# Case 1: 40yo with R-sided cranial nerve defects

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GLOBAL OUTREACH

# Case presentation

A 40 yrs old male, a known alcoholic, smoker and seropositive on HAART presented himself to our OPD in December with C/O- slurred speech, Headache, R-side deviation of angle of mouth, difficulty in swallowing and hard of hearing.

Started Atripla in January 2015, CD4 230 in September (nadir or VL not known). HAART stopped in late December.

# O/E

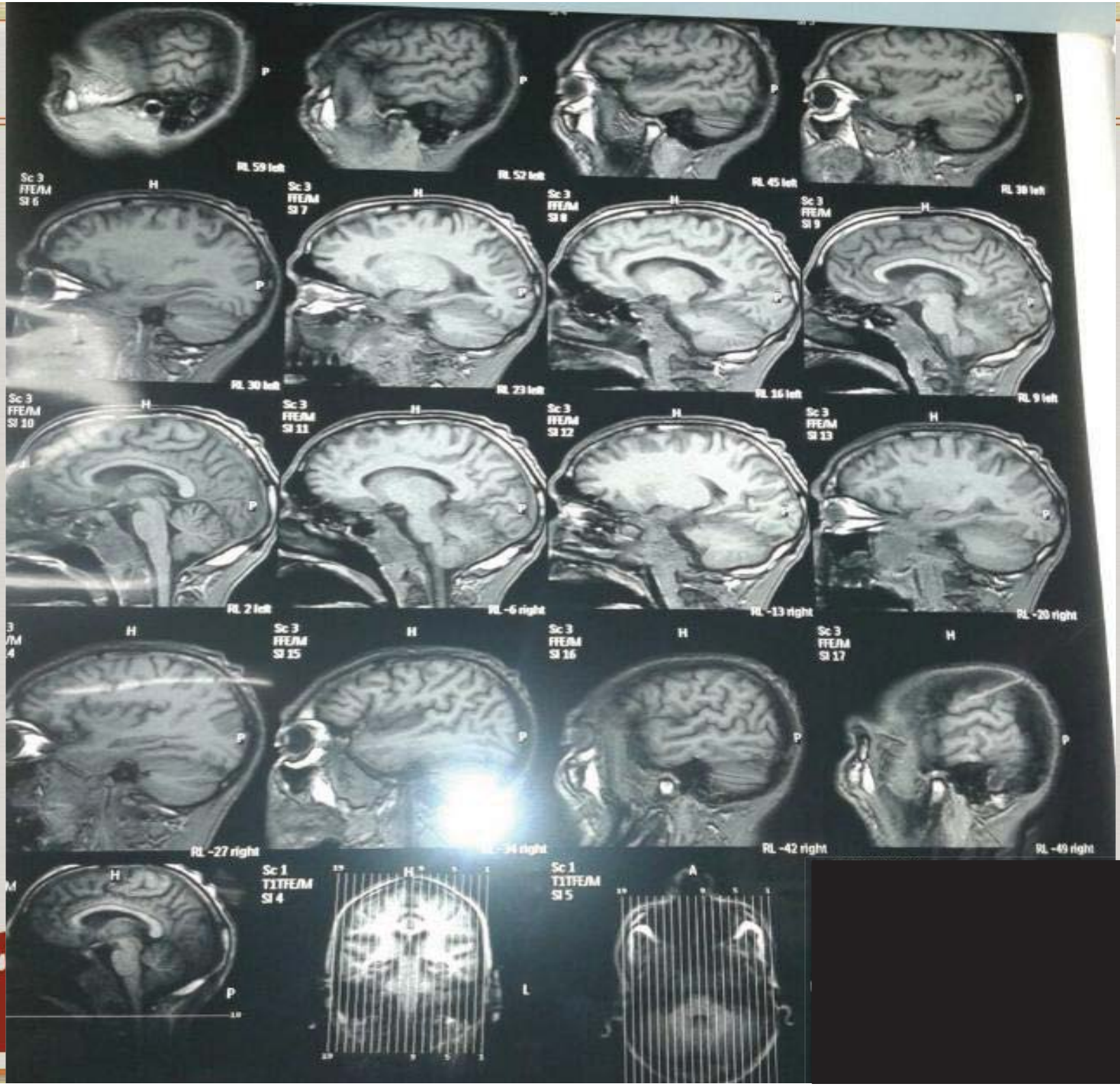
- G/E- Dehydrated, emaciated, pallor.
- CVS-NAD.
- RS-B/L-Lung fields Rhonchi(+).
- P/A-Soft.
- Oral cavity- candidiasis.
- CNS-GCS-15/15.
- Reflexes-Intact.
- Sensory- Intact.
- Motor
- Power-5/5, Tone- Normal in all 4 limbs.

# Cranial nerves

- Drooping of eyelid and difficulty in movement of eyeball on R-side, difficulty in chewing & facial muscle wasting (CNs- III, IV, V, VI & VII).
- Hard of hearing & Loss of equilibrium (CN-VIII).
- Difficulty in swallowing and loss of taste (CNs- IX & XI).
- Difficulty in shrugging of shoulder joint (CN-XI)
- Frozen and atrophic tongue (CN-XII).

# Supportive care

- Started on I.V ABX – suspected pneumonitis.
- Ryle's tube intubated to avoid further aspiration pneumonia.
- Started on I.V Dexamethasone and later on changed to prednisolone.
- I.V fluids- dehydration.
- Baseline blood investigations.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Sc 3 FFE/M SI 13
RL 2 left
RL -6 right
RL -13 right
RL -20 right
Sc 3 FFE/M SI 15
Sc 3 FFE/M SI 16
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RL -27 right
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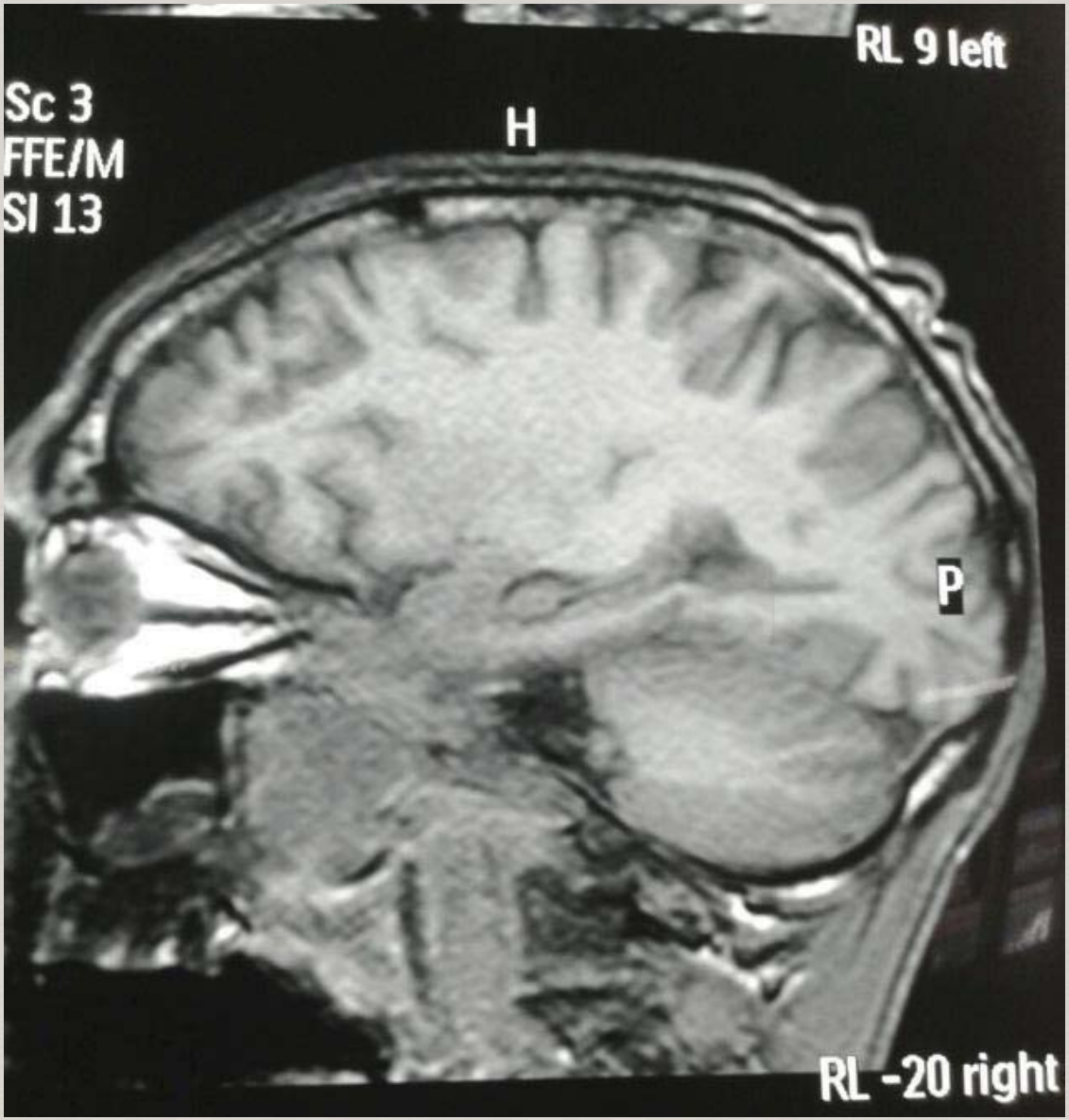
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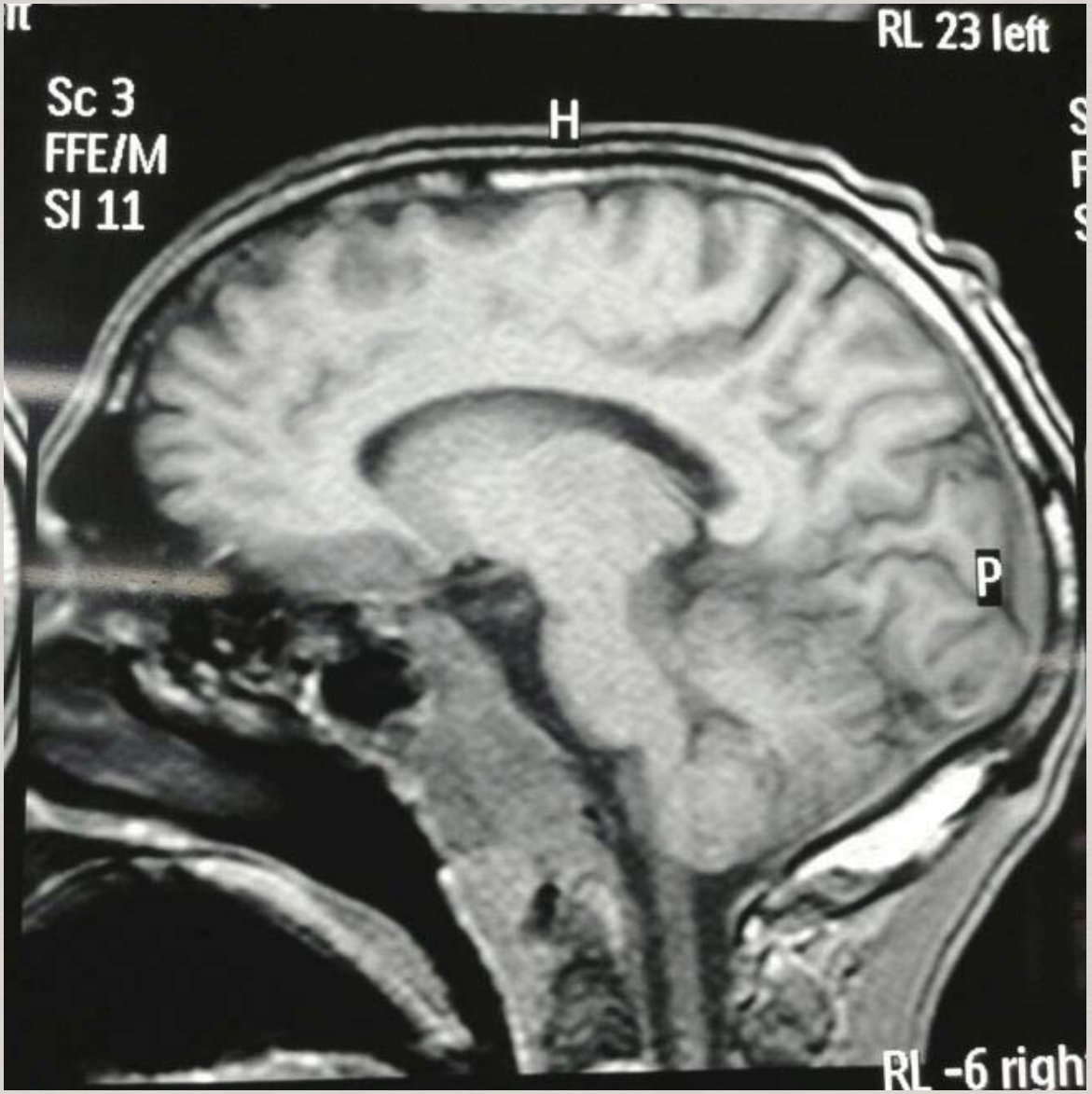
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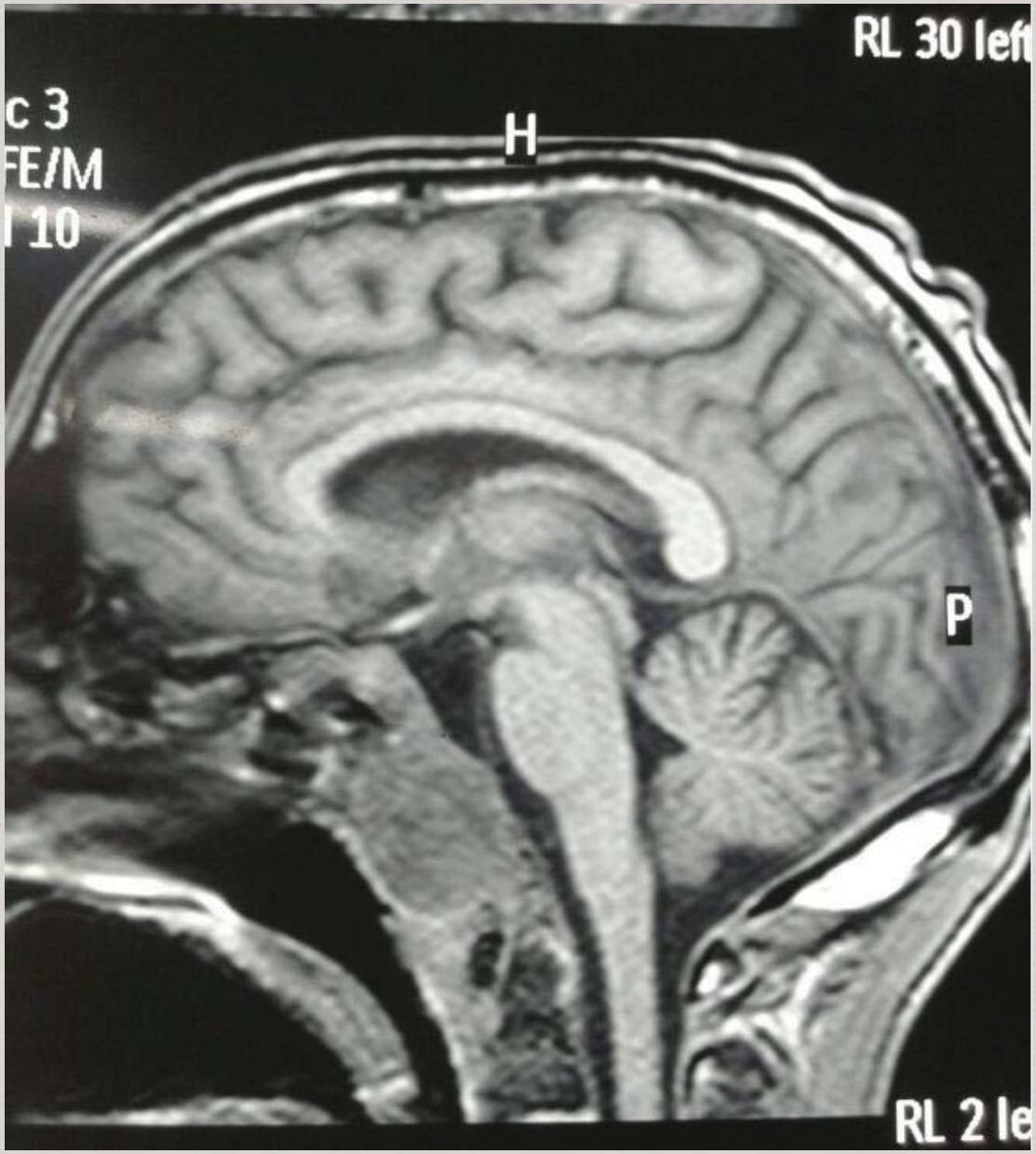
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# Imaging

- **CXR-** S/O Aspiration pneumonitis.
- **CT** Scan brain in late December- Bone destruction found at the clivus. Chordoma is suggested with Severe paranasal sinusitis.
- **MRI** Brain in early January- A mass, 3.8x2.2 cm found in the clivus. Bone destruction in base of the skull and lesion found invade the sphenoid and it suggested chordoma of skull base.

# Discussion

# Background

- **Rare** tumors, that **arise from embryonic notochordal remnants** along the length of the neuraxis at developmentally active sites.
- These sites are the ends of the neuraxis and the vertebral bodies.
- **<0.2**% of **CNS** tumors.
- Relatively **slow-growing**, **low-grade** malignancies.

# Epidemiology Incidence

- Chordomas are rare neoplasms.
- Constitute 0.2% of all CNS tumors.
- Generally occur in **4 locations**, they arise from
- Sacrum- 50%–60%.
- Skull base region (spheno-occipital/nasal) 25%–35%.
- Cervical vertebrae- 10% of cases, and
- Thoracolumbar vertebrae in approx 5%.

- **M/F** ratio is **2:1**.
- Intracranial chordomas present in a much younger age group than their spinal counterparts.
- The **average age** at diagnosis of all patients with chordomas was **56** years, with an age range of 27-80 .

# Etiology

- Thought to arise from primitive notochordal remnants along the axial skeleton.
- Most exhibit complex abnormal karyotypes including whole or partial losses of chromosomes 3, 4, 10, and 13, gains in chromosome 7, and rearrangements of chromosome 1p.

# Pathophysiology

- Characterized by **slow growth**, with **local destruction** of the bone and **extension** into the **adjacent** soft tissue.
- **Low metastatic** potential; however, **distant** metastasis to **lung**, **bone**, **soft tissue**, **lymph node**, **liver**, and **skin** has been reported in up to 43% of patient
- Eventually, they may be responsible for mortality.

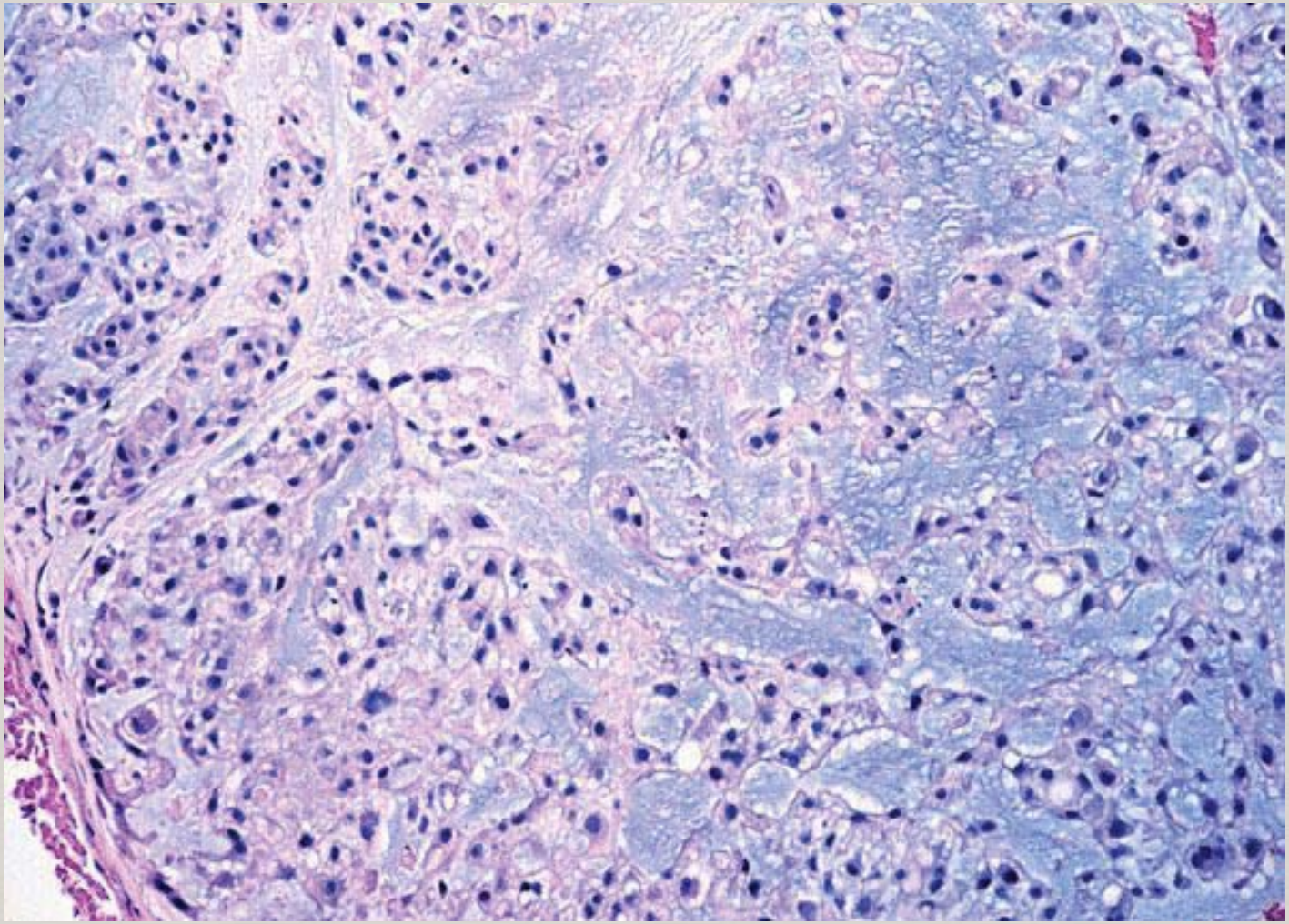
# Presentation

- **The clinical presentation is entirely dependent on the location of the chordoma.**
- With intracranial tumors, the most common presenting symptoms are **diplopia** and **headache**.
- **Neurologic signs** occur in >50% of the patients, **primarily as cranial nerve palsies**. Palsies of cranial nerve VI and the sensory branch of V are the most common.

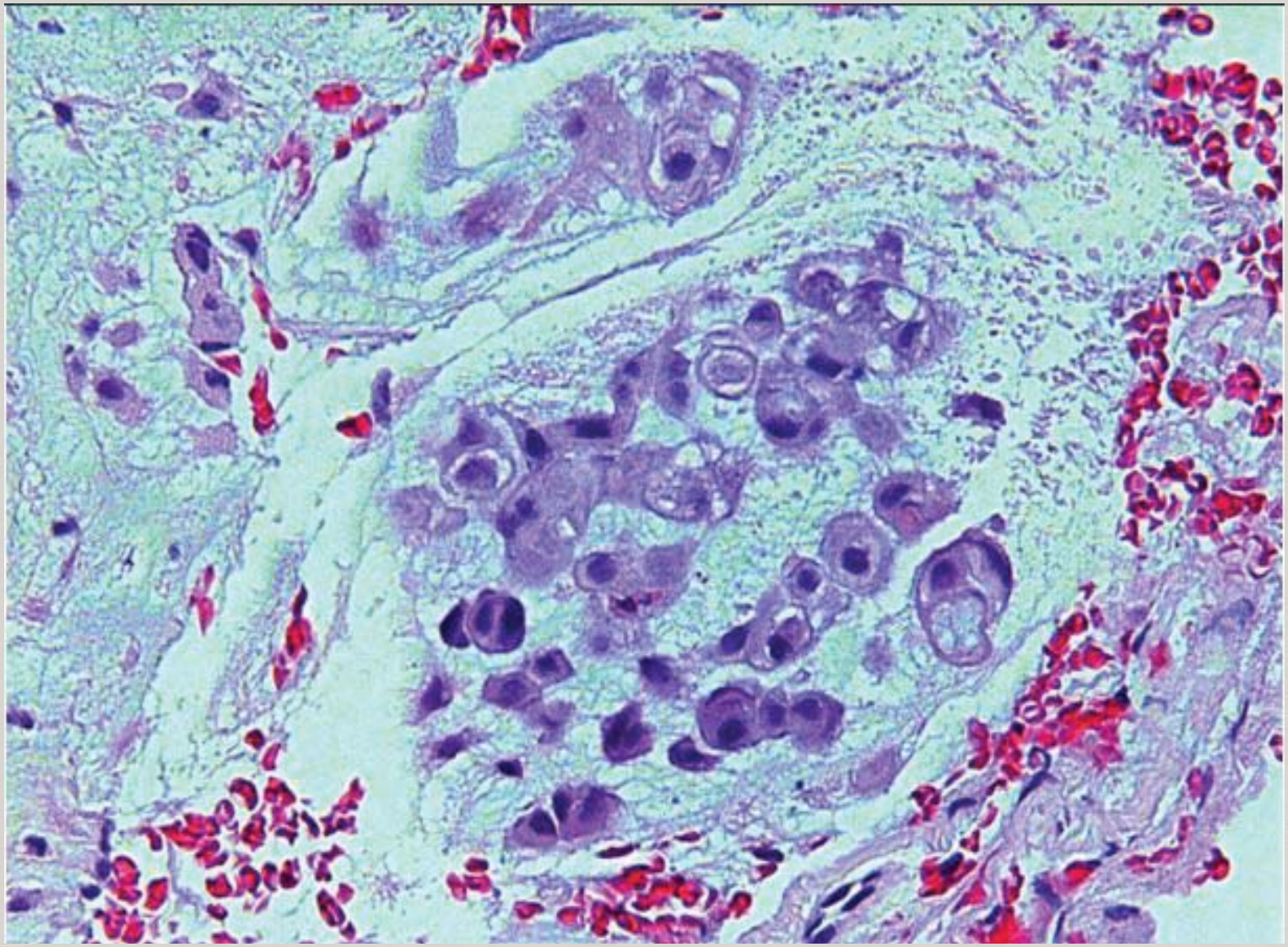
# Radiographic features

- **MRI and CT scan have complementary roles in the evaluation of chordoma**.
- **CT** evaluation is needed to assess the degree of **bone involvemen**t or **destruction** and to detect patterns of **calcifications** within the lesion.
- **MRI** provides excellent **3-D analysis** of the posterior fossa (especially the brainstem), sella turcica, cavernous sinuses, and middle cranial fossa.

# Light microscope, H&E Physaliferous cells & mucinous matrix



# Higher mag LM, H&E showing physaliphorous cells



# Management

- **Surgery continues to be the primary modality in the management as they continuously grow, albeit slowly, and erode bone and adjacent soft tissue, causing marked destruction of surrounding tissues.**
- Rates of local recurrence, as well as survival, appear to be dependent on the achievement of negative surgical margins, with recurrence rates on the order of 70% in cases where negative margins are not achieved.
- **Tzortzidis et al**. used aggressive surgical approaches to achieve total resection in up to 70% of patients, resulting in long-term control in >50% of cases.

# Contraindications

- Excision of a chordoma primarily are related to general health of the patient, Surgical accessibility and preexisting medical conditions.

# Role of RTP

- Chordomas are considered **radioresistant** tumors and require doses > **60 Gy**.
- **Conventional** RT with high-energy photons up to a dose of 50–55 Gy does **not** provide a **high local control**, because of the proximity of chordomas to vital neurological structures such as the brain stem, optic pathway limits the dose of radiation that can not be safely delivered.
- Therefore, highly focused radiation such as **Proton** Therapy and **carbon ion** therapy are more **effective** than conventional x-ray radiation.

- A meta-analysis by **Di Maio et al.** confirmed that both **5-yr PFS and OS** of skull-base chordomas are **enhanced** by **complete resection** of the tumor.
- Furthermore, this analysis suggests that **adjuvant RT** is of no additional benefit to total surgical resection, but is **warranted** in cases of **incomplete resection**. The actuarial 5-yr local control rate was 73% using tumor dose.

# Role of systemic therapy

- There are no drugs currently approved to treat chordoma, however, the advent of **molecularly targeted therapies** has raised interest for their use in low-grade malignancies with poor response to chemotherapy. a clinical trial conducted in Italy using the **PDGFR** inhibitor **Imatinib** demonstrated a modest response in some chordoma patients.
- The same group in Italy found that the combination of **imatinib** and **sirolimus** caused a response in several patients whose tumors progressed on imatinib alone.

- **Casali et al.** treated 6 chordoma patients with **imatinib** at 800 mg daily and observed nondimensional tissue responses, marked by **hypodensity** and **decreased** contrast **uptake** on CT scan (and concordant changes on MRI).
- **Casali et al**. also reported that the addition of low-dose cisplatin to the treatment of patients with chordoma who progressed on imatinib restored sensitivity of the tumor, suggesting **synergism** between **imatinib** and **cisplatin**.

# Prognosis

- Surgical outcomes are dependent on **location** and **tumor size** at diagnosis.
- The overall median survival with chordoma has been estimated to be approx. 6yrs, with a survival rate of 70% at 5 years, falling to 40% at 10 years.

# Conclusion

- Chordomas are **rare** primary bone tumors with a **high risk for local recurrence** and modest propensity for distant metastasis.
- **Surgery is the primary modality** to achieve the best long-term control. However, the location of these tumors makes en bloc excision to achieve adequate negative margins technically challenging.
- **Conventional RT** has a proven role; however, the high doses required for these **radioresistant tumors** lead to significant toxicity to surrounding normal tissues and limit its therapeutic value.
- **Newer** techniques and **charged particle** radiotherapy allow for **better dose** delivery, and hence better **disease control**.
- **Chemotherapy** has virtually **no role** in this disease; however, **molecularly targeted** therapy is showing **significant promise** and is an area of great potential.

THANK YOU

# Case 2: 50yo with femur fracture

Dr. Garcia

Oncologist

Francistown

26 January, 2016

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# History of Present Illness

- 50 y/o male patient admitted at NRH in October 2015 for fracture in left femur

- X-ray of legs showed complete fracture of left femur with multiple image radio-transparent that suggested a lot of bone tissue mass

# History of Present Illness

- Patient underwent operation and fracture was reduced and bone was fixed with internal device

- Patient successfully recovered and came to O.P.D. of oncology in Jan 2016 for f/u.
  - Walking with crutches
  - No complaints referred

# Lab Test Results

- WBC: 7,08 x $10^3$; Hb: 13.6 g/l;
  Platelet: 357 x $10^3$; Neutrophils: 3,1
- Alkaline Phosphatase: 179 u/l (35-10)
- Total Protein: 84g/l (60-80)

# Treatment Received

- HIV + on treatment
- Patient is now under chemotherapy for 6 cycles
  - Includes Cisplatin 100mgBS plus Adriamycin 70mgBS