Skull Tumors

PATHOLOGY

1. BONE FORMING TUMORS:
   1) OSSIDOMA (most common primary tumors of calvaria) - growths of mature dense lamellar cortical bone (outer or inner table), typical appearance - nodus of osteoid tissue in background of osteoblastic connective tissue, which is enclosed completely by reactive bone.
   2) OSSIDOMA-OSSIDOMA.
   3) OSSIDOMA-FIBRIBOSIS - spindles with varying amounts of woven bone; tumor periphery is composed of mature lamellar bone.
   4) OSSIDOMA-FIBRIBOSIS - fibrous stroma with irregular osteoid deposition.
   5) OSSIDOMA-FIBRIBOSIS - secondmost frequent malignant skull tumor after multiple myeloma) - malignant spindle cell stroma, which directly produces osteid or immature bone (osteoblastic, chondroblastic, or fibroplastic form), association with prior radiation exposure, Paget disease, fibrinoid dispiration, chronic osteomyelitis.

2. CARCINOMA FORMING TUMORS:
   1) CARCINOMA (endodermal, squamous to osteosarcoma, osteosarcoma) - mature hyaline cartilage; arise from cartilaginous portion of bones formed by enchondral ossification (skull base and parasinal sinuses).
   2) CARCINOBLASTOMA - chondroid and myxoid differentiation with lobular growth.
   3) CARCINOBLASTOMA - immature cartilage cells.
   4) CARCINOBLASTOMA - third most common malignant skull tumor; often associated with abnormalities of chromosomal 10 and 12; low-grade type (neurofibrosarcoma) - chondroid and immature cartilage deposition in areas of myomatosus change and cystic degeneration; high-grade type (mesenchymal chondrosarcoma) - absence of cartilage lobules and presence of fibrousarcotous areas (groups of chondromalcal cells lose their usual lobulation and begin to spout out), both types are vimentin positive.

3. CONNECTIVE TISSUE TUMORS:
   1) EOSINOPHILIC GRANULOMA - giant cells around hemorrhagocic foci, numerous spindel shaped fibroblastic cells, and new bone formation; tumor cells are smaller than those of giant cell tumor of bone, whereas stromal cells resemble each other.  
   2) NONOSSEOUS FIBROMA - fibroblast proliferation with multinucleated giant cells.
   3) XANTHOMA - foamy xanthomacous cells.
   4) WING SARCOMA - uniform, densely packed small cells with indistinct cytoplasmic borders.
   5) GIANT CELL TUMOR (OSTEOSARCOMA) - well vascularized tissue mass of pump, spindel, or ovoid stroma cells together with uniformly dispersed, numerous, large, multinucleated giant cells.

5. TUMORS OF BLOOD OR BLOOD VESSEL ORIGIN:
   1) EOSINOPHILIC GRANULOMA (common) - nonregenerative brownish red lesions under skull periosseum; microscopically - capillaries, cavernous, or venous blood vessels.  
   2) NEOPLASTIC PLASMA CELL GRANULOMA (rare) - lymph nodes; characterized Langerhans or X cells)

6. TUMORS OF NEUROEPITHELIAL ORIGIN:
   1) ISCHEMIC-INDUCED LESION.

7. TUMORS OF SQUA MUS CELL ORIGIN:
   1) OSSIDOMA CARCINOMA (nasal sinuses and temporal bone)

8. Tumors of Apocrine Gland Origin (salivary, lacrimal glands); propensity for perineural spread.

9. METASTASES (skull is common site!); data in effective barrier - brain invasion is rare!

10. OTHER TYPES:
    1) OSSIDOMA DISPLASIA.  
    2) OSSIDOMA - internalized increased osteoclastic activity (bone resorption) - increased osteoblastic activity (bone formation).
    3) OSSIDOMA EBERHARD TUMORS (one of most common benign skull lesions in children)  
    4) OSSIDOMA-CARTILAGE CYST - large vascular spaces (lack endothelial lining) separated by trabecular of connective tissue and bone; locally aggressive lesions - continue to expand until treated.
    5) OSSIDOMA-CARTILAGE CYST.

   6) OSSIDOMA-LIPOMA.

   7) OSSIDOMA-MEDULLARY CYST - 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 tumor
     1) single, small, roundly rounded oval lesion
     2) peripheral sclerosis
     3) intradacral calcifications
     4) peripheral bone vasculaturity

   • malignant transform to osteosarcoma, chondrosarcoma, or fibrosarcoma) - in 2% Paget disease and 0.5% OSSIDOMA DISPLASIA cases.

   • Lesion Location is of little differential diagnostic value, but certain tendencies exist.
     lesions of developmental origin - strong midline propensity; OSSIDOMA - parasinal sinuses, frontal bone; OSSIDOMA - frontotemporal region.
     OSSIDOMA GRANULOSIS, OSSIDOMA - meningeal origin.
     OSSIDOMA - skull base, usually multicentric.


cartilage tumors - skull base;  
GIANT CELL GRANULOMA - spheno, temporal, and ethmoid areas;  
HEMANGIOMAS (more common in vertebral column):  
GLOBULAR VARIETY - skull base;  
SESSIONID, TEMPORAL, AND ETHMOID AREAS;  
Sessile type - frontotemporal region;  
GLOBULAR VARIETY - cerebellopontine angle, parasellar region, calvaria (neoplasms 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 disfigurement.  
- 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 meningiomas.

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, OSSIFYING FIBROMA, GIANT CELL GRANULOMA or malignant tumor.  
- malignant tumors without pain - MULTIPLE MYELOMA, OSSIFYING FIBROMA.

2. Cranial nerve deficits (if tumor involves skull base), e.g. visual and hearing loss.

3. Dural erosion, direct brain compression.

4. Recurrent 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).

SYNDROMES  
Gardner syndrome:  
1) multiple osteomas of skull, sinus, mandible  
2) soft tissue fibromas of skin  
3) colon polyps

McCune-Albright syndrome - postzygotic mutation (spontaneous mutation) of GNAS1gene - involved in G-protein signaling - mutation prevents downregulation of cAMP signaling  
1) polyostotic fibrous dysplasia  
2) “autonomous production” of hormones - precocious puberty, hyperthyroidism, Cushing syndrome  
3) unilateral hyperpigmented skin macules (“café-au-lait”) - jagged “coast of Maine” borders, and tendency to respect midline and follow developmental lines of Blaschko

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)  
- b) radiopaque (osteoblastic) - OSSIFYING FIBROMA, INTRAOSSEOUS MENINGIOMA, scierotic form of FIBROUS DYSPLASIA, later stages of PAGET DISEASE, some METASTASES (e.g. prostate, breast, bladder, hypernephroma).
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 (spontaneous osteoma may be radioslucent, osteoid osteoma - radiolucent nidus with surrounding dense sclerosis).

NONOSSIFYING FIBROMA - initial lesion is radiolucent, but progressively becomes radiopaque, with sharp margins and dilated vascular channels.

INTRAOSSEOUS MENINGIOMA - well-demarcated nonenhancing lytic lesion with smooth calcified margins.

CHONDROMA - well-circumscribed lytic lesion eroding surrounding bone; stippled calcification helps to distinguish from metastasis or chondroma.

CHONDROBLASTOMA - radiolucent with tissue calcification.

DENSELPLASTIC FIBROMA - well-defined lytic and expansile lesions with typical soap bubble appearance; causes thinning of overlying cortex without periosteal reaction.

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

NONOSSIFYING FIBROMA, XANTHOMA - radiolucent with sclerotic margins and bony trabecular with soap bubble appearance.

XENOPHILIC GRANULOMA - 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 within area of bony destruction (central density may also be present).

HEMANGIOMA - well-defined nonenhancing lytic lesion with characteristic honeycomb or trabecular appearance; 35% 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); dilated is preserved.

Hemangiomas of skull vault (A - lateral radiograph; B - CT, bone window) - well-defined lucent in parietal bone has typical “spoke wheel” appearance (due to prominent vascular impressions)

LIPOPHAGHOMA - cystic bone defect.

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

OSTEOID/DEHISIEN - 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.

FIBROMATOSIS - see below.

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

OSTEOSARCOMA - osteolytic soft-tissue extension; may have calcification; typical (but not frequent) appearance in sun-ray picture.

A. Contrast CT - calcified mass within medial right parietal-occipital lobes with massive extracranial soft tissue swelling.
B. CT bone window - thinning and erosive changes of calvarium with several large areas of calcification and ossification within extracranial soft tissue in right parietal-occipital region

CHONDROSARCOMA - no reliable radiological features (lytic and sclerotic changes within poorly defined margins).

FIBROSARCOMA - lytic lesion with thinning and widening of cortex.
**ANGIOSARCOMA** - destructive lesion with cortical erosion and reactive ossification; CT - heterogeneous enhancement with focal necrosis.

**Giant Cell Tumors** - involve sphenoid bone and commonly erode sellar region; CT - hyperdense, contrast-enhancing masses.

**Metastatic Neuropathy**
- osteoblastic - sclerosis and thickening (e.g. prostate, breast, bladder, hypernephroma).
- osteoclastic - bone destruction and lucency (e.g. lung, uterus, GI tract, thyroid, melanoma, neuroblastoma).
- combined (sclerotic and lytic) lesions - prostate, breast.

Metastases from breast carcinoma (lateral plain skull film) - numerous irregular lytic defects in cranial vault associated with large vascular groove.

**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 (OSTEOMAS, OSSIFYING FIBROMAS, OSSIFYING FIBROSARCOMAS, 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. Encephalohlele, meningoencephalohlele
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 OSSEous OSTEOID)
2. **Surgical excision**
   - Benign tumors – for symptomatic relief, cosmetic reasons, or cranial nerve decompression.
   - 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 excision is preferred (with extensive margins for malignant tumors).
     - Preoperative embolization is recommended for ANGIOSARCOMAS (to reduce intraoperative blood loss).
     - Unresectable lesions → curettage, Gamma Knife and CyberKnife.
3. **Radiosurgery** - for some partially resected benign lesions with high recurrence rates (OSTEOMAS, OSSIFYING FIBROMAS, OSSIFYING FIBROSARCOMA, ASENTEAL BONE CYST). Radiosurgery is primary treatment for secondary OSSIFEROUS OSSIFYING FIBROMAS (esp. in elderly patients), OSSIFEROUS OSSIFYING FIBROSARCOMA, OSSIFYING FIBROPLASTIC OSSIFYING FIBROMA.
4. **Chemotherapy** (combinations including CYCLOPHOSHAMIDE, CARMUSTINE, LOMUSTINE) – for OSSIFEROUS OSSIFYING FIBROMAS, OSSIFYING FIBROSARCOMAS, MULTIPLE MYELOMA (first choice of treatment); efficacy in CHONDROSARCOMA unknown.

### Prognosis

**Recurrence rates**
- ASSENTEAL BONE CYST: 40-50%
- OSSIFYING FIBROMA: 20-30%
- GIANT CELL GRANULOMA: 12-16%

**5-year survival rates**
- OSSIFEROUS OSSIFYING FIBROMA: 20-50%
- CHONDROSARCOMA: 10-year survival 30-80%
- OSSIFEROUS OSSIFYING FIBROMA: 10-year survival 40%
- Ewing Sarcoma: 40-65%
- ANGIOSARCOMA: 90%

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**Fibrous Dysplasia**

Benign FIBROUS LESIONS of bone:
1. Fibrous dysplasia
2. Osteofibrous dysplasia (ossifying fibroma)
3. Nonossifying fibroma
SKULL TUMORS

ONC40 (5)

PHYSIOLOGY
- 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.

Characteristics 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:

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
SKULL TUMORS

**Onc40 (7)**

- 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 exophthalmia or ophthalmoplegia.
- 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 diploe and cortical bone, without a sclerotic border.
- isodense to hyperdense on CT.
SKULL TUMORS

MRI
- isointense to hyperintense on T1, markedly hypointense on T2.
- DWI: plasmacytomas - restriction, whereas multiple myeloma - increased diffusion.
- avid contrast enhancement.

Radioisotope bone scanning
- “cold” lesion
- relatively high false-negative rate.

Angiography - tumor blush from ECA branch feeders.

TREATMENT
Solitary plasmacytomas → 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).

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