT with thin-cut reconstructions
  - Needed to confirm presence of pulmonary AVMs
- Upper GI study ordered due to decreased hemoglobin
- Genetic testing ENG, ACVRL1, and SMAD4 for cause of mutation recommended

Disposition

- Difficult to establish care with HHT center due to uninsured status
- One follow-up visit where jaundice resolved and had no new complaints
- Interventional radiology and neurovascular specialist consults requested to evaluate possible embolization of AVMs
- Two months after initial evaluation, he passed away from an acute intracranial hemorrhage with uncal herniation (shown in figures 2 and 3)

IMAGING

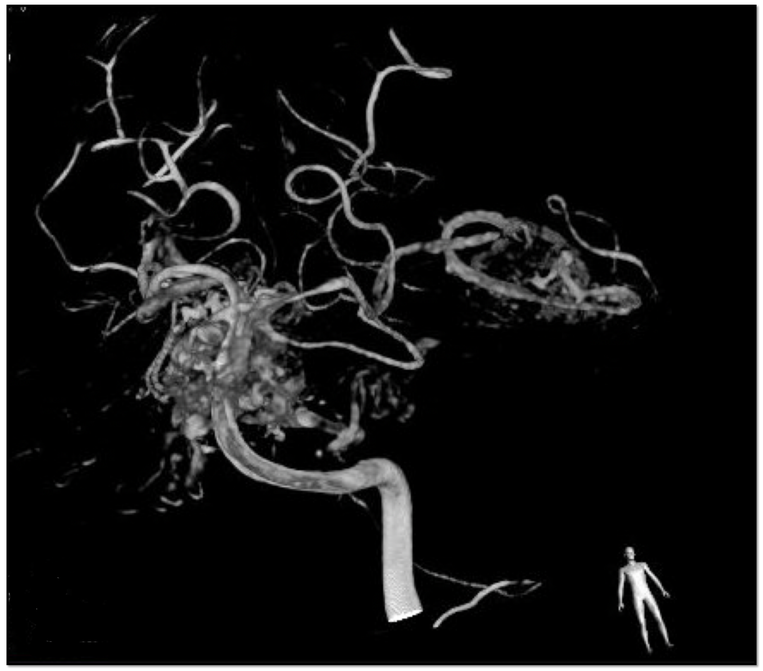

Figure 1: IR Cerebral Arteriogram showing multiple AVMs obtained 8 months prior. High flow AVMs of pons and left occipital region. Additional AVMs in right inferior frontal lobe, right parasagittal posterior frontal lobe, left mesial temporal lobe, and right inferior cerebellar lobe. Prominent venous varicosities in right pontine AVMs.

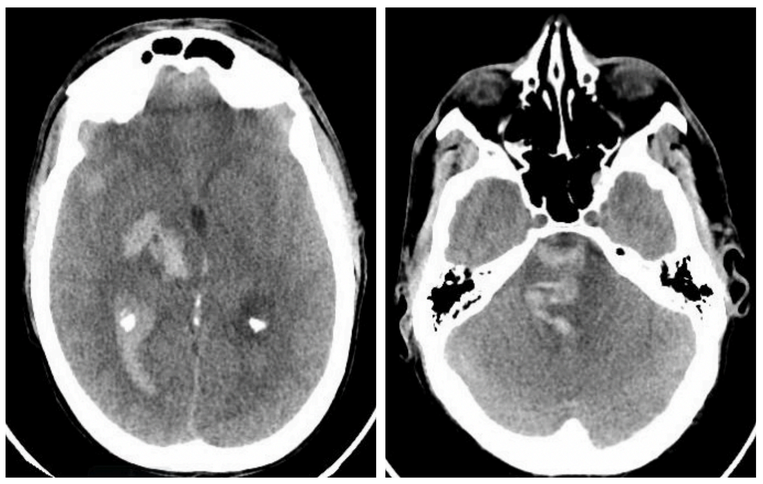

Figure 2. *Figure 3.*

Figures 2 & 3: CT brain without contrast showing extensive hemorrhage involving the medulla, pons, right thalamus, and right basal ganglia with intraventricular extension. Also seen is a subarachnoid hemorrhage, obstructive hydrocephalus, cytotoxic edema, and uncal herniation.

CONCLUSION

Many physicians who manage the complications of this disease are unfamiliar with the genetic condition, therefore, this leads to HHT being underdiagnosed.

Curacao Criteria for diagnosis of HHT

1. Spontaneous and recurrent epistaxis
2. Multiple telangiectasia in nose, mouth, lips, face, or hands
3. AVMs in one or more internal organ
4. First-degree relative with diagnosis or genetic diagnosis

Definite Diagnosis of HHT: 3 or more are met
Suspected Diagnosis of HHT: 2 are met
Unlikely Diagnosis: 0 or 1 are met

Evaluation for HHT

- Obtain thorough history inquiring about nose bleeds
- Perform a physical exam looking for mucocutaneous telangiectasias
- Conduct a thorough history asking about family history of symptoms
- Suspect HHT →
  - Screen for cerebral and pulmonary AVMS with imaging
  - Doppler ultrasound for hepatic AVMs to establish baseline
- 1 -2 Curacao criteria met (inconclusive/no genetic testing available) →
  - Order Doppler ultrasound to evaluate hepatic AVMs.

Factors Leading to Delayed Diagnosis

- Our patient was never asked about his nose bleeds until his initial Bedlam visit
  - indicated screen for hepatic AVMs (1 Curacao Criteria)
- Suspect multiple site telangiectasias were present (2 criteria)
  - screens for cerebral AVMs obtained sooner
- Imaging after Hemorrhagic stroke showed multiplicity of AVM
  - Indicative of underlying genetic disorder but no further evaluated obtained
- Increased familiarity of HHT presentation and complications by medical providers could have resulted in an earlier diagnosis

Consequences of Delayed Diagnosis

- Continued epistaxis and anemia
- Suffered life-threatening GI bleed, likely due to hepatic vascular malformations
- Experienced hemorrhagic stroke with residual neurologic and cognitive deficits
- Lived with seizure disorder, right-sided weakness, and emotional liability
- Died due to another hemorrhagic stroke

If diagnosed earlier with HHT, physicians could have continually screened and evaluated him to prevent serious complications and possibly untimely death.

REFERENCES

- Faughnan ME, Palda VA, Garcia-Tsao G, et al. International guidelines for the diagnosis and management of hereditary haemorrhagic telangiectasia. Journal of Medical Genetics. 2011;48(2):73-87.
- Maher CO, Piepgras DG, Brown Jr RD, Friedman JA, Pollock BE. Cerebrovascular manifestations in 321 cases of hereditary hemorrhagic telangiectasia. Stroke. 2001;32(4):877-882.