Cerebral Vascular Malformations in Hereditary Hemorrhagic Telangiectasia

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Children's Hospital of Georgia
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Acknowledgments

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Hereditary Hemorrhagic Telangiectasia (HHT)

- Osler-Weber-Rendu disease
- Affects 1.4 million people world-wide
- Mucocutaneous telangiectasias, visceral arteriovenous malformations, epistaxis
- Inherited in autosomal dominant fashion
  - HHT1 = Endoglin (ENG) gene
  - HHT2 = Activin-like kinase receptor 1 gene
  - JPHT = SMAD4 gene

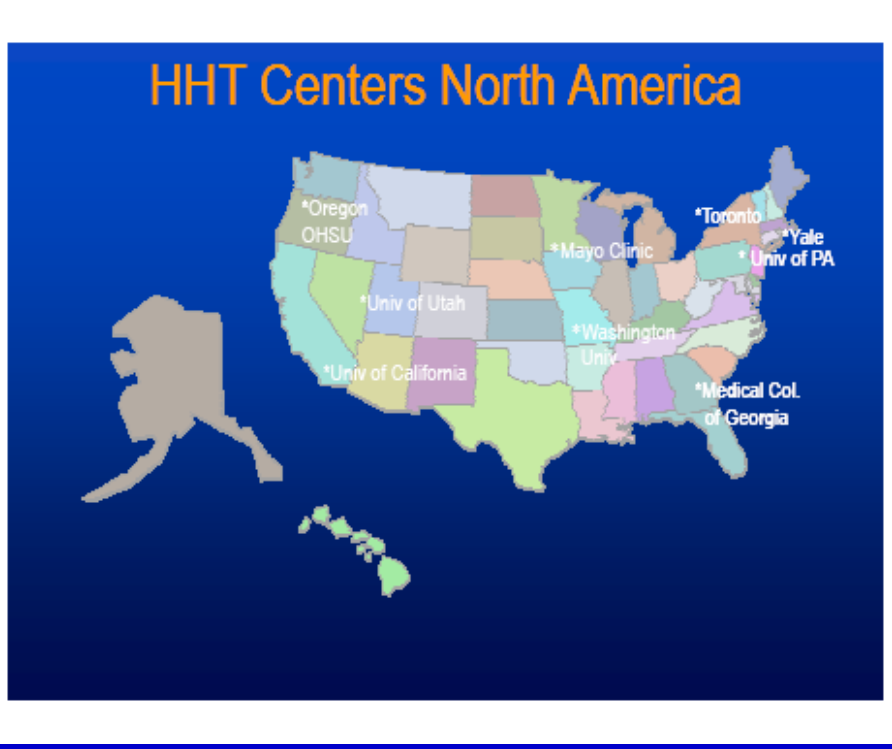
Cerebral Vascular Malformations (CVM)

- 5-20% of people with HHT
- Cerebral arteriovenous malformations (AVM), spinal AVM, ischemic stroke, brain abscess, intracerebral hemorrhage, migraines, seizures
- Annual spontaneous hemorrhage rate of sporadic AVM is ~ 2-4%
- Current guidelines: screen children in the 1st 6 months of life (or time of Dx) with MRI

Faughnan, ME et al. *J Med Genet* 2011

HHT Foundation

- GRU is one of 16 US centers (35 worldwide)
- Jim Gossage (Dir. of Pulm. Vasc. Dis. At GRU) is Med. Dir. of HHT Foundation
- Multidisciplinary program
  - Pulmonology
  - Genetics
  - Interventional radiology
  - Gastroenterology
  - Otolaryngology
  - Neurosurgery
  - Neurointerventional surgery



Characterization of CVM in HHT

- Retrospective review of database from 8/2002 – 10/2009
- 167 pediatric patients < 21 years of age
- Data collection:
  - History, physical exam, radiographic studies
  - 3 Tesla MRI/MRA with and without gadolinium with gradient echo sequences
- AVMs analyzed with regard to size, location, eloquence of cortex

Results

- Average age of referral 9.6 years
  (range 0.1 to 20.7 yr)
- 76 patients with definite HHT, of these 68 had screening MRI/MRA brain
- CVM in 11 patients
  - 7 cerebral AVM
  - 2 developmental venous anomalies
  - 1 cavernous malformation
  - 1 capillary telangiectasia

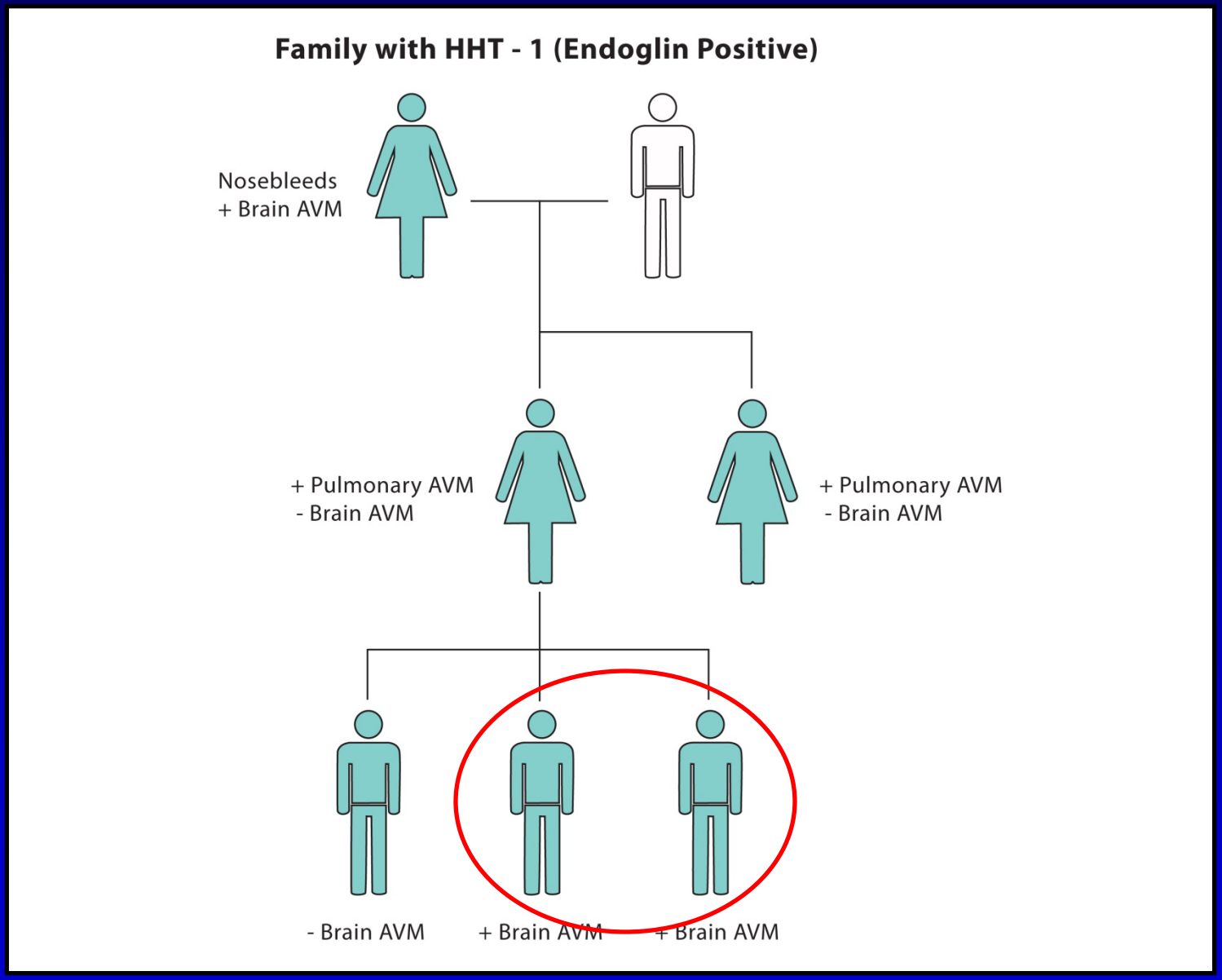
HHT AVM Characteristics

Age/Sex	Size	Location	Eloquence	Venous Drainage	Treatment	Outcome	DNA
5 F	<3cm	Cerebellum	No	Superficial	None	Thrombosed	No
5 M	<3cm	R Temporal	No	Superficial	Embo x 2 + Surgery	Recurred, Obliteration	ENG
7 M	<3cm	R Frontal	No	Superficial	Embo + Gamma	Obliteration	ENG
8 F	<3cm	R Temporal	No	Superficial	Embo	Obliteration	ENG
8 F	<3cm	L Frontal	Yes	Superficial	Surgery	Obliteration	ENG
12 M	<3cm	R Frontal	No	Superficial + Deep	Embo	Obliteration	ENG
15 F	<3cm	R Frontal	No	Superficial	Gamma	Obliteration	No

HHT AVM Characteristics

- 5 AVMS were Spetzler-Martin Grade 1
- 2 AVMS were Spetzler-Martin Grade 2
- Treatment:
  - Gamma knife (1)
  - Surgery (1)
  - Embolization (3)
  - Embolization and gamma knife (1)
  - Autothrombosed on follow up (1)

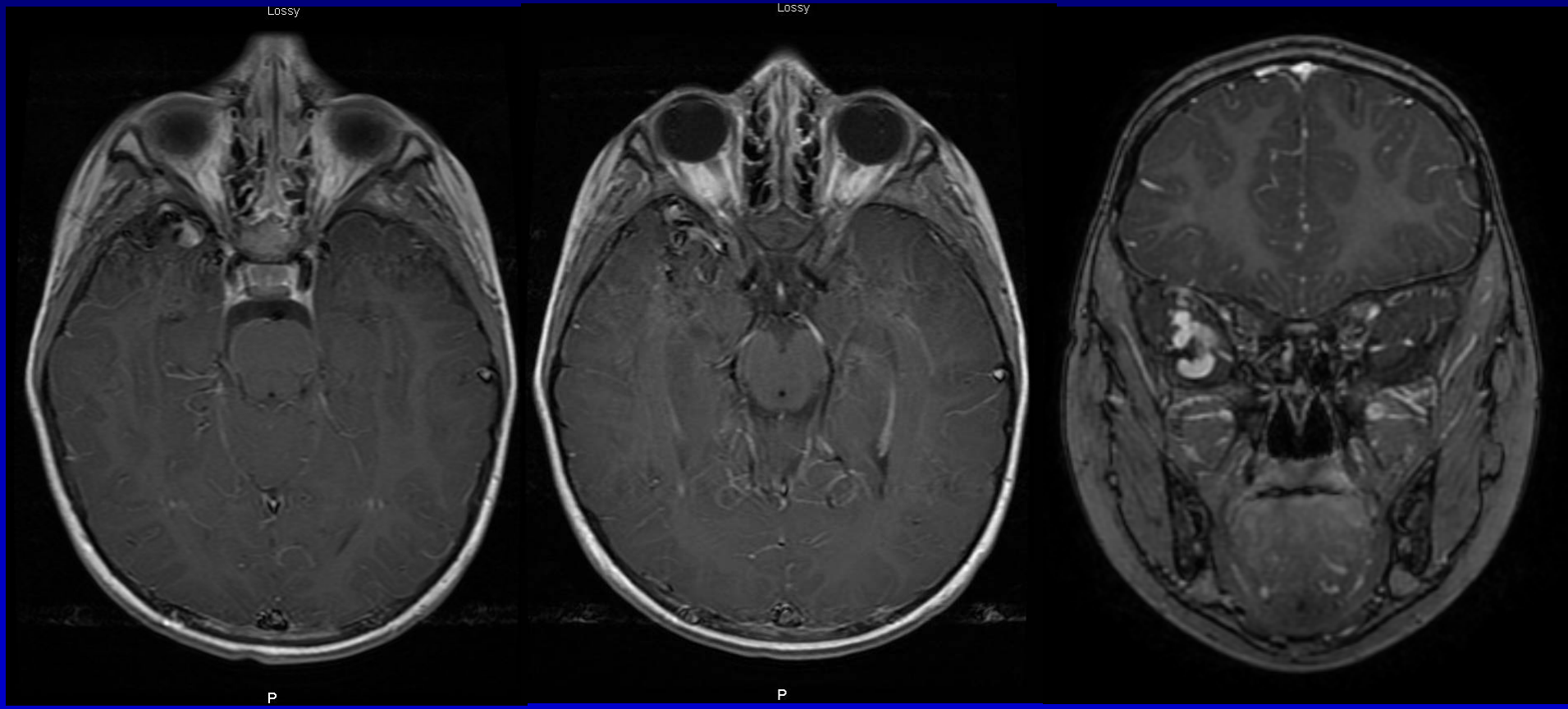
Cerebral AVMs in a Family with HHT



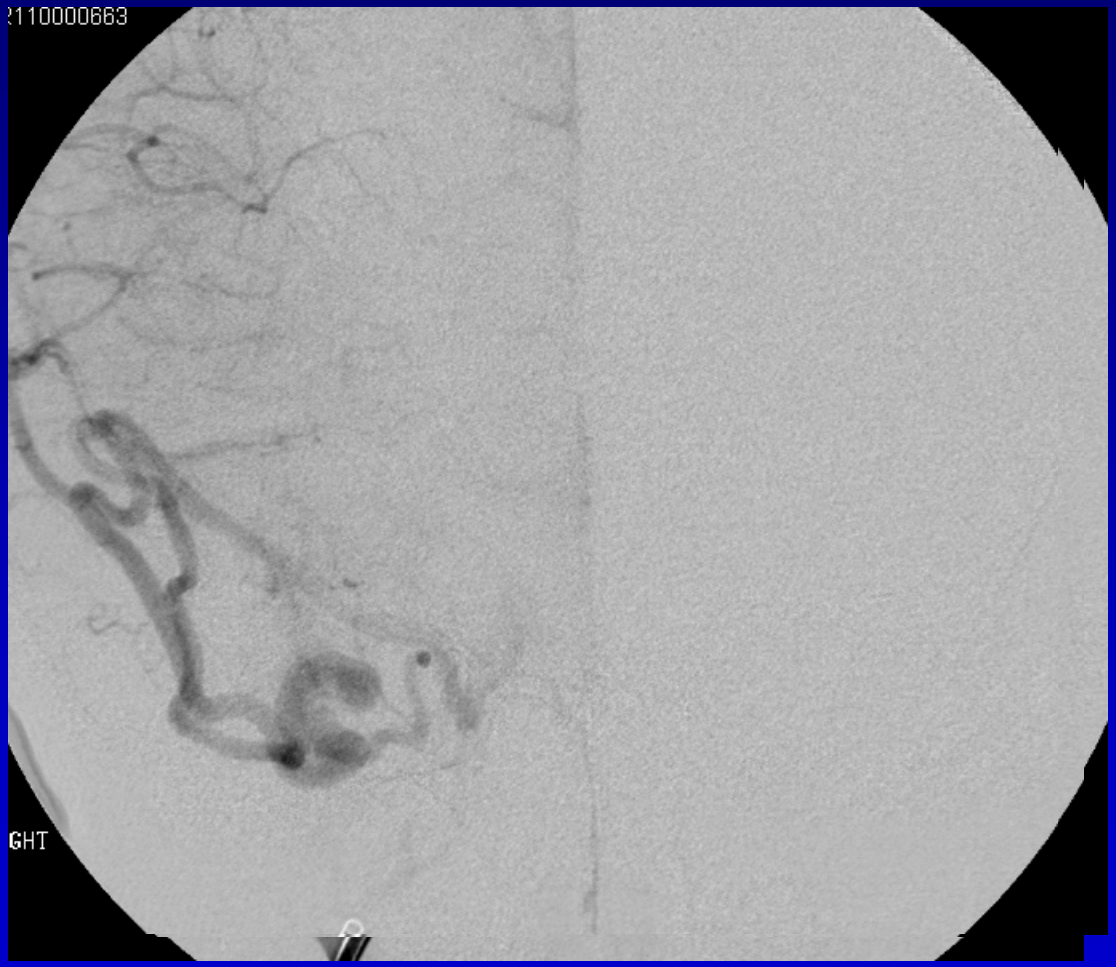
Patient #1

- 5 y/o M with epistaxis since age 1 or 2, which occurs several times per week
- No overt signs of HHT

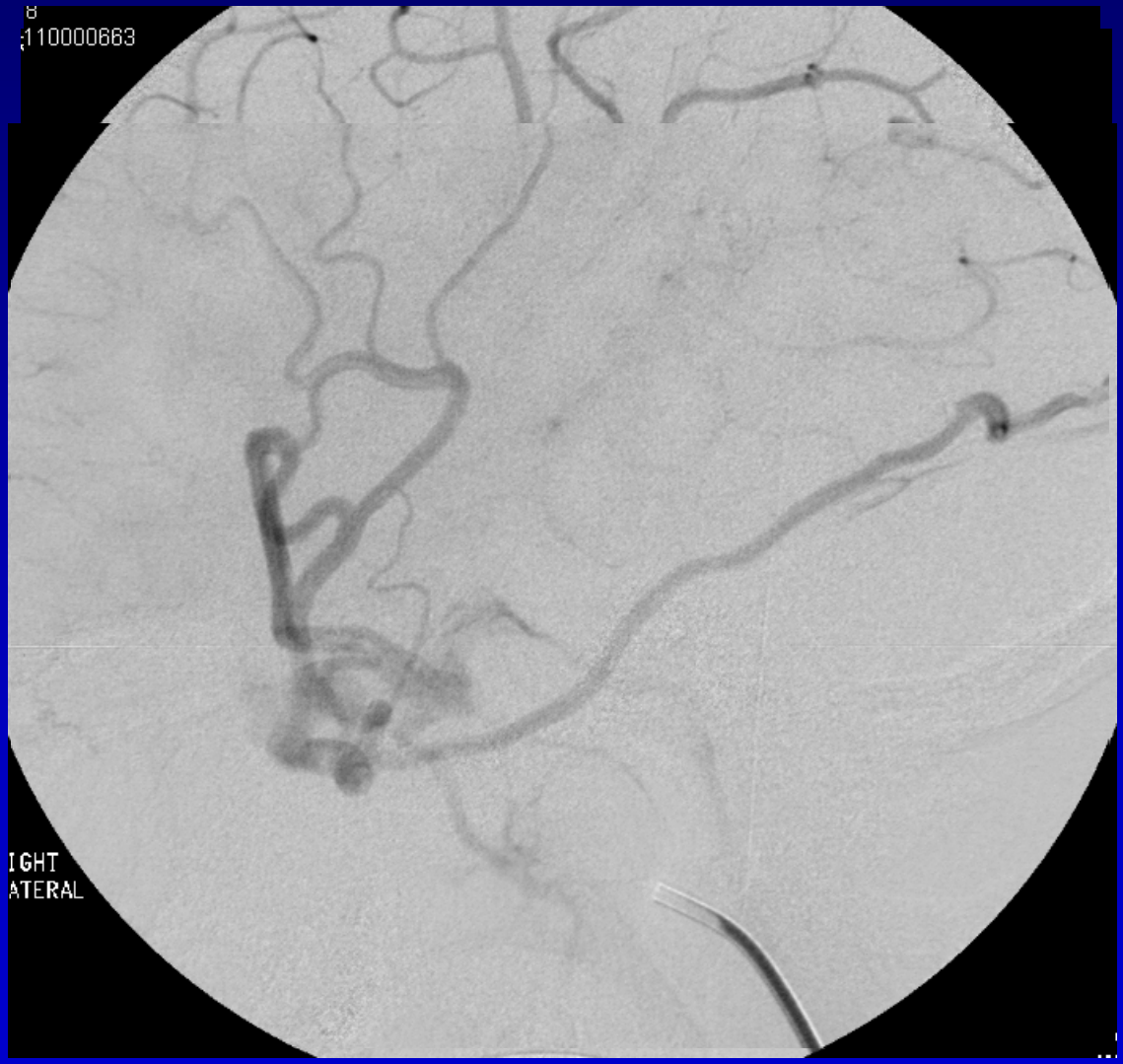
Screening MRI



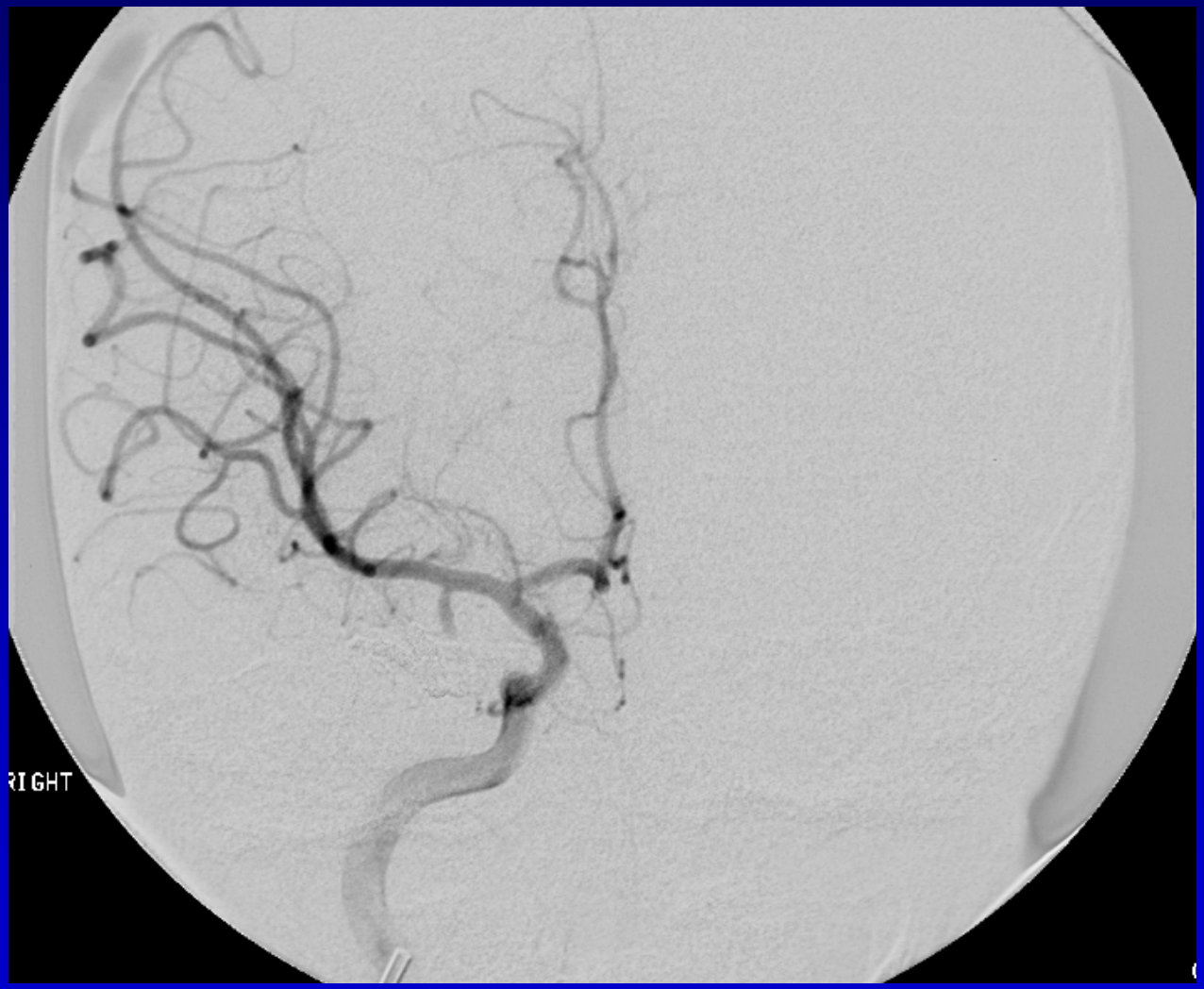
Initial Cerebral Angiogram



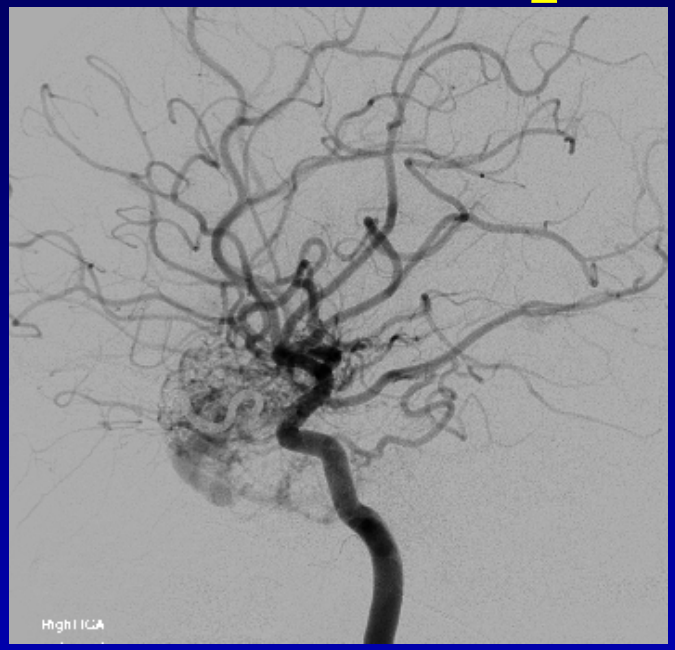
Initial Cerebral Angiogram

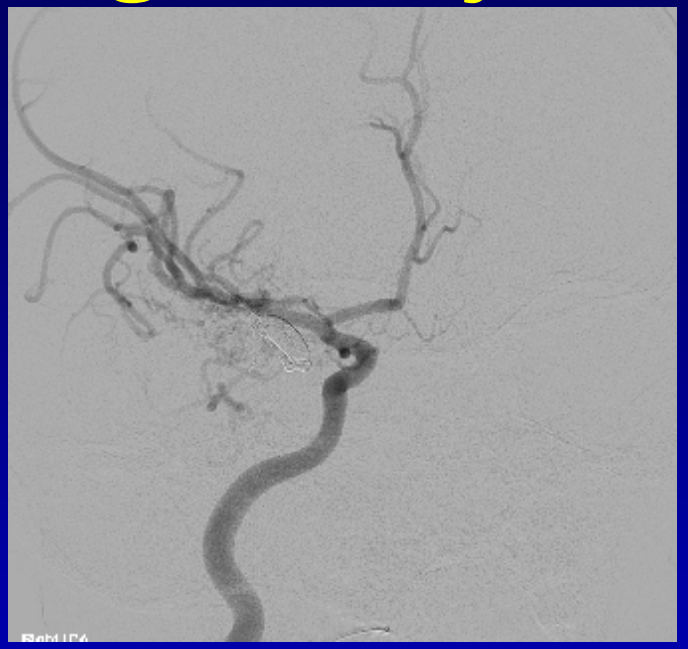


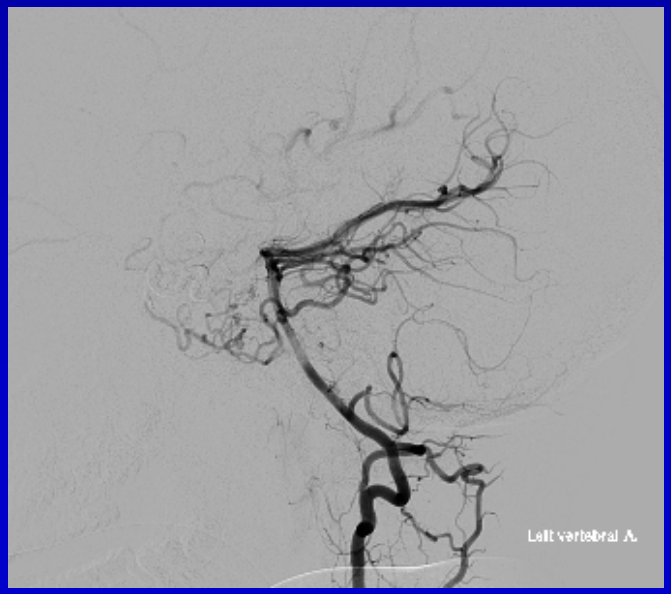
Treatment with Glue Embolization

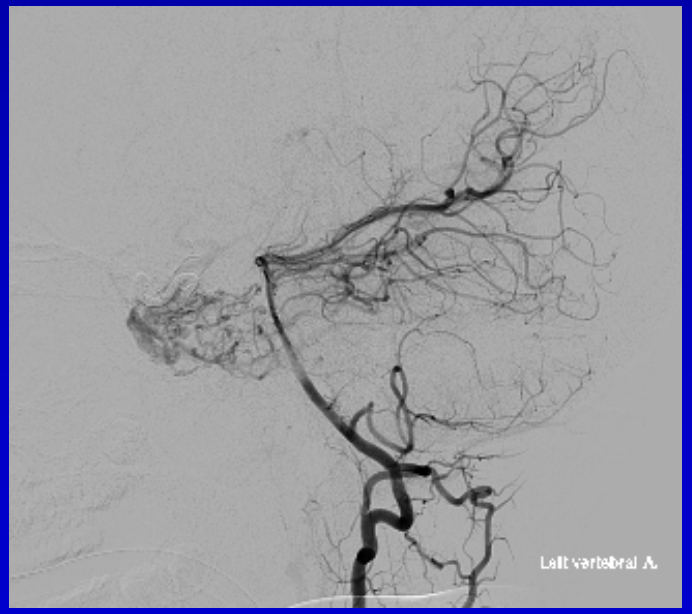


Follow Up Angiogram 2 yrs

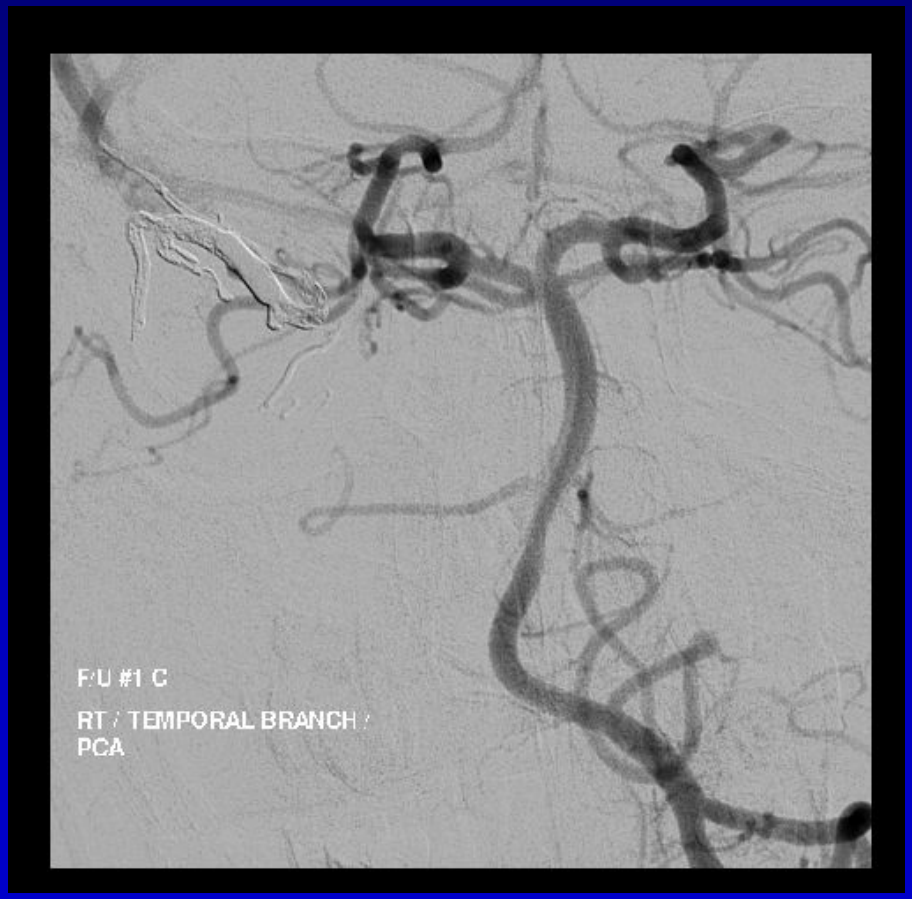


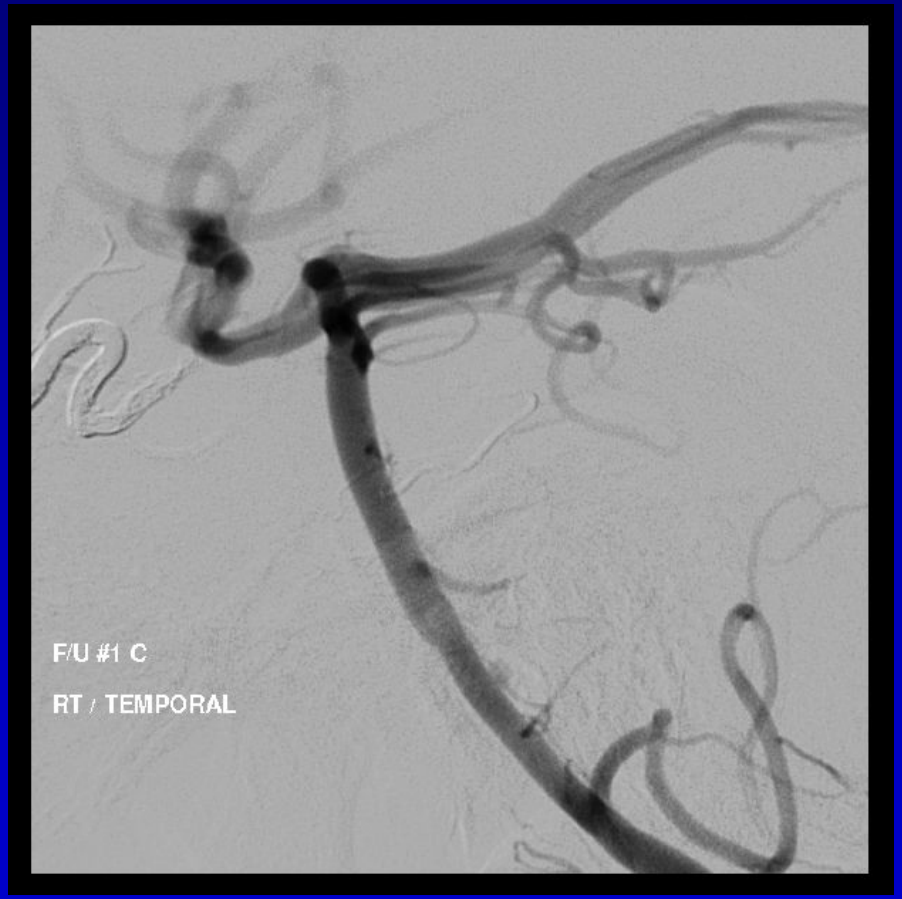




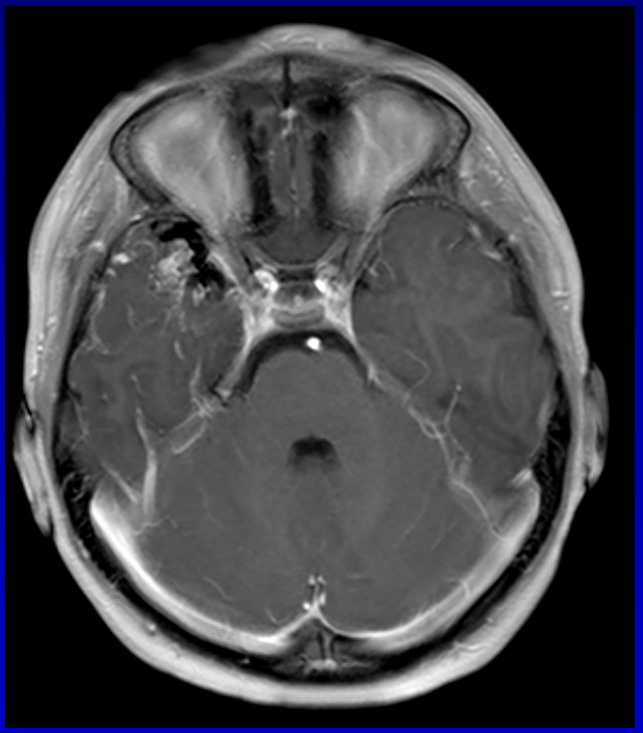
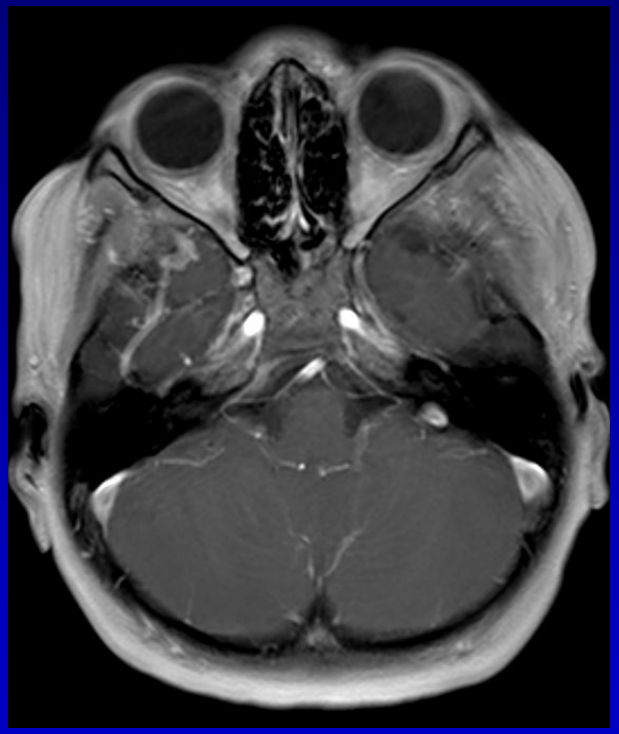
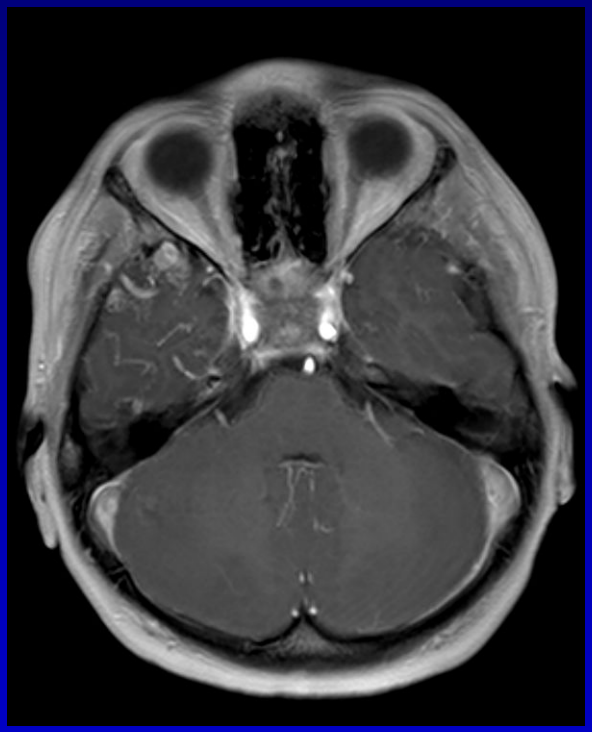


Retreatment with Glue Embolization

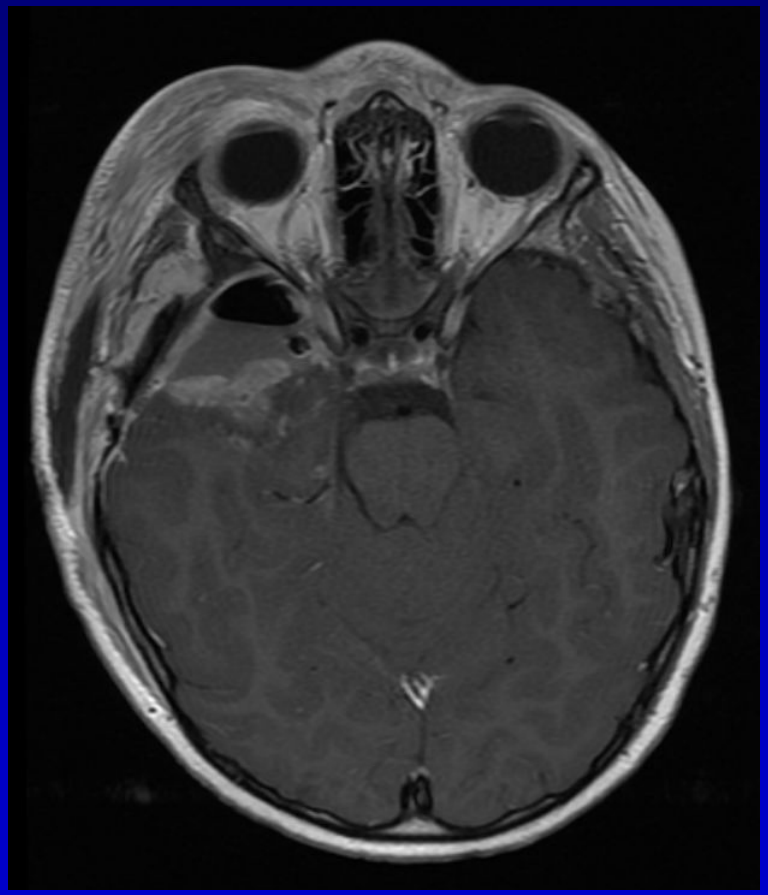


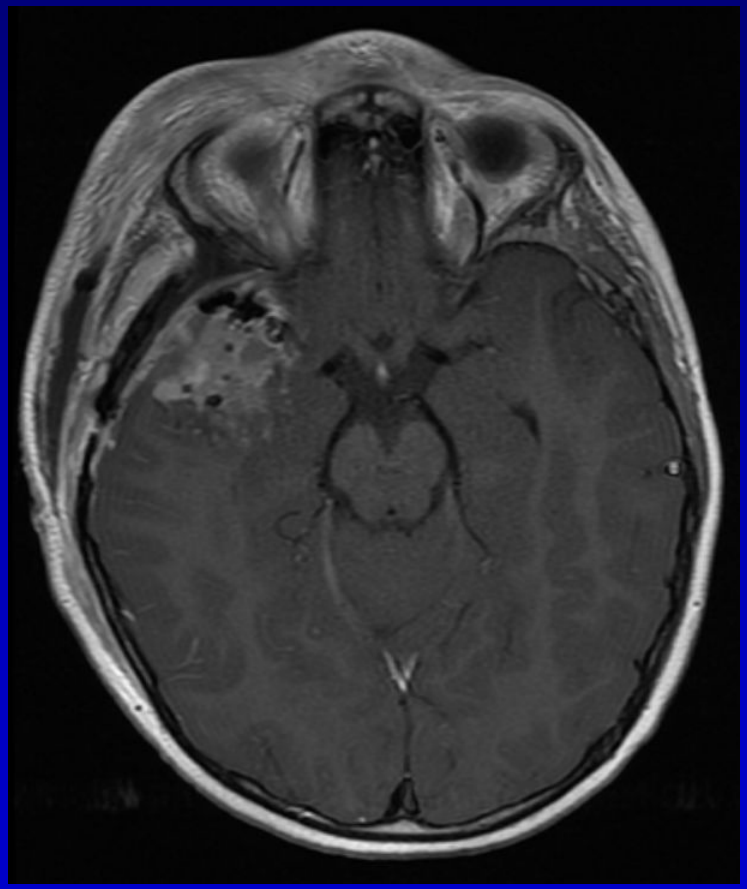


Residual AVM

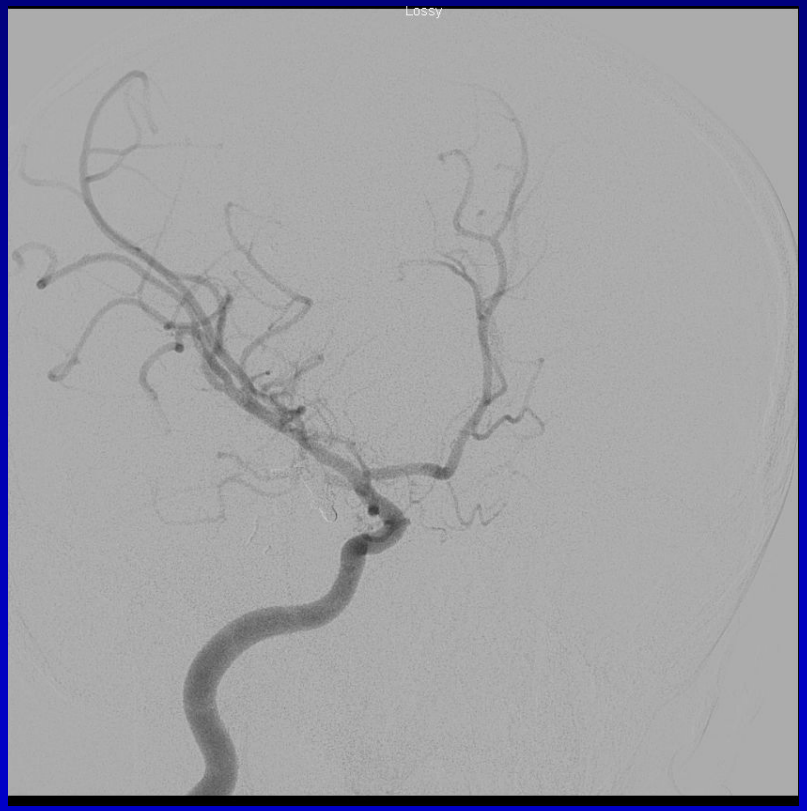




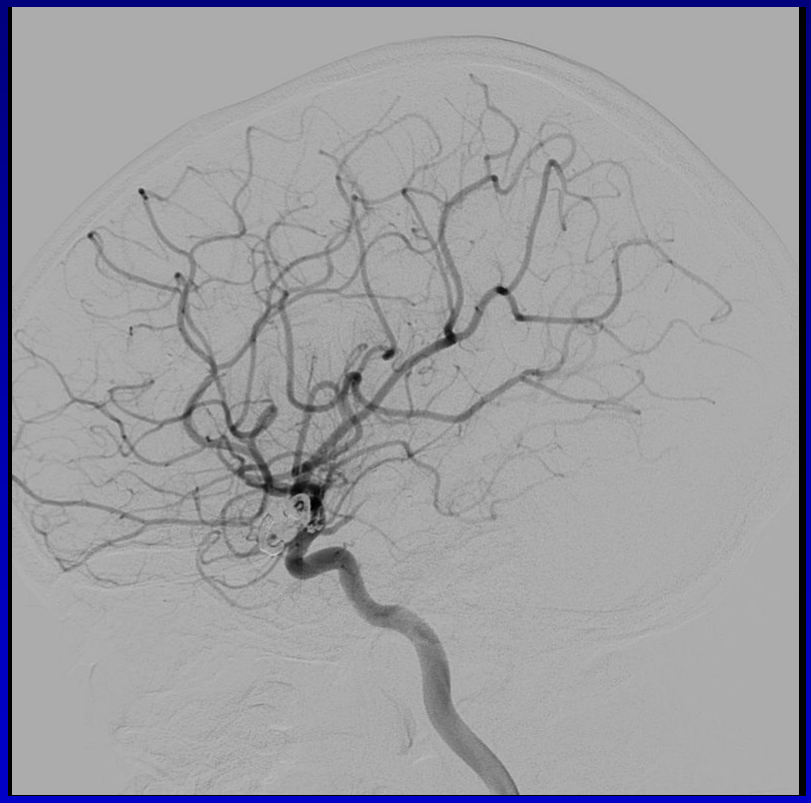
Surgery for Residual AVM





Final Angiogram

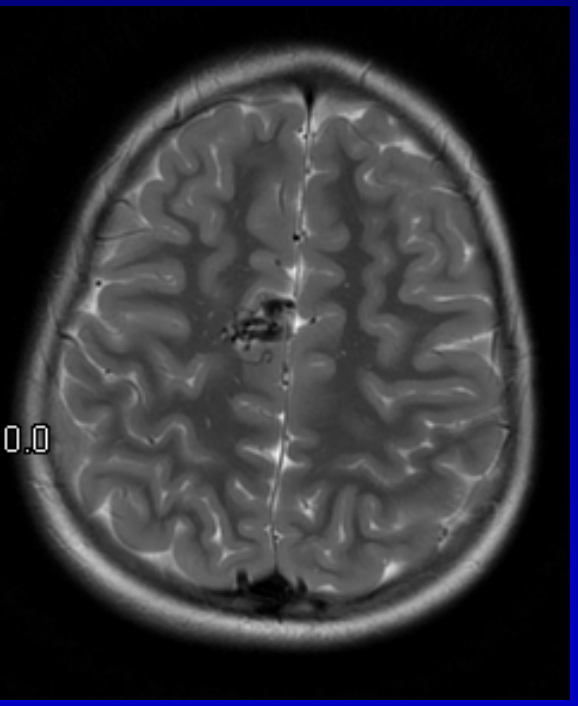


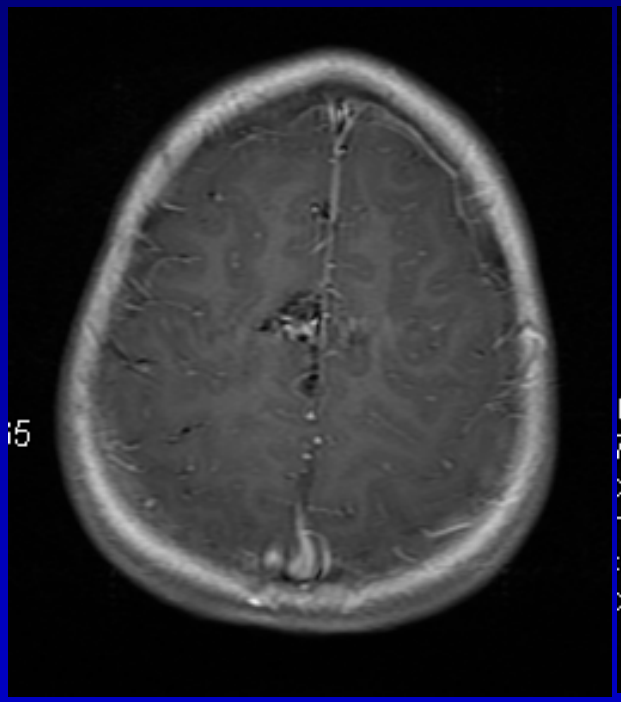


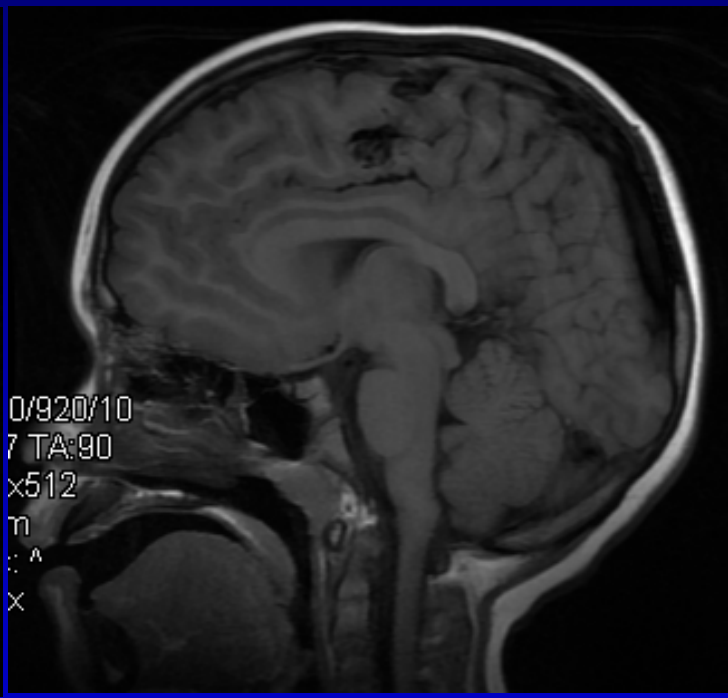
Patient #2

- 7 y/o M with epistaxis from 2 years, which have been fairly mild. The epistaxis typically occurs less than once per month, and he has occasional HA
- No other overt manifestations of HHT

Screening MRI







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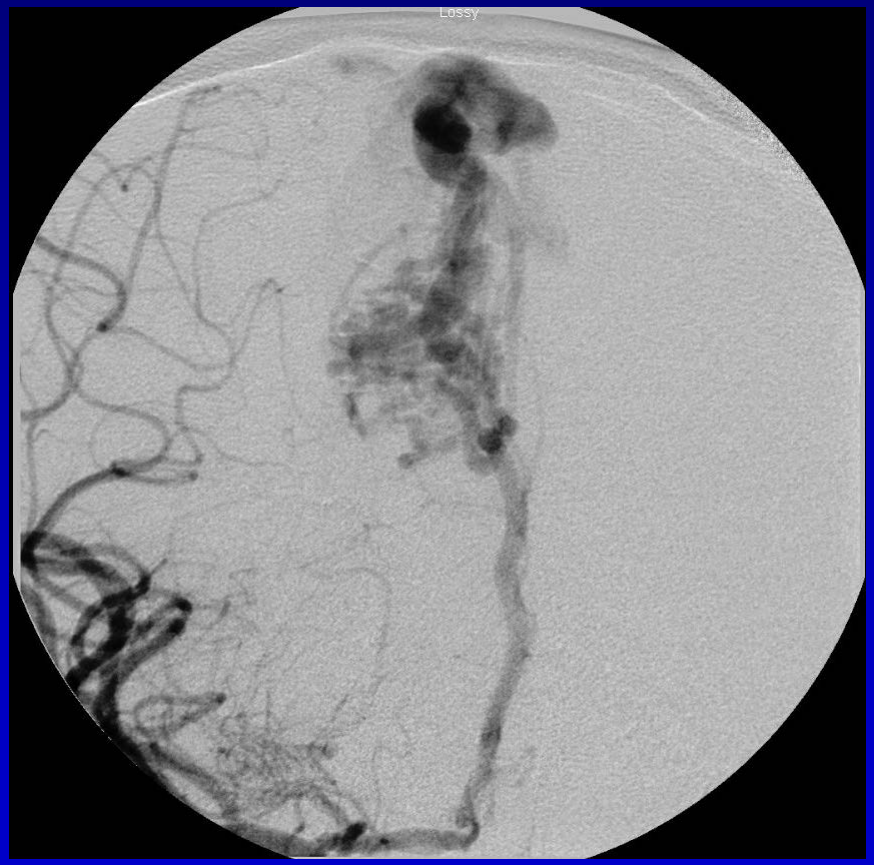
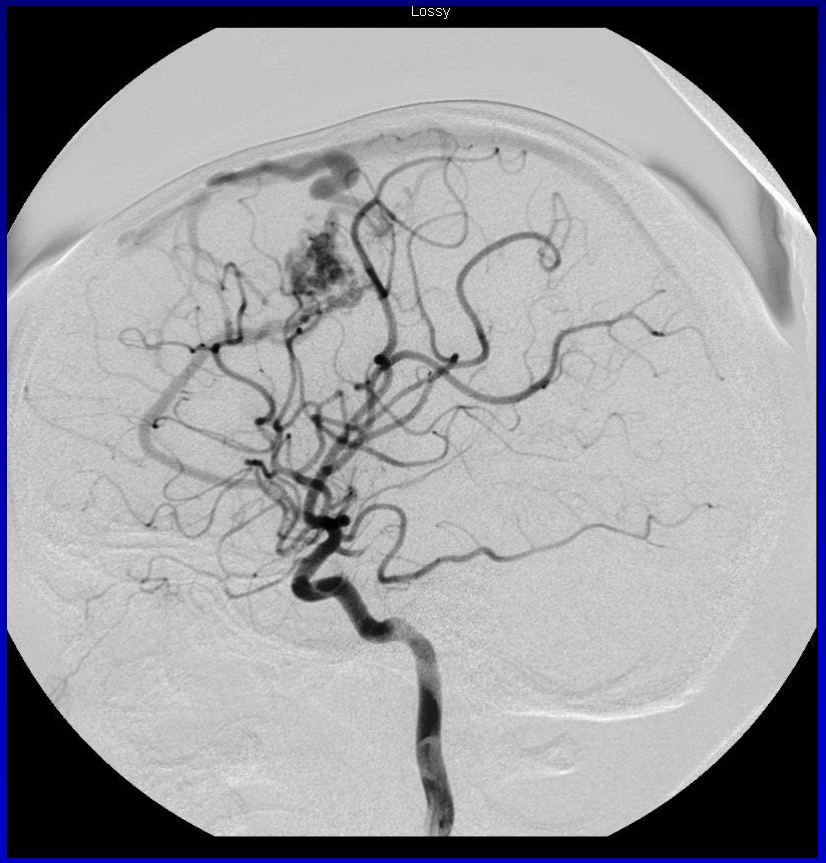
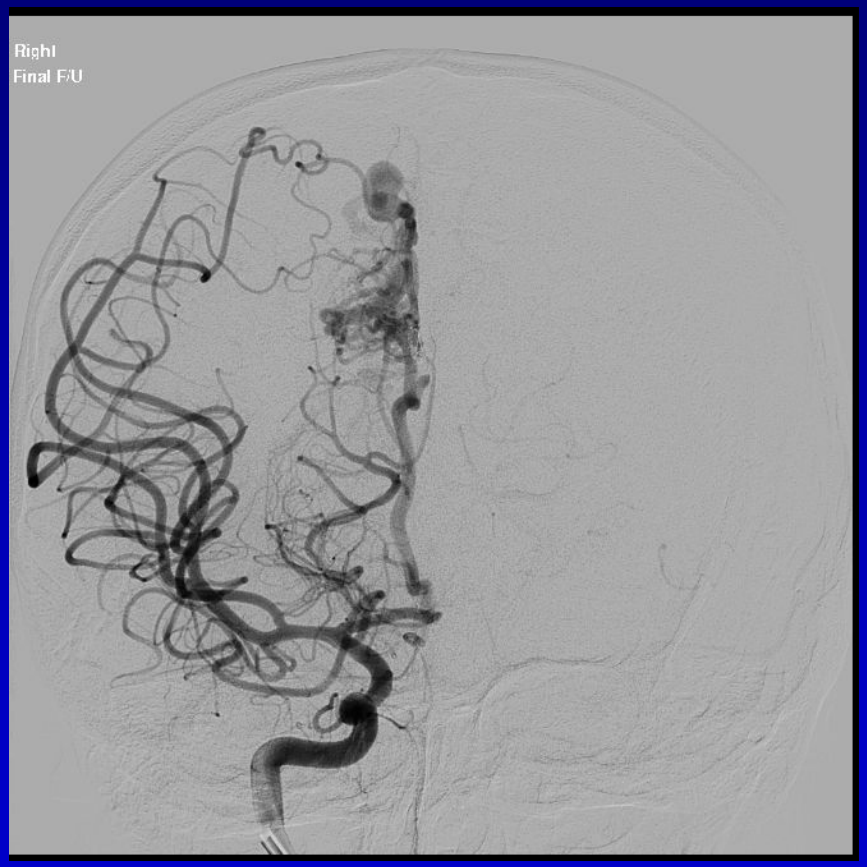
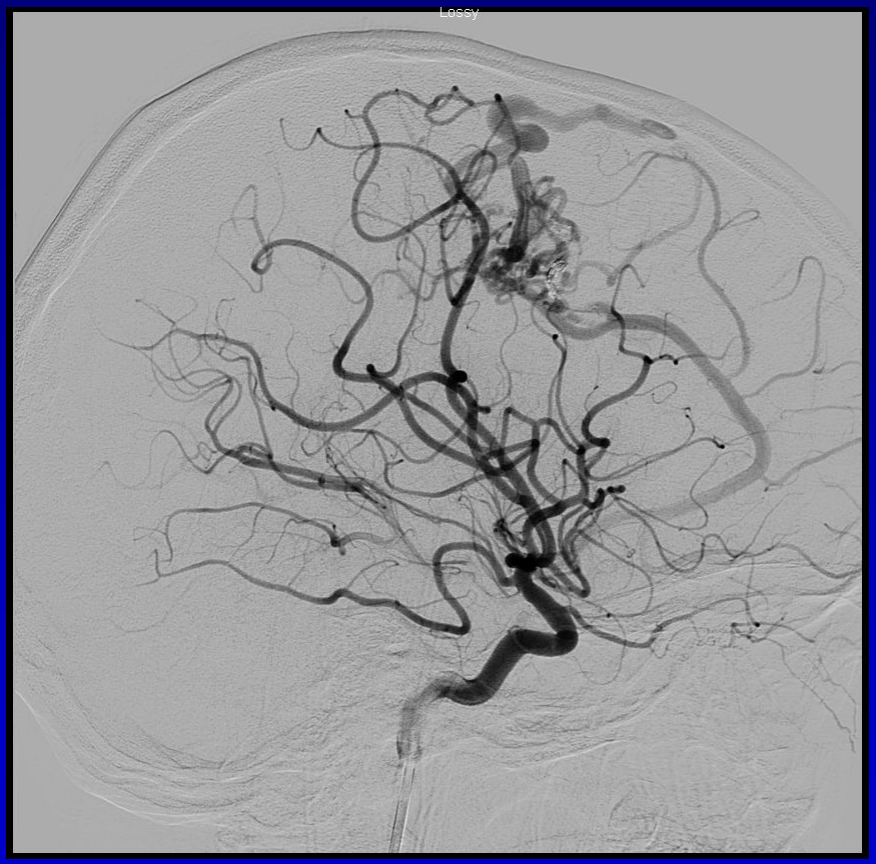


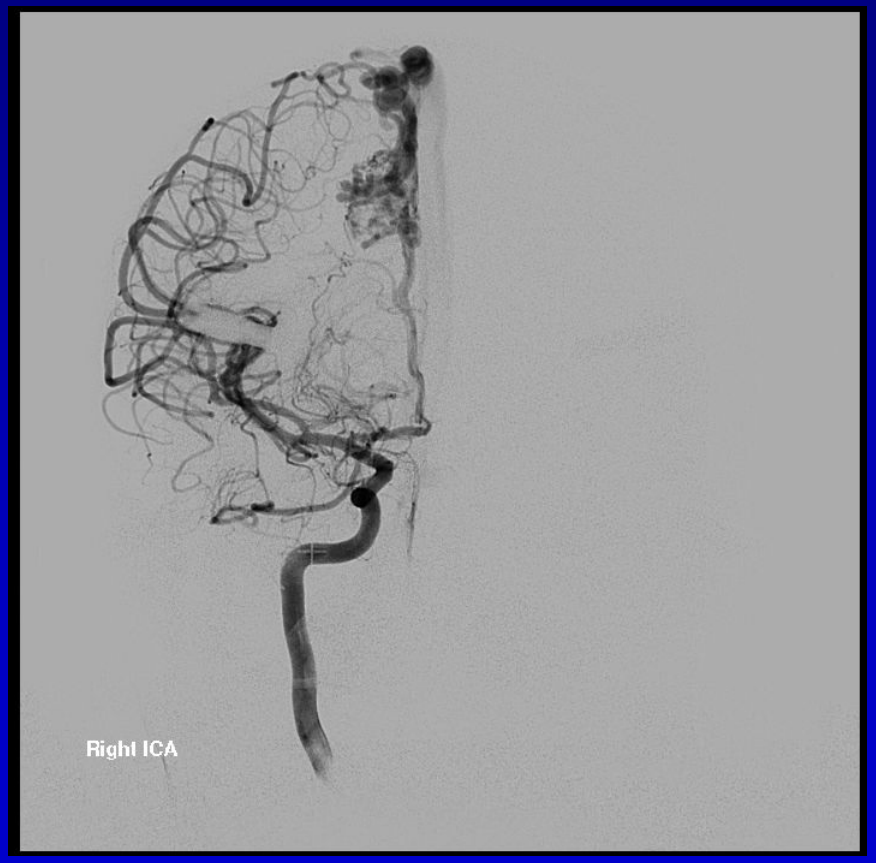


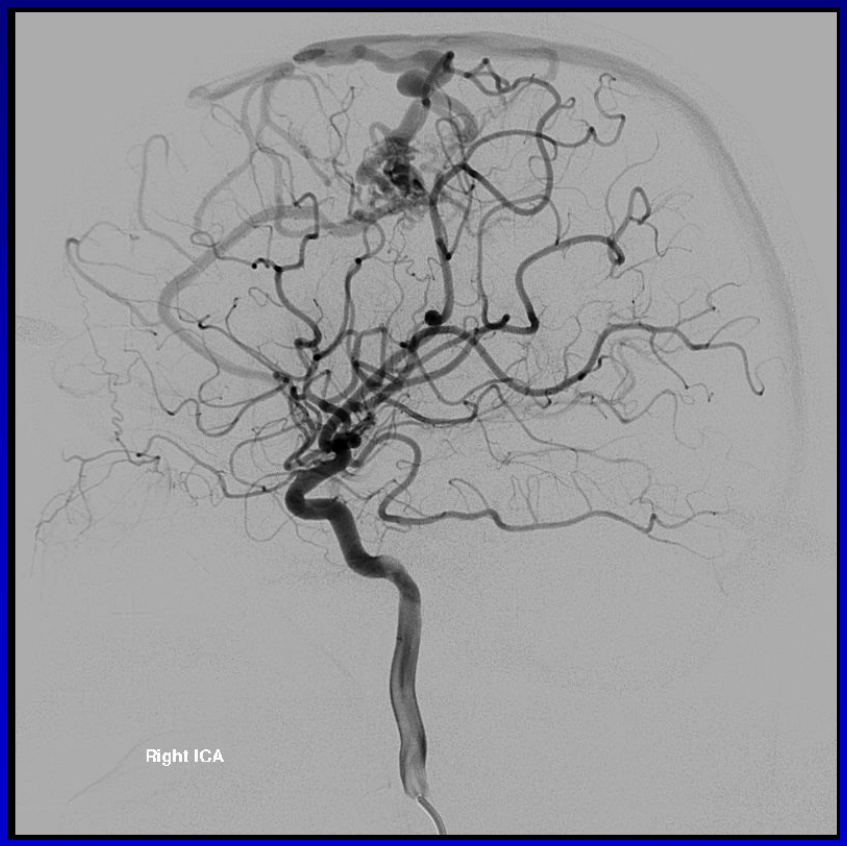
Glue Embolization



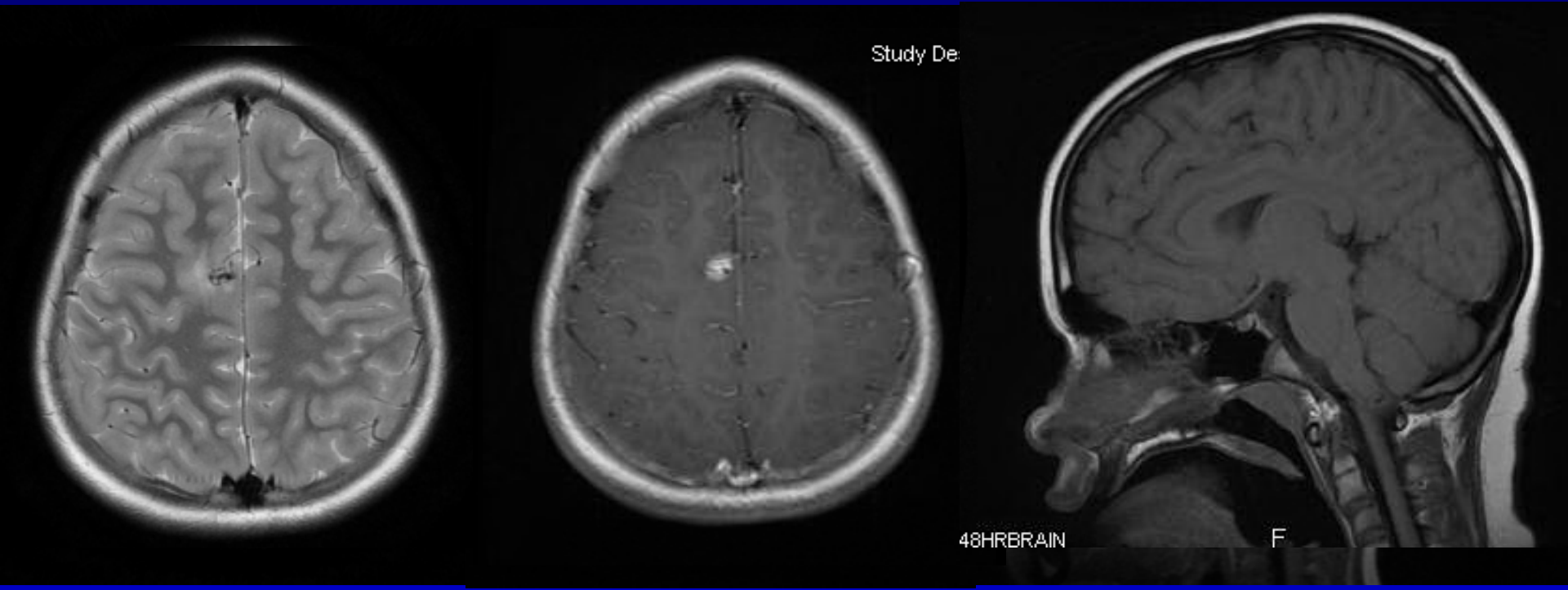


Gamma Knife Treatment





Follow Up MRI 1 yr



Conclusions

- 14.5% HHT patients had CVM
- 9.2 % HHT patients had AVM
- 2.6% HHT patients had DVA
- 1.3% HHT patients had a cavernous malformation
- 1.3% HHT patients had a capillary telangiectasia
- HHT AVMs were found to be small in size and superficial in location

Future Directions

Determine the natural history of CVM in HHT in order to guide treatment decisions

Determine whether routine screening and treatment for CVM in HHT is better than the natural history

Thank you