Case Presentation

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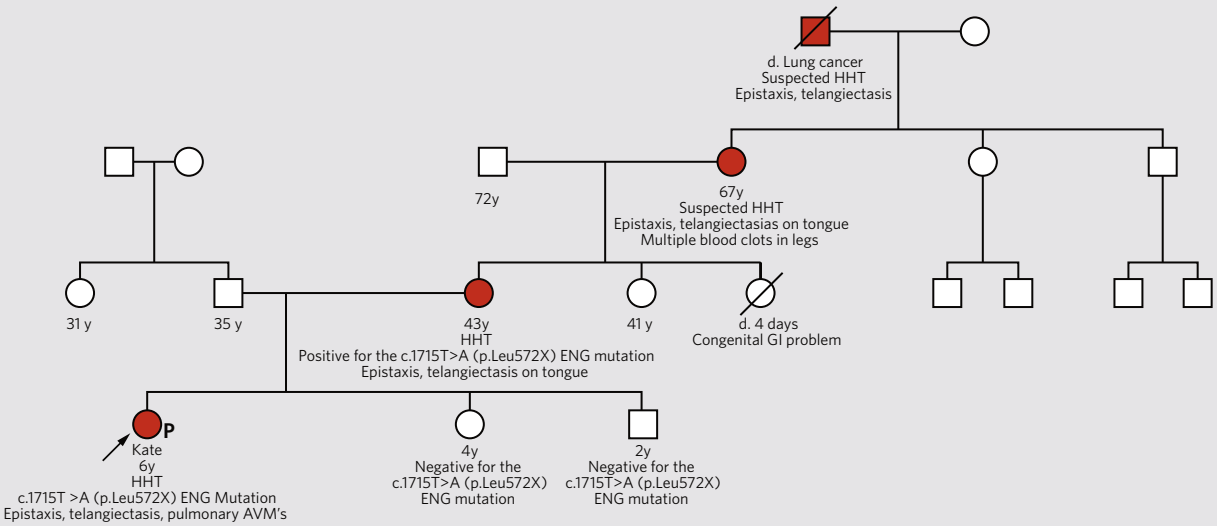
Kate is a happy and active six-year-old with hereditary hemorrhagic telangiectasia (HHT). She was born borderline-preterm, delivered at 36 weeks gestational age. She had a large head circumference and a skin hemangioma at birth. Further evaluation demonstrated that Kate had congenital hydrocephalus secondary to a grade III intraventricular hemorrhage (IVH) in utero requiring an intraventricular shunt. IVH is a common complication of early prematurity but not at Kate's gestational age. Due to her unusual presentation, she was referred to a geneticist at nine months and her genetic screening tests at the evaluation were all normal. However, a significant family history of epistaxis was uncovered requiring, cauterization in her mother and maternal grandmother. In addition, the geneticist noted telangiectasia on both her mother's and maternal grandmother's tongue. At that time, molecular testing for HHT was sent that confirmed the suspected clinical diagnosis of HHT and that demonstrated a nonsense mutation; with a single change at c.1715T>A in exon 12 of the endoglin (ENG) gene located at chromosome 9q34 locus resulting in "stop" (written as p.Leu472X or L472X).

Unfortunately, Kate was lost to follow up for four years. With the development of the HHT Center of Excellence at UPMC, Kate's case was recovered and the family was re-introduced to the multistep clinical screening process. A team of physicians, specializing in HHT, has worked to ensure that Kate receives the best in HHT preventative and cutting edge care. Kate was evaluated by the HHT Pediatric Center's diagnosticians to characterize the extent of her ear nose and throat (ENT), pulmonary, neurologic, and gastrointestinal involvement. Her ENT evaluation demonstrated the development of intermittent epistaxis, treated with humidification and intranasal saline. She now is followed by the HHT Center's ENT expert to monitor and manage complications as this disease progresses.

Kate underwent pulmonary screening with a contrast transthoracic echocardiogram, which demonstrated delayed presentation of saline bubbles into the left atrium after five cardiac cycles, suggestive of a possible AVM. Kate then underwent a CT angiogram of her chest which demonstrated four tiny AVMs within her lung parenchyma. Her case was reviewed by the HHT center's interventional radiologist, who assessed that none of the lesions were of a clinically significant size to require coiling. She will require close observation to check for the progression of these lesions, antibiotic prophylaxis to prevent possible intracranial "seeding" that could result in brain infections during elective procedures, and filtered IV solutions to prevent air bubble embolization. Finally, Kate's blood picture shows that she is normocytic with age appropriate hemoglobin as well as iron stores and has no history of bloody stools. Therefore, no further gastrointestinal screening is warranted at this time.

Cerebral and pulmonary AVMs appear to be more commonly associated with mutations in the ENG gene. There are only a few reported cases of IVH due to cerebral AVMs in children. Therefore, Kate's history of IVH at birth is highly suggestive that she had intracranial AVM which bled in utero even though her screening brain MRI/MRA demonstrated no specific lesions of HHT at this time. Going forward, the HHT team at UPMC will work to individualize Kate's care to ensure she stays healthy throughout her life. Due to her unfortunate presentation, her family members have been identified as HHT gene carriers and now will receive the appropriate screening and care in our adult HHT Center of Excellence.



At least four generations are afflicted by HHT. The diagnosis of HHT unveiled and brought to surface by our 9 month old Kate, the proband is shown by the arrow. Please see the intra-familial variability of HHT. The two siblings tested negative and do not warrant surveillance for varied manifestations of HHT.