THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER

Difficult neurosurgical issues in managing hemangioblastomas in VHL

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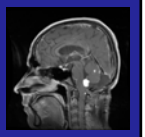
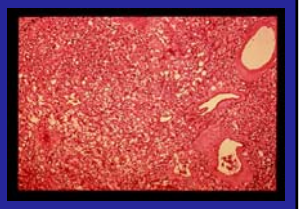


Hemangioblastoma

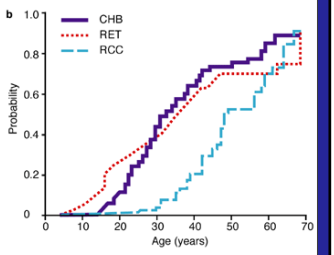
- Cell of origin: "embryonic hemangioblast"
- Sharp margin
- Associated with pial surface
- Very vascular
- In 65%, von Hippel-Lindau disease is present



Tumor initiation over time in VHL

List of tumours and cysts that can develop in VHL disease:

- Cerebellar haemangioblastoma
- Retinal angioma
- Spinal haemangioblastoma
- Renal cell carcinoma and renal cysts
- Phaeochromocytoma
- Pancreatic islet cell tumour and pancreatic cysts
- Endolymphatic sac tumour of the inner ear
- Epididymal cysts



Distribution of hemangioblastomas in VHL

244 tumors in 25 patients

- 45% cerebellum
- 47% spinal cord

From Park et al, *PLoS* 2007

New standard surveillance imaging suggested by the VHL Family Alliance

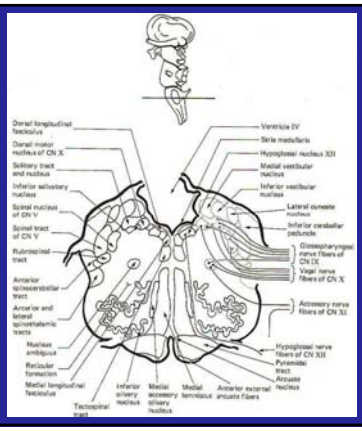
- Where are CNS tumors? [per NIH series]
  - Posterior fossa (cerebellum and brainstem): 60%
  - Spinal cord (cervical): 20%
  - Spinal cord (thoracic): 13%
  - Spinal cord (lumbar): 7%
  - ELST seen in 11-16% of VHL patients
- Recommended surveillance scan:
  - "MRI of brain and cervical spine, with thin cuts through posterior fossa, attention to inner ear/petrous temporal bone"….. which detects both ELST and 80% of hemangioblastomas

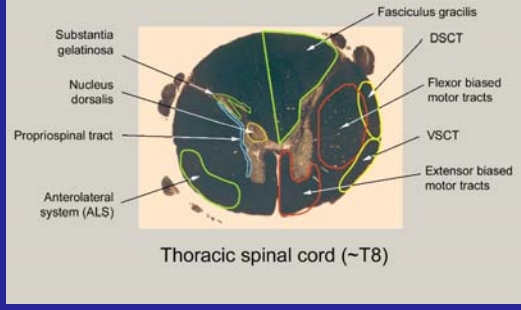
Ammerman et al, *J Neurosurg* 2006

Difficult issue #1:

Locations of these tumors are *quite* sensitive

Brainstem





Symptoms and Signs at the Time of Evaluation

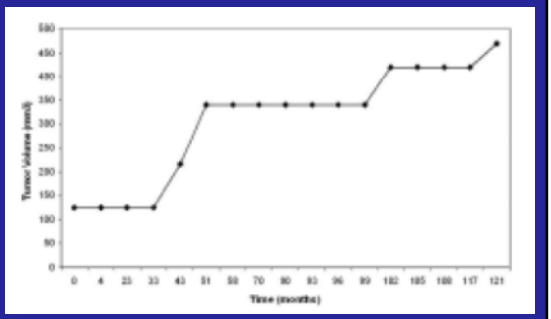
Symptom or Sign	Number of Patients (%)
Sensory disturbance of posterior columns and spinothalamic pathway	17 (94.4)
	15 (83.3)
Motor weakness	15 (83.3)
Abnormality of reflexes	15 (83.3)
Muscle atrophy	5 (27.8)
Localized pain	9 (50)
Sphincter disturbance	6 (33.3)
Impotence	1 (5.6)
Cranial nerve signs	1 (5.6)

Difficult issue #2:

Patient selection

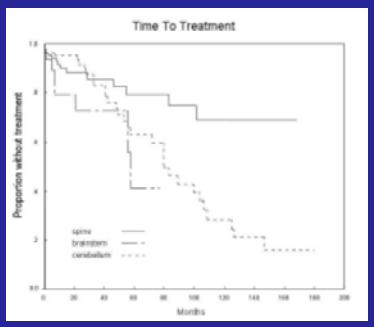
Smaller tumors managed conservatively show unpredictable patterns of progression

Untreated tumors show step-wise growth



From Ammerman et al, *J Neurosurg* 2006

What happens if you watch and wait?



Treatment is needed within 5 years in tumors of ...

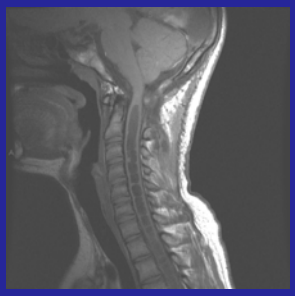
Cord: 20%
Cerebellum: 38%
Brainstem: 60%

From *J Neurosurg* 2006

Difficult issue #3:

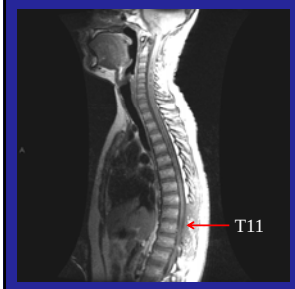
What is the best management of a tumor-associated syrinx?

The syrinx can be large



- Tumor is at T11
- Syrinx extends through entire cord
- *Myelopathy is from syrinx > tumor*

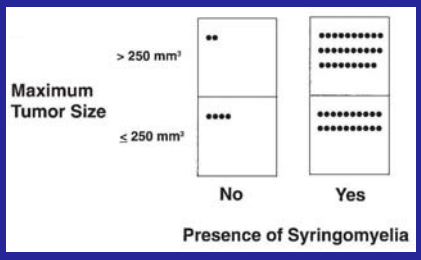
The syrinx is reversible



- Removing tumor clears syrinx
- Takes 4-12 weeks
- Mechanism unknown

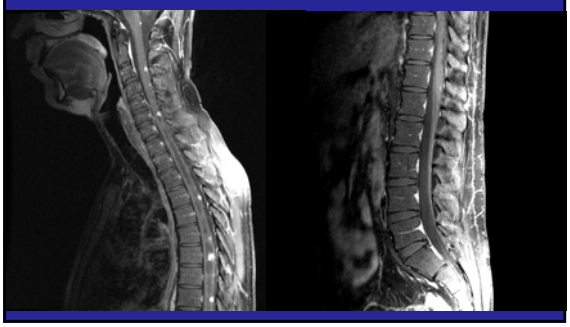
- If syrinx does not clear, suspect residual tumor!

Even small tumors can make a syrinx

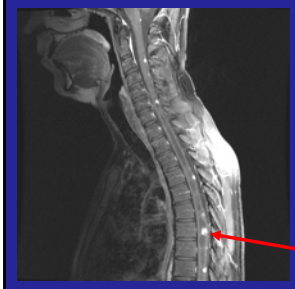


Lonser et al, *J Neurosurg* 86 (2003)

Which tumors sustain the syrinx?

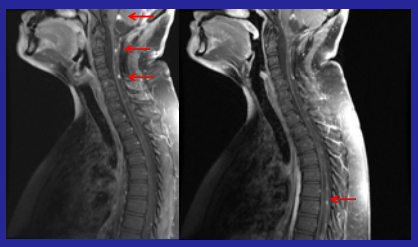


Pick your battles



- Multiple small tumors
- Too many to remove at once
- Syrinx makes the symptoms
- One tumor is primarily responsible for syrinx
- Treat <u>that</u> tumor first

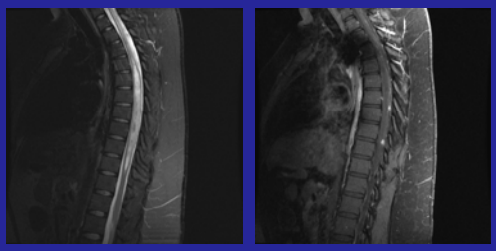
When tumors are multiple, but there is no syrinx



Upper 3 tumors were removed

Not the lower one(s)

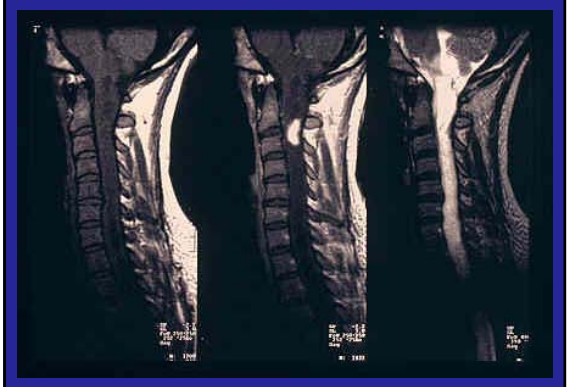
Syrinx persisted, so lower tumors had to be removed

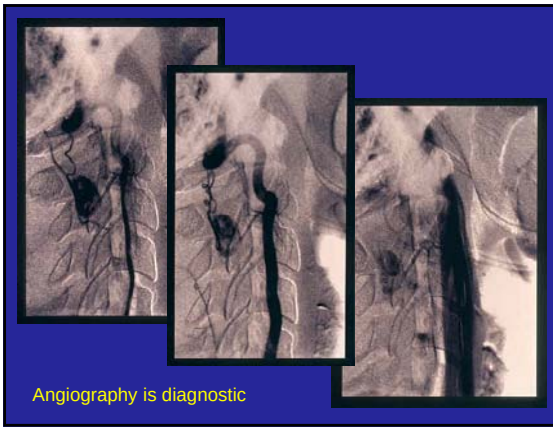


16 months after first operation

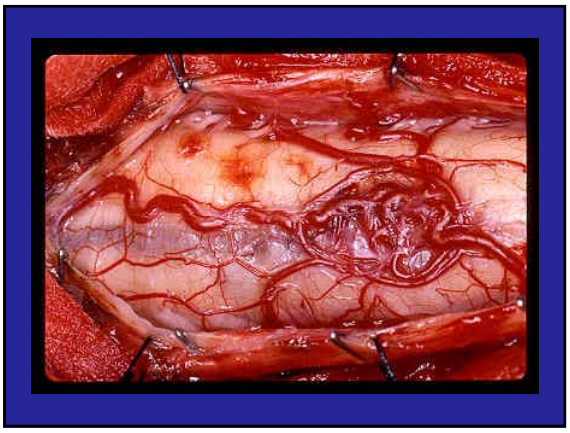
Difficult issue #4

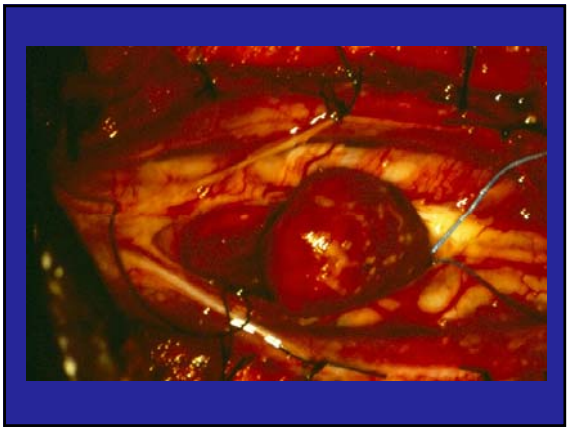
The hypervascularity of hemangioblastomas

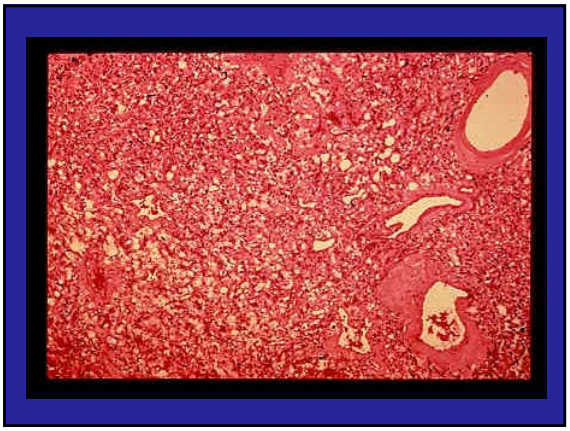




Angiography is diagnostic



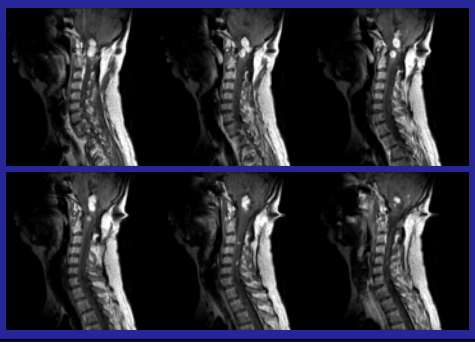




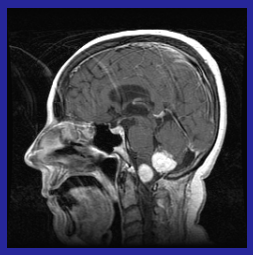
Difficult issue #5

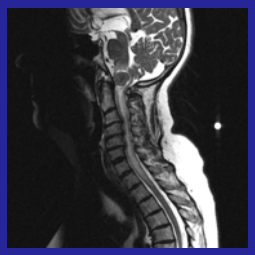
Large, complex tumors in tricky places

The cervicomedullary junction



This patient did *not* have tumor removal

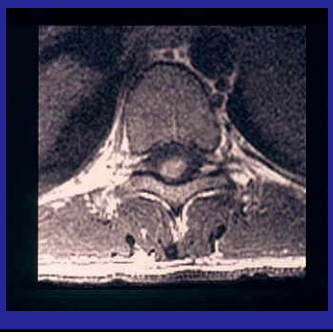




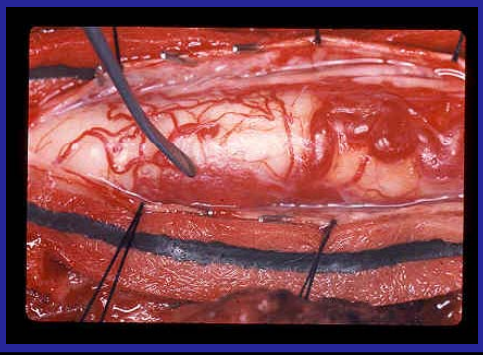
Cervicomedullary tumor + Cervical spinal stenosis

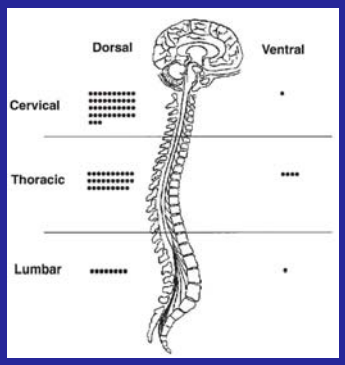
The spinal cord…not too difficult?

Looks accessible on MRI …but…



It comes to the surface laterally





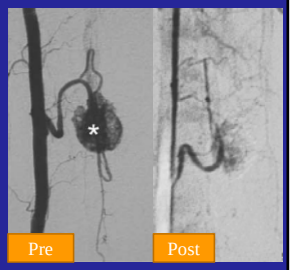
86 tumors
All operated

7% are ventral

Lonser et al, *J Neurosurg* 86 (2003)

Embolization? [answer: no]

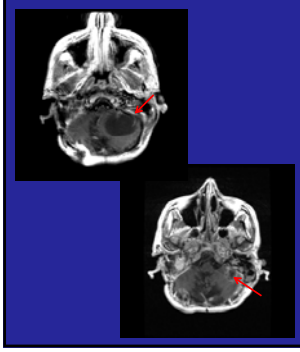
- Series are small
- ?Danger of spinal stroke
- Risk of bleeding with particulate emboli
- Not curative
- Requires high level of expertise



Difficult issue #6

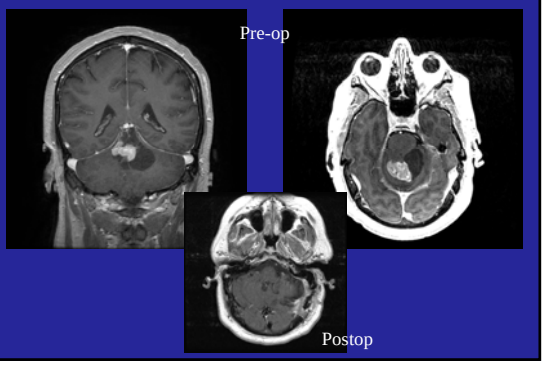
Dealing with a tumor-associated cyst in the brain

What to do about a tumor cyst



- 55% of tumors in large series have an peritumoral cyst
- If you remove the tumor nodule, the cyst will *always* resolve itself
- Stripping out cyst lining:
  - is unnecessary
  - can cause brain injury
  - will not prevent the cyst from coming back

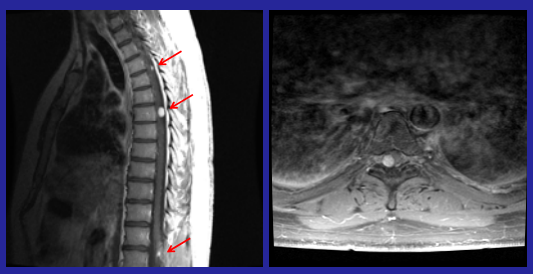
Sometimes a cyst is helpful!



Difficult issue #7

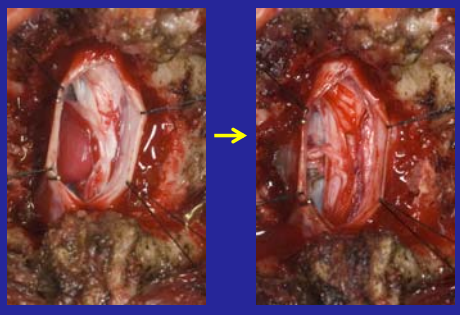
The optimal management of tumors *outside* the cord or brain

Some patients have tumors on nerve roots

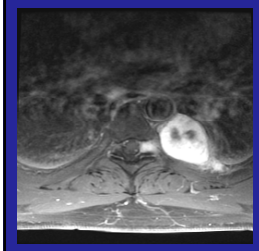


~ 20 cases have been reported

In surgery, they look like this

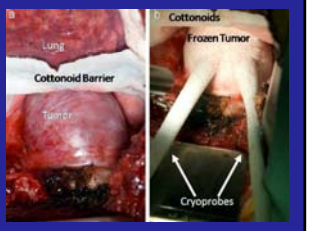


Tumor on nerve root going into chest



Big and vascular tumor

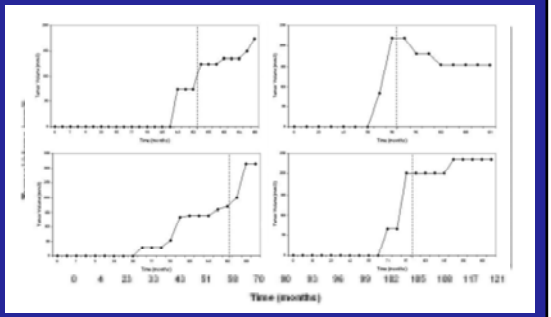
Cryoablation !



Difficult issue #8

Can radiosurgery replace surgery?

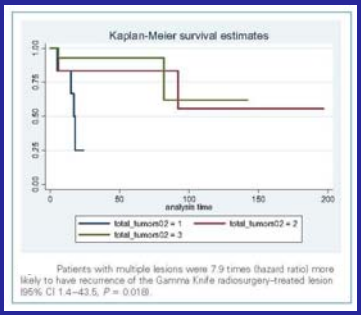
In many, radiosurgery does not work well



From *J Neurosurg* 2006

University of Virginia series

Radiosurgery for hemangioblastoma



Note:
89% of patients with VHL have multiple hemangioblastomas

Local tumor control rates were:
1 yr 89%
5 yr 74%
10 yr 50%

Sayer et al, *World Neurosurgery* 2010; Ammerman et al, *J Neurosurg* 2006

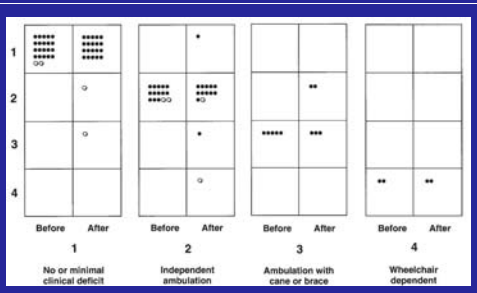
Difficult issue #9

The neurological complications of surgery

Immediate neurological decline after surgery is seen, usually as new sensory dysfunction, but it is not inevitable….

Most maintain their function.

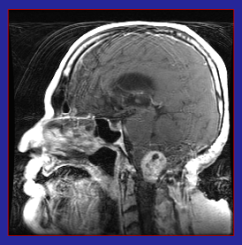
Neurological status before and after surgery in hemangioblastoma patients



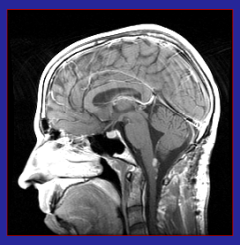
Open circles = ventral tumor

Lonser et al, *J Neurosurg* 86 (2003)

Recovery depends on *which symptom* and on *degree of preop deficit*



Weakness



Intractable nausea

The better the neurological condition of the patient is before surgery, the better the condition will be after surgery.... and the more rapid and complete the recovery.

Therefore, waiting for profound clinical decline is unwise.

We need a good drug—but which?

Baseline

After Rx (pazopanib)