Skull Tumors

PATHOLOGY

1. BONE FORMING TUMORS

1) OSSIFYING FIBROMAS - giant cells around hemorrhagic foci, numerous spindle-shaped fibroblastic cells, and new bone formation; tumor cells are smaller than those of giant cell tumor of bone, whereas stromal cells and giant cells resemble each other.

2) NONOSSEOUS FIBROMAS - fibroblastic proliferation with multilamellar giant cells.

3) XANTHOMA - foamy xanthomatous cells.

4) ENGEL'S SARCOMA - uniform, densely packed small cells with indistinct cytoplasmic borders.

5) GIANT CELL TUMOR (OSTEOCLASTOMA) - well-vascularized tissue mass of plump, spindle, or oval stoma cells together with uniformly dispersed, numerous, large, multinucleated giant cells.

2. CARTILAGE FORMING TUMORS:

1) CHONDROMA (enchondroma, juxtaarticular chondroma, osteochondroma) - mature hyaline cartilage; arise from cartilaginous portion of bone formed by enchondral ossification (skull base and parasphenial sinuses).

2) CHONDROMYXOID FIBROMA - chondroid and myxoid differentiation with lobular growth.

3) CHONDROBlastoma - immature cartilage cells.

4) CHONDROSARCOMA (third most common malignant skull tumor); often associated with abnormalities of chromosomes 10 and 22; low-grade type (myxochondrosarcoma) - chondroid and immature cartilage deposition in areas of myxomatous change and cystic degeneration; high-grade type (mesenchymal chondrosarcoma) - absence of cartilage lobules and presence of fibrocartilagenous areas (groups of chondromatous cells lose their usual lobulation and begin to spindle out); both types are vimentin positive.

3. CONNECTIVE TISSUE TUMORS

1) DERMATOFIBROMA (very rare) - fibrous connective tissue origin marked by collagen formation.

2) FIBROMYCOSIS (very rare) - varying amounts of collagen production and absence of bone, osteoid, or cartilage; medullary subtype has better prognosis than peripheral subtype.

4. HISTIOCYTIC TUMORS (very rare):

1) APOCRINE GLAND CARCINOMA - gland cells around hemorrhagic foci, numerous spindle-shaped fibroblastic cells, and new bone formation; tumor cells are smaller than those of giant cell tumor of bone, whereas stromal cells and giant cells resemble each other.

2) PALAIS GRANULOMA - immature cartilage cells.

3) XANTHOMA - foamy xanthomatous cells.

4) ENGEL'S SARCOMA - uniform, densely packed small cells with indistinct cytoplasmic borders.

5) GIANT CELL TUMOR (OSTEOCLASTOMA) - well-vascularized tissue mass of plump, spindle, or oval stoma cells together with uniformly dispersed, numerous, large, multinucleated giant cells.

5. TUMORS OF BLOOD OR BLOOD VESSEL ORIGINS

1) EOSINOPHILIC GRANULOMA (common) - mononuclear histiocytes* mixed with eosinophils; giant cells and areas of hemorraghe or necrosis may be observed.

*Histiocytes stain positive for protein S-100; on electron microscopy, Birbeck granules (that characterize Langerhans or X cells) are noted

2) HEMANGIOMA (10% of benign skull tumors) - non progressive brownish red lesions under skull peristome, microscopically - capillary, cavernous, or venous blood vessels.

3) LYPHANGIOMA (rare) - consist of lymph vessels.

4) ANgiOlysinOSIS (hemangiopericytoma or hemangioblastoma) - irregular anastomosing vascular channels lined by one or more layers of atypical endothelial cells and pericytes, which have anaplastic immature appearance.

6. TUMORS OF NEUROEPITHELIAL ORIGIN

1) CHONDROSARCOMA - arise from cartilaginous portion of bones formed by enchondral ossification (skull base and paranasal sinuses).

2) CHONDROMYXOID FIBROMA - fibroblastic proliferation with multilamellar giant cells.

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7. TUMORS OF SQUAMOUS CELL ORIGIN

1) SQUAMOUS CELL CARCINOMA (nasal sinuses and temporal bone)

8. TUMORS OF APOCRINE GLAND ORIGIN (salivary, lacrimal glands); propensity for perineural spread.

9. METASTASIS (skull is common site!); dura is effective barrier - brain invasion is rare!

10. OTHER TYPES

1) FIBROUS DysPLASIA - see below

2) Paget Disease - initially increased osteoclastic activity (bone resorption) - increased osteoclastic activity (bone formation)

3) Paget Disease - see p. 122

4) ANGiomATOUS BONE CYSTS - large vascular spaces (lack endothelial lining) separated by trabeculae of connective tissue and bone; locally aggressive lesions - continue to expand until treated.

5) INTRADURAL MYELOMAs

6) MULTIPLE MYELOMA - widespread osteolytic bone destruction by dense tumor cells that look like plasma cells clustered in close aggregates.

• 19% are benign and 81% - malignant.

• Features of benign tumors:

1) single, small, grossly round / oval lesion

2) peripheral sclerosis

3) intratrabecular calcifications

4) peripheral bone vascularity

5) malignant transformation (to osteosarcoma, chondrosarcoma, or fibrosarcoma) - in 2% Paget Disease and 0.5% Fibrous Dysplasia cases.

• Lesion LOCATION is of little differential diagnostic value, but certain tendencies exist:

1) lesions of developing origin - strong midline propensity;

2) osteomas - parasanal sinuses, frontal bone;

3) ossifying fibromas - frontotemporal region;

4) Paget Disease - see above

5) fibrous dysplasia - see above

6) multiple myeloma - widespread osteolytic bone destruction by dense tumor cells that look like plasma cells clustered in close aggregates.

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• Features of benign tumors:

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**SKULL TUMORS**

**Eosinophilic Granuloma** causing *MENINGIOMA* - frontoparietal area; *PAGET DISEASE* - skull base, usually multicentric; *carotid tumors* - skull base; *Giant Cell Granulomas* - sphenoid, temporal, and ethmoid areas; *hemangiomas* (more common in vertebral column; *globular variety* - skull base; *sexicide type* - frontotemporal region). 

**Sphenoid and dermoids** - cerebellopontine angle, parasellar region, calvaria (dermoids prefer midline).

**Hyperostoses** - local overgrowth of skull bones: 
- **a)** induced by *INTRACRANIAL MENINGIOMAS*
- **b)** nonneoplastic

- Hyperostoses may involve either outer or inner tables;
  - outer table involvement is insignificant except for possible disfiguration.
  - hyperostoses of inner table rarely grow enough to compress intracranial contents.

**Hyperostosis frontalis interna** - asymptomatic symmetric hyperostosis of inner table of frontal bone - common incidental finding in women > 40 yrs; diploe and external table are not affected; differentiate from *en plaque MENINGIOMA*.

**Epidemiology**
- account for ≈ 1% of all bone tumors.
- most manifest in young adults! (except *INTRAOSSEOUS MENINGIOMA*, *PAGET DISEASE*, *MULTIPLE MYELOMA*, *SQUAMOUS CELL CARCINOMA* - affect older adults).

**Clinical Features**
1. **Enlarging skull mass ± pain / tenderness** (due to periosteal involvement).
   - **Osteoid Osteoma** - nocturnal local tenderness relieved by NSAIDs.
   - **Rapidly growing mass** - *ANEURYSMAL BONE CYST*, *CHONDROBLASTOMA*, *CHONDROMYXOID FIBROMA*, *DESMOPLASTIC FIBROMA*, *GIANT CELL GRANULOMA* or malignant tumor.
   - **Malignant tumors** without pain - *MULTIPLE MYELOMA*, *OSTEOSARCOMA*.
2. **Cranial nerve deficits** (if tumor involves skull base), e.g. visual and hearing loss.
3. **Dural erosion**, direct brain compression.
4. **Recurrence sinusitis, CSF rhinorrhea** - if tumor obstructs sinus ostium → mucocele (encapsulated, thick fluid collection); mucocele may erode through base of skull to compress intracranial structures.
5. **Subdural collections** - associated with malignant tumors invading dura (esp. metastatic).

**Hand-Schüller-Christian disease:**
1) diabetes insipidus
2) exophthalmos
3) bone lesions

**Ollier syndrome** - multiple enchondromas.

**Maffucci syndrome:**
1) enchondromas
2) dyschondroplasia
3) cavernous hemangiomas of soft tissues / viscera

**Diagnosis**
Plain skull radiography with special projections, CT (extent of intracranial extension):
- **a)** *radiolucent (osteolytic)* - most tumors (benign and malignant)
malignant tumors - irregular poorly defined borders, no periosteal reaction.

OSTEOMA — condensation of cortical bone (circumscribed homogeneous bone density) which may project external to skull (exostosis) or towards cranial cavity (enostosis); arises from outer table without involvement of diploë (infract OSTEOMA may be radiolucent; OSTEOMA — radiolucent nodule with surrounding dense sclerosis).

OSTEOMAS — well-demarcated, non-enhancing lytic lesion with smooth calcified margins. OSTEOMAS — well-demarcated osteoid lesion with varying degrees of calcification.

DESMOPLASTIC FIBROMA - well-defined lytic and expansive lesions with typical soap bubble appearance; causes thinning of overlying cortex without peritumoral reaction.

GIANT CELL GRANULOMA - radiosclerotic, well demarcated, multiloculated, with expansion and thinning of bone cortex; CT - isodense lesion, which may erode overlying cortical bone.

NONOSTEOMATOSO FIBROMA, XANTHOMA - radiolucent with sclerotic margins and bony trabeculae with soap bubble appearance.

XANTHOMA - radiolucent, oval, well-demarcated lesion without sclerosis; appearance of punched-out defect or doughnut-shaped lesion that involves both inner and outer table; CT - soft tissue mass with area of bony destruction (central density may also be present).

Hemangiomata - well-defined nonenhancing lytic lesion with characteristic honeycomb or trabecular appearance; 33% show peripheral sclerosis; 10-15% show classic "sunburst" or "spoke wheel" pattern (spicules radiate from central point); intralesional calcifications are common, prominent vascular groove may be seen in vicinity (external carotid arteriography sometimes shows blush); diploë is expanded, but inner table is preserved!

Hemangiomata of skull vault (A - lateral radiograph, B - CT, bone window - well-defined lucency in frontal bone typical "spoke wheel" appearance (due to prominent vascular compression).

EMANGIOMA - cystic bone defect.

ANEXOPHALIC BONE CYST - well-demarcated lesion that arises from diploë (expands both inner and outer tables; CT - multiloculated expansile lesion with characteristic fluid level.

ENEXOPHALIC BONE CYST - round lytic lesion arising within diploë; may expand inner and outer tables away from each other; sharp dense sclerotic borders that involve all three layers of bone; CT - hypodense nonenhancing lesion with irregular borders.

FIBROUS DISPLASIA — see below.

PAGET DISEASE — expansion of skull base by thickened abnormal bone: sharply demarcated lytic lesions (osteoporosis circumscripta) — enlarged, coarsened trabeculae, thickening of cortex, and nonhomogeneous patchy densities (semble cotton wood) with varying degrees of bone formation and no clear edges — sclerosis-lytic appearance (can be confused with fibrous dysplasia, but occurs in older age).

OSTEOIDES Ancylostroma — osteosclerotic soft-tissue extension; may have calcification; typical (but not frequent) appearance is "sun-burst" pattern.

A. Noncontrast CT — calcified mass within medial right parietal-occipital lobes with massive extracranial soft tissue swelling
B. CT bone window - thinning and atrophy changes of calvarium with several large areas of calcification and ossification within extracranial soft tissues in right parietal-occipital region.
CHONDROSARCOMA - no reliable radiological features (lytic and sclerotic changes within poorly defined margins).

FIBROBLASTOMA - lytic lesion with thinning and widening of cortex.

ERoding SARCOMA - typical onion skin appearance (laninated perilous change); CT - isodense mass surrounded by hypodense area and hyperostosis, contrast enhancing.

ANGIOBLASTOMA - destructive lesion with corrugation and reactive ossification; CT - heterogeneous enhancement with focal necrosis.

PLASMACTOMA/MULTIPLE MYELOMA - multiple lytic lesions that involve both inner and outer tables, as well as dipoil from which they arise; CT - hyperdense, homogeneous enhancing lesions.

GIANT CELL TUMORS - involve sphenoid bone and commonly erode sellar region; CT - hyperdense, contrast-enhancing masses.

METASTATIC NEOPLASMS:
   a) osteoblastic - sclerosis and thickening (e.g. prostate, breast, bladder, hypernephroma).
   b) osteoclastic - bone destruction and lucency (e.g. lung, uterus, GI tract, thyroid, melanoma, neuroblastoma).
   c) combined (sclerotic and lytic) lesions - prostate, breast.

Metastases from breast carcinoma (hair tuft skin film) - numerous irregular lytic defects in cranial vault associated with large vascular grooves.

MRI - hypointense on T1, hyperintense on T2.
   • some degree of contrast enhancement is common.

Bone scanning with Tc-99m — “hot” area of increased radioisotope uptake (OSTEOSARCOMA, OSSIFYING FIBROMAS, OSSIFYING FIBULOSARCOMA, all malignant tumors).

Arteriography - high vascularity (tumors of vascular origin, MULTIPLE MYELOMA); not helpful in diagnosis of other tumors.

Biopsy - paramount importance!

DIFFERENTIAL DIAGNOSIS
1. Encephalocoele, meningiopencephalocoele.
2. Venous lakes of skull, pacchionian depression.
3. Fractures, surgical defects.
4. Osteomyelitis, tuberculosis, sarcoidosis, syphilis.
5. Hyperparathyroidism, osteoporosis, congenital hemolytic anemia

TREATMENT
No treatment is required for asymptomatic benign lesions unless diagnostic concerns exist!

1. Pain control (aspirin or NSAIDs for OSTEOSARCOMA)
2. Surgical excision:
   a) Design tumors – for symptomatic relief, cosmetic reasons, or cranial nerve decompensation.
   b) malignant tumors - treatment of choice for cure (except MULTIPLE MYELOMA); if other means cannot control tumor expansion, surgery is still option in metastatic disease!
      • complete en bloc resection is preferred (with extensive margins for malignant tumors).
      • preoperative embolization is recommended for ANGIOSARCOMA (to reduce intraoperative blood loss).
      • unresectable lesions --> curettage, Gamma Knife and CyberKnife.
3. Radiotherapy - for some partially resected benign lesions with high recurrence rates (OSTEOSARCOMA, OSSIFYING FIBROMA, HEMANGIOMA, OSSUARIAL BONE CYST).
   Radiosurgery is primary treatment for secondary OSSIFYING SARCOMA (esp. in elderly patients), MULTIPLE MYELOMA (if chemotherapy fails).
   • not indicated for ANGIOSARCOMA and FIBROBLASTOMA use in CHONDROSARCOMA controversial.
4. Chemotherapy (combinations including CIPXILATIN, CYCLOPHOSPHAMIDE, CARMUSTINE, LUDOMUSTINE) for OSSIFYING SARCOMA, FIBROBLASTOMA, MULTIPLE MYELOMA (first choice of treatment); efficacy in CHONDROSARCOMA unknown.

PROGNOSIS

Reurrence rates:
   OSSUARIAL BONE CYST - 40-50%
   DESMOPLASTIC FIBROMAS - 20-30%
   GIANT CELL GRANULOMAS - 12-16%

5-year survival rates:
   OSSIFYING SARCOMA - 20-50%
   CHONDROSARCOMA - 10-year survival 30-80%
   FIBROBLASTOMA - 10-year survival 40%
   ERoding SARCOMA - 40-65%
   OSSIFYING FIBROMA - 50%
Special Types

CHONDROSARCOMA

FIBROUS DYSPLASIA

Benign FIBROUS LESIONS of bone:
1) fibrous dysplasia
2) osteofibrous dysplasia (ossifying fibroma)
3) nonossifying fibroma

PATHOLOGY
- Skeletal dysplasia - developmental anomaly (not true neoplasm) - normal bone formation arrested at woven stage → lamellar bone is not formed → typical overgrowth of fibrous tissue among woven bone; portions of the bone are replaced by fibrous connective tissue and poorly formed trabecular bone.
- Process originates in the medullary cavity.
- May occur in single (70-80%) or multiple (20-30%) bones (monostotic and polyostotic fibrous dysplasia).
- Polyostotic form is part of McCune-Albright syndrome see above
- Any bone but is most common in proximal femur, tibia, ribs, and skull.

Characteristic thin, irregular (Chinese character-like) bony trabeculae and fibrotic marrow space:

ETIOLOGY
- Postzygotic (nonhereditary) mutation in guanine nucleotide stimulatory protein (GNAS1) gene.

CLINICAL FEATURES
- Most commonly presents in the teens or 20s.
- Most are asymptomatic.
- May cause painful swelling, repeated pathologic fractures or severe bone deformity (e.g. "shepherd's crook" varus deformity of the proximal femur).

Mauricio Saravia, a Uruguayan artist:
**IMAGING**

**Plain radiographs** - lytic lesion with a "ground glass" appearance, bone expansion, endosteal erosion, periosteal reaction usually is absent (unless there is a pathologic fracture).

**CT** - "ground glass" skull lucency with patches of increased density; multilobulated intradiploic lesion (can be confused with Paget disease, but occurs in younger age group); 3 different forms:
- **cystic form** - involves mainly outer table;
- **sclerotic form** - characterized by bone thickening;
- **mixed form** - manifests after third decade.

Fibrous dysplasia of orbit and ethmoid sinus (CT with bone windows):

Fibrous dysplasia of left temporal bone (large arrowheads) and sphenoid bone (small arrowheads) - expansion and sclerosis.

Fibrous dysplasia of the right zygomatic bone:
**DIFFERENTIAL DIAGNOSIS**
1. Nonossifying fibroma
2. Unicameral bone cyst
3. Aneurysmal bone cyst
4. Chondromyxoid fibroma

**TREATMENT**
Symptomatic patients:
1) bisphosphonate therapy
2) curettage, bone grafting, and stabilization.
   - autograft should not be used because it will be resorbed.

**PROGNOSIS**
- deformity of fibrous dysplasia progresses with skeletal growth → static after growth ceases (may be reactivated with pregnancy)
- often recurs after curettage and bone grafting.
- 0.5% FIBROUS DYSPLASIA cases undergo malignant transformation (to osteosarcoma, chondrosarcoma, or fibrosarcoma).

**SOLITARY PLASMACYTOMA / MULTIPLE MYELOMA**

**Plasmacytoma**
- solitary benign neoplasm of monoclonal plasma cells.

**Multiple Myeloma**
- disseminated malignant form of plasmacytoma, potentially fatal.
- more often found in the vertebral column, thoracic cage, and long bones; involvement of the cranial vault is not infrequent.
- involvement of the skull base is a strong positive predictor for progression from solitary plasmacytoma to multiple myeloma.
- plasmacytoma affects patients in the late 5th decade; vs. MM occurs in the late 6th decade.

**PATHOLOGY**
- smooth and lobulated but can cause irregular destruction of the involved bone
- made up of abnormal plasma cells that produce monoclonal immunoglobulins.
- widespread osteolytic bone destruction by dense tumor cells that look like plasma cells clustered in close aggregates.
- plasmacytomas may be of low (plasmacytic), intermediate, or high (plasmablastic) grade based on histologic findings.

**CLINICAL FEATURES**
- cranial neuropathies may be caused by mass effect or direct infiltration with myelomatous cells.
- involvement of the orbit may result in exophthalmus or ophthalmoparesis.
- headaches of increased intracranial pressure.
- intradural extension may give rise to seizures.

**DIAGNOSIS**
- It is essential to perform both CT and MRI.
  - thorough evaluation to exclude multiple myeloma (particularly if the lesion is at the skull base) - bone marrow evaluation, a skeletal survey, a bone scan, and serum and urine protein electrophoresis.
- Plain radiography and CT
  - multiple myeloma - well-defined lytic lesions involving the diploë and cortical bone, without a sclerotic border.
  - isodense to hypodense on CT
**MRI**
- Isointense to hyperintense on T1, markedly hypointense on T2.
- DWI: plasmacytomas - restriction, whereas multiple myeloma - increased diffusion.
- Avid contrast enhancement.

**Radiosotope bone scanning**
- "Cold" lesion.
- Relatively high false-negative rate.

**Angiography** - tumor blush from ECA branch feeders.

**Treatment**

**Solitary plasmacytoma** → surgical resection → irradiation (plasmacytoma is a radiosensitive lesion).
- Tumors are often quite vascular - significant blood loss should be anticipated (preoperative embolization may be helpful).
- Indications for radiotherapy alone (after biopsy):
  a) Prohibitive medical comorbid conditions
  b) Lesions of the skull base.

**Multiple myeloma** - not treated by surgical resection.
- **chemotherapy** with C-VAD (cyclophosphamide, vincristine, Adriamycin, and dexamethasone), along with stem cell transplantation and **palliative irradiation**, forms the mainstay of treatment.
- median survival: 3 years (several months to 10 years).

**BIBLIOGRAPHY** for ch. “Neuro-Oncology” — follow this [LINK](#)