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Chondromyxoid Fibroma Arising in Craniofacial Sites

A Clinicopathologic Analysis of 25 Cases

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颅面骨软骨性肿瘤的特点

- 软骨肉瘤：好发于副鼻窦或眼眶周围骨壁，靠近颅底的部位，而非颌骨，所以肿瘤常充满鼻腔鼻窦或眼眶
- 颌骨内出现肿瘤性软骨首先要排除骨肉瘤
- 颅面骨几乎没有良性内生性软骨瘤

- 软骨母细胞瘤：颅面骨的软骨母细胞瘤几乎都位于颞骨外侧部，容易导致听力丧失，或者波及颞颌关节
- 组织学形态和其他部位一样
- 主要鉴别诊断：颞颌关节的腱鞘巨细胞瘤

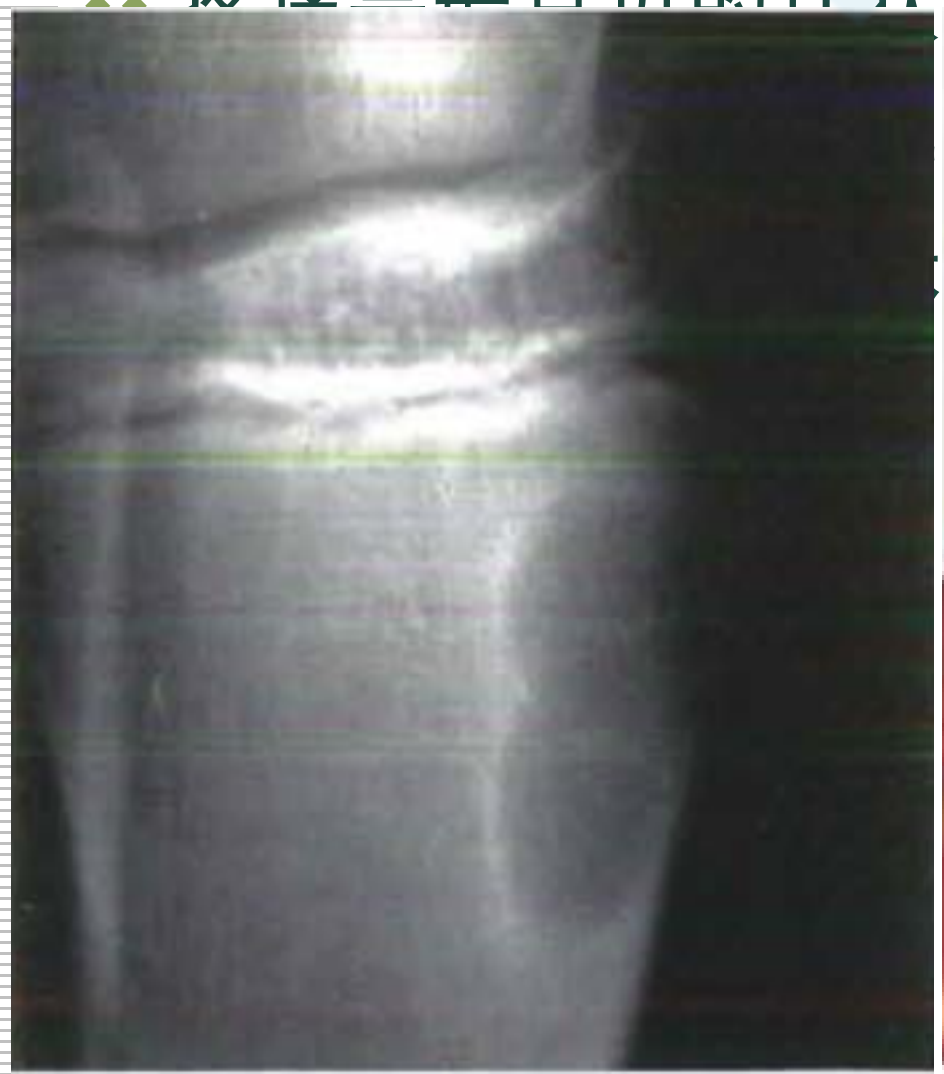
参考上海交通大学附属第六人民医院病理科蒋智铭老师的课件

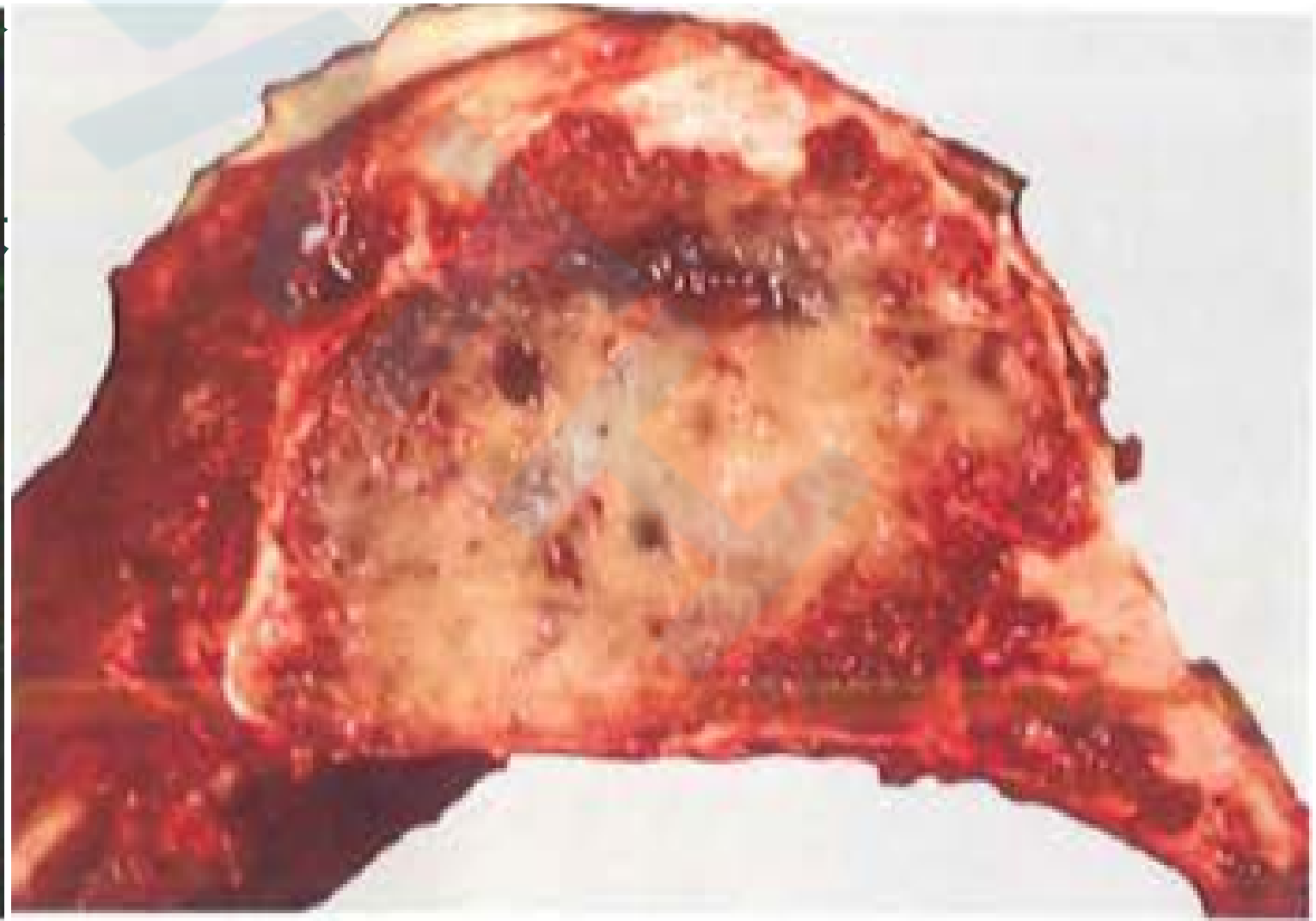
- 颌骨是间叶软骨肉瘤最好发部位
- 颅面骨几乎没有透明细胞软骨肉瘤的报告
- 颅面骨软骨性肿瘤的诊断陷阱：
  - 软骨肉瘤和软骨母细胞性骨肉瘤的鉴别
  - 软骨肉瘤和鼻中隔反应性结节状软骨增生鉴别
  - 颅底部软骨肉瘤和软骨样脊索瘤的鉴别
  - 骨软骨瘤与髁上突的鉴别

参考上海交通大学附属第六人民医院病理科蒋智铭老师的课件

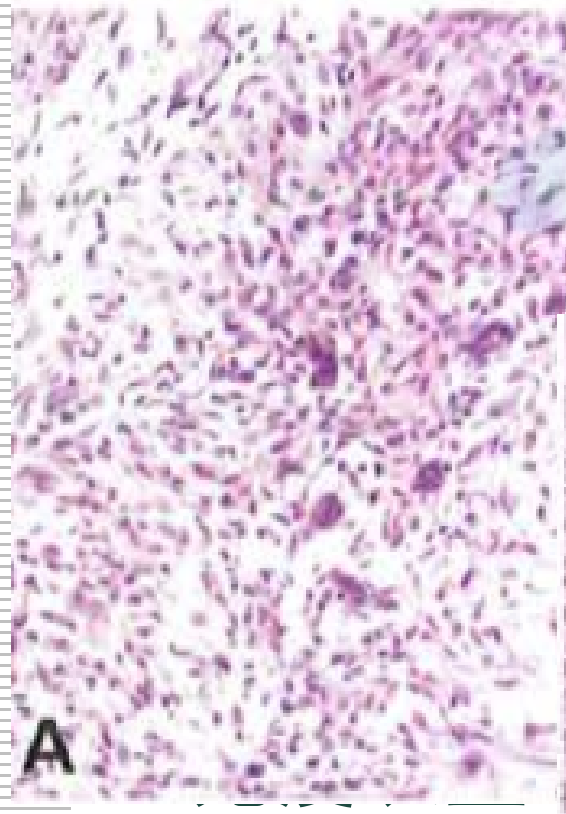
软骨黏液样纤维瘤

- ICD-O编码：9241/0；中间性，局部侵袭
- 几乎发生在任何骨，长骨最常见，尤其胫骨近端和股骨远端，其次在髂骨，足部的跖骨，其他部位包括肋骨、椎骨、颅面骨和手部的管状骨等
- 疼痛是最常见的症状

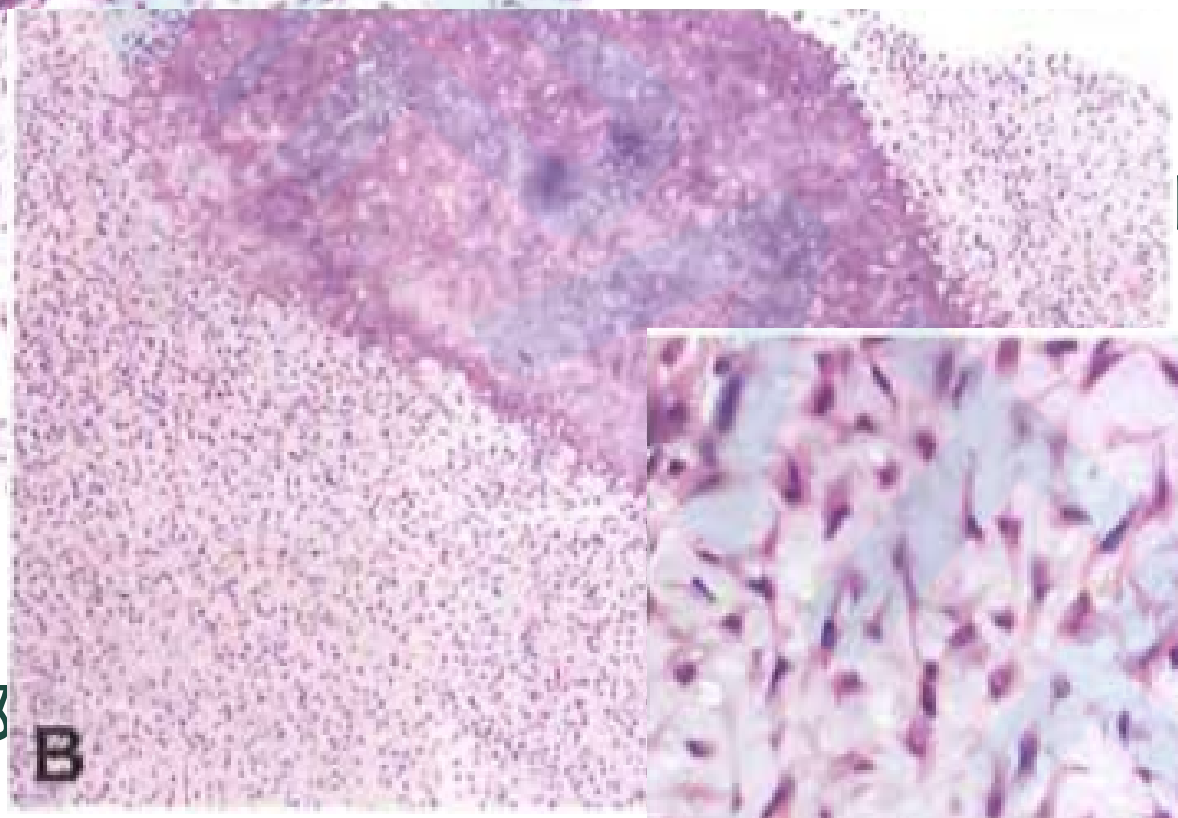




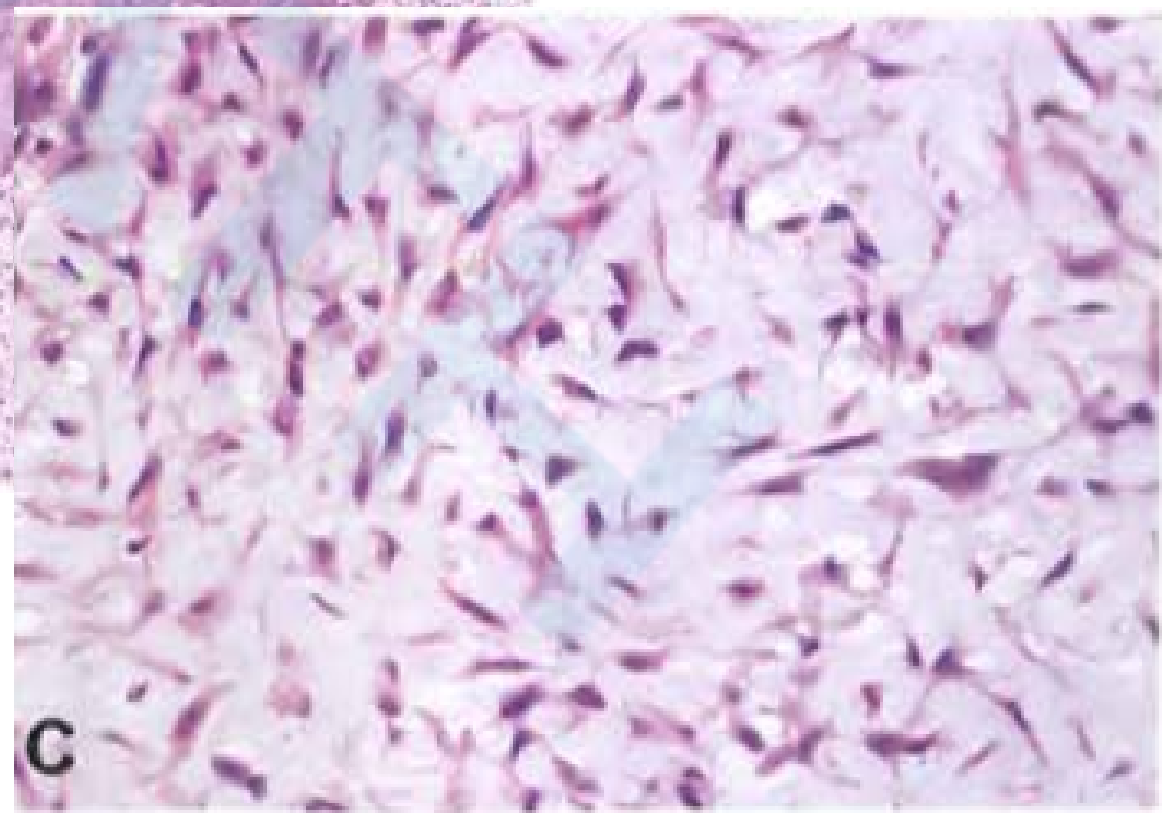
- 主体与蓝灰色或白色的膨胀性肿物



界限分明，分叶状的排列方式，
伏细胞，小叶中央细胞稀疏，而



嗜酸性胞质界限



边区域

- 一般经刮除

MATERIALS AND METHODS

- Case Selection and Clinical Features
  - Brigham and Women's Hospital, Boston, MA
    All cases (n = 25) diagnosed as CMF arising in craniofacial regions
  - Between January 1997 and April 2017 were retrieved
  - From routine hospital and consult files of 1 of the authors (C.D.M.F.)

- All cases were carefully examined and specific morphologic features were annotated, including
  - Cytologic atypia
  - Mitotic count (as mitotic figures per 10 high-power fields [HPFs], or 2.4 mm^2)
  - Presence of necrosis
  - Calcification
  - Presence of hyaline cartilage
  - Intratumoral bone matrix
  - For excisions, margin status was recorded when possible

Clinical Features

- The patient's age and sex
- Anatomic location of tumor
- Type and duration of preceding symptoms
- Size of tumor (maximal dimension)
- Sampling modality (biopsy vs. excision)
- Clinical, radiologic, and follow-up information, including
  - imaging studies
  - additional treatment
  - presence of recurrence and/or metastasis
  - the status of the patient at last follow-up (alive or deceased; with or without evidence of tumor)

Immunohistochemistry

TABLE 1. Immunohistochemistry: Sources, Clones, Dilutions, and Pretreatment Conditions

Antibody	Source	Clone	Dilution	Pretreatment
AE1/AE3	Dako	AE1+AE3	1:200	10 min protease digestion
B-catenin	BD	14	1:1000	Pressure cooker
Brachyury	Santa Cruz	Polyclonal	1:300	Pressure cooker
Cam5.2	Dako	CAM5.2	1:50	10 min protease digestion
CD34	Dako	QBEcuol 10	1:400/1:200 AP	None
CD99	Santa Cruz	013	1:150	Pressure cooker
Desmin	Sigma	PE-U-10	1:5000	Pressure cooker
EMA	Dako	E29	1:200	None
GFAP	Dako	Polyclonal	1:15,000	Citrate buffer, pressure cooker
p63	Biocare Medical	4A4	1:100	Pressure cooker
Pankeratin	Dako	MNF-116	1:700	10 min protease digestion
S-100 protein	Dako	Polyclonal	1:1000	None
SATB2	Sigma	Polyclonal	1:1000	Pressure cooker
SMA	Sigma	IA4	1:20,000	None

RESULTS

- Clinical Features
- Pathologic Features
- Immunohistochemistry
- Treatment and Outcome

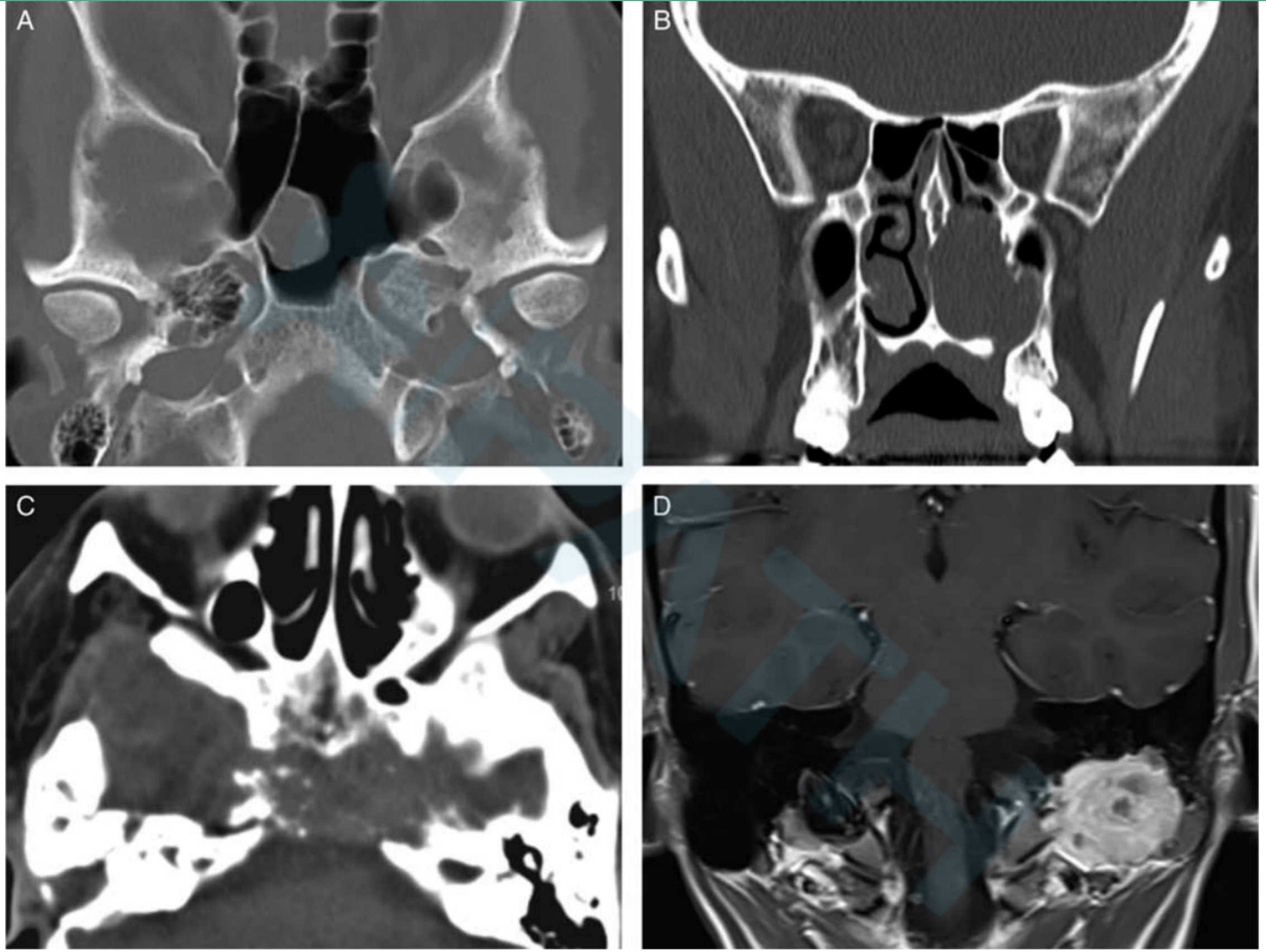


FIGURE 1. Radiographic examples of craniofacial CMF. Many tumors occurred superficially within existing sinus cavities (A) with some showing focal bony erosion and extension into adjacent sinuses (B). C, Occasional tumors demonstrated frank destruction of involved bones. D, T2-weighted magnetic resonance imaging image of a lesion occurring within the mastoid region with intracranial extension.

TABLE 2. Clinical and Pathologic Features of Cranial Chondromyxoma (n = 25)

Features	N/Total (%)
Age (median [range]) (y)	44 (5-83)
Sex	
Male	14/25 (56)
Female	11/25 (44)
Anatomic site	
Sphenoid	7/25 (28)
Ethmoid	5/25 (20)
Maxilla	3/25 (12)
Occipital	2/25 (8)
Nasal septum	2/25 (8)
Palatine	2/25 (8)
Temporal	2/25 (8)
Orbit	1/25 (4)
Undisclosed skull	1/25 (4)
Relation to bone	
Superficial	15/21 (71)
Intraosseous	6/21 (29)
Bone erosion/destruction (imaging)	13/16 (81)
Tumor size (median [range]) (cm)	2.0 (0.8-6.0)
Stromal features	
Calcifications present	14/24 (58)
HPC-like vessel pattern	14/24 (58)
Hyaline cartilage	2/24 (8)
Mitotic count (median count [range]) (per 10 HPFs)	0 (0-2)
Giant cells/nuclear atypia	3/24 (13)
Follow-up (median [range]) (mo)	18 (0-132)
Alive, NED	13/15 (87)
Recurrence	5/15 (33)
Metastasis	0/15 (0)

HPC, indicates hemangiopericytoma; NED, no evidence of disease.

- Biopsy(1) excision (14)
- fragments of polypoid or lobulated soft tissue, with a firm or rubbery, white/tan to pink/red cut surface admixed with bone
- No necrosis was observed in any case
- Infiltration of adjacent bone(6 cases) superficial cortical erosion or subcompartmentalizatio n(6 cases)

Clinical Features

- Most patients were either asymptomatic or complained of headaches and region-specific symptoms (eg, epistaxis, tinnitus, visual deterioration)
- The reported duration of symptoms ranged from days to > 10 years
- Suggested clinical diagnoses included both benign (mucocele, aneurysmal bone cyst, dermoid cyst, papilloma, chondroma, neurofibroma) and malignant (chondrosarcoma, chordoma, osteosarcoma) entities
- Most patients underwent piecemeal excision or curettage (5/5 positive margins when reported). A single case of recurrent tumor within the clivus was radiated after initial resection

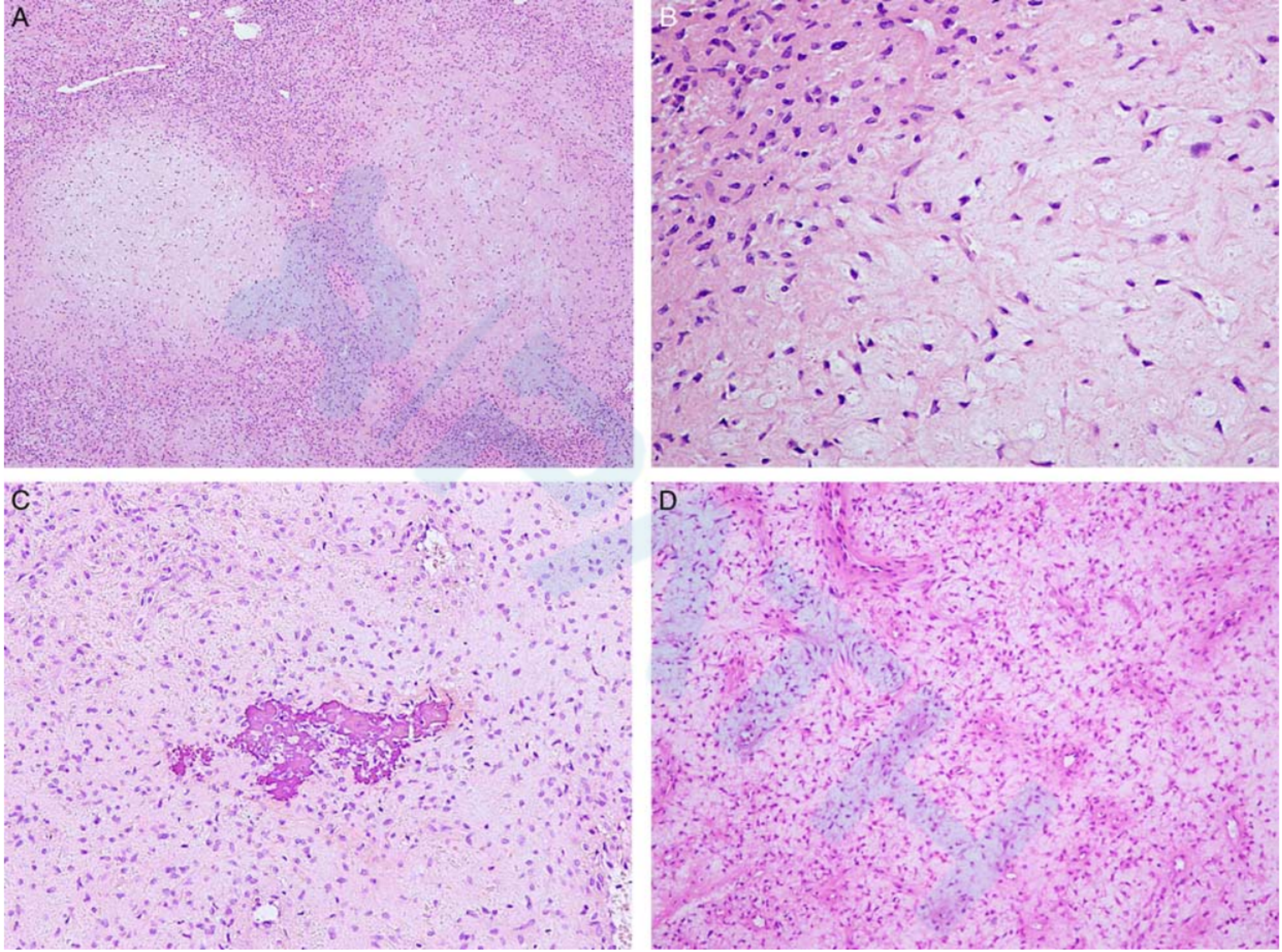


FIGURE 2. Common histologic features of craniofacial CMF. A, Most tumors exhibited classic features of CMF including a lobulated growth pattern with zones of hypercellularity. B, The central zones of loose myxoid matrix contain spindled to stellate cells that transition to a more ovoid morphology at the more densely cellular periphery. C, Coarse, irregular calcifications are usually present to varying degrees. D, CMF arising in nasopharyngeal bones frequently contained a hemangiopericytoma-like vasculature pattern, as well as rounded, variably hyalinized thicker-walled vessels.

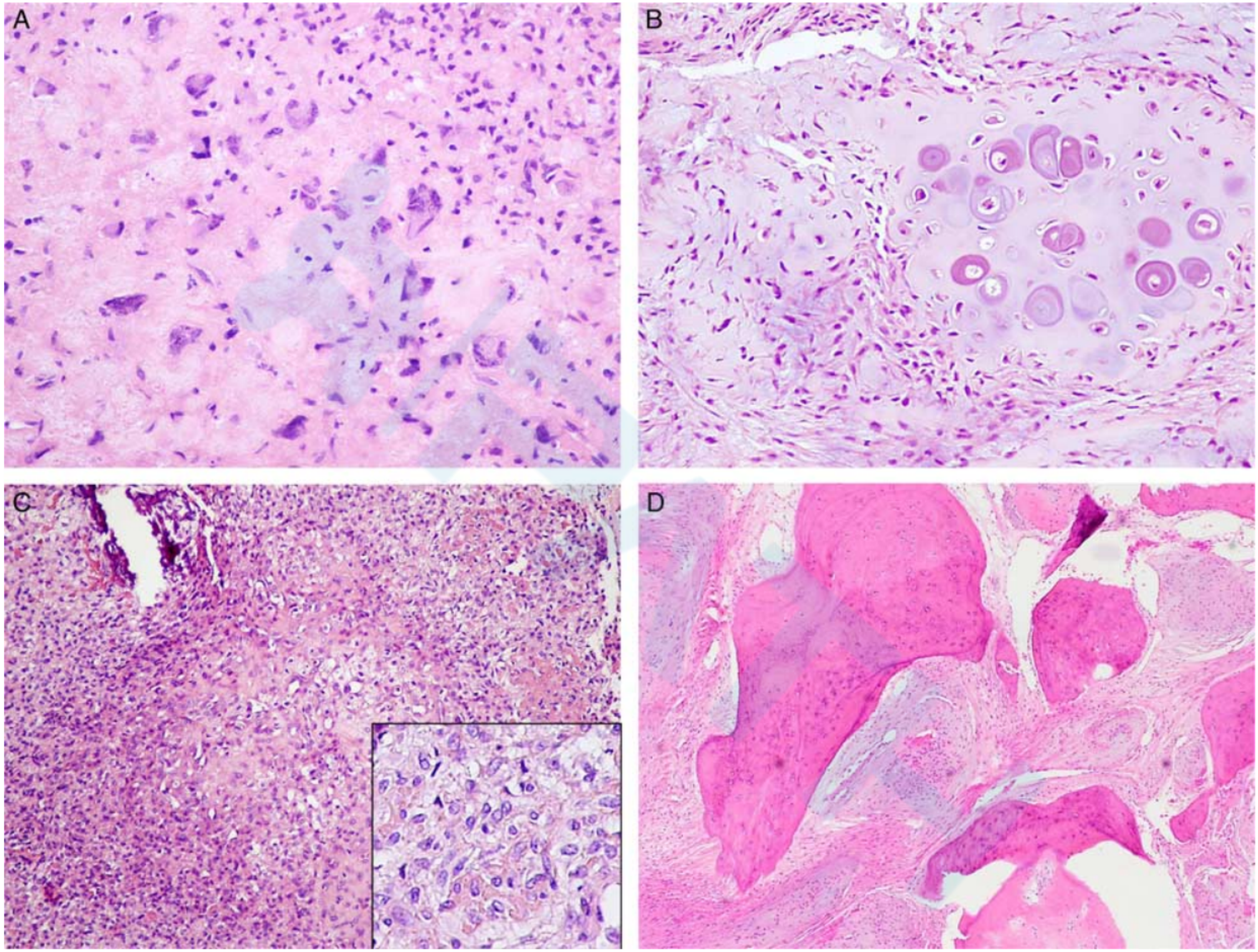


FIGURE 3. Potentially worrisome features in craniofacial CMF. A, Although uncommon, some lesions showed focally prominent nuclear atypia and aggregates of giant cells. B, Foci of mature cartilage can mimic chondrosarcoma, especially in prominently myxoid tumors. C, A single tumor exhibited chondroblastoma-like morphology, with epithelioid cells containing clear cytoplasm and slightly irregular round to ovoid nuclei (inset, 40x). D, Six cases showed infiltration of bone.

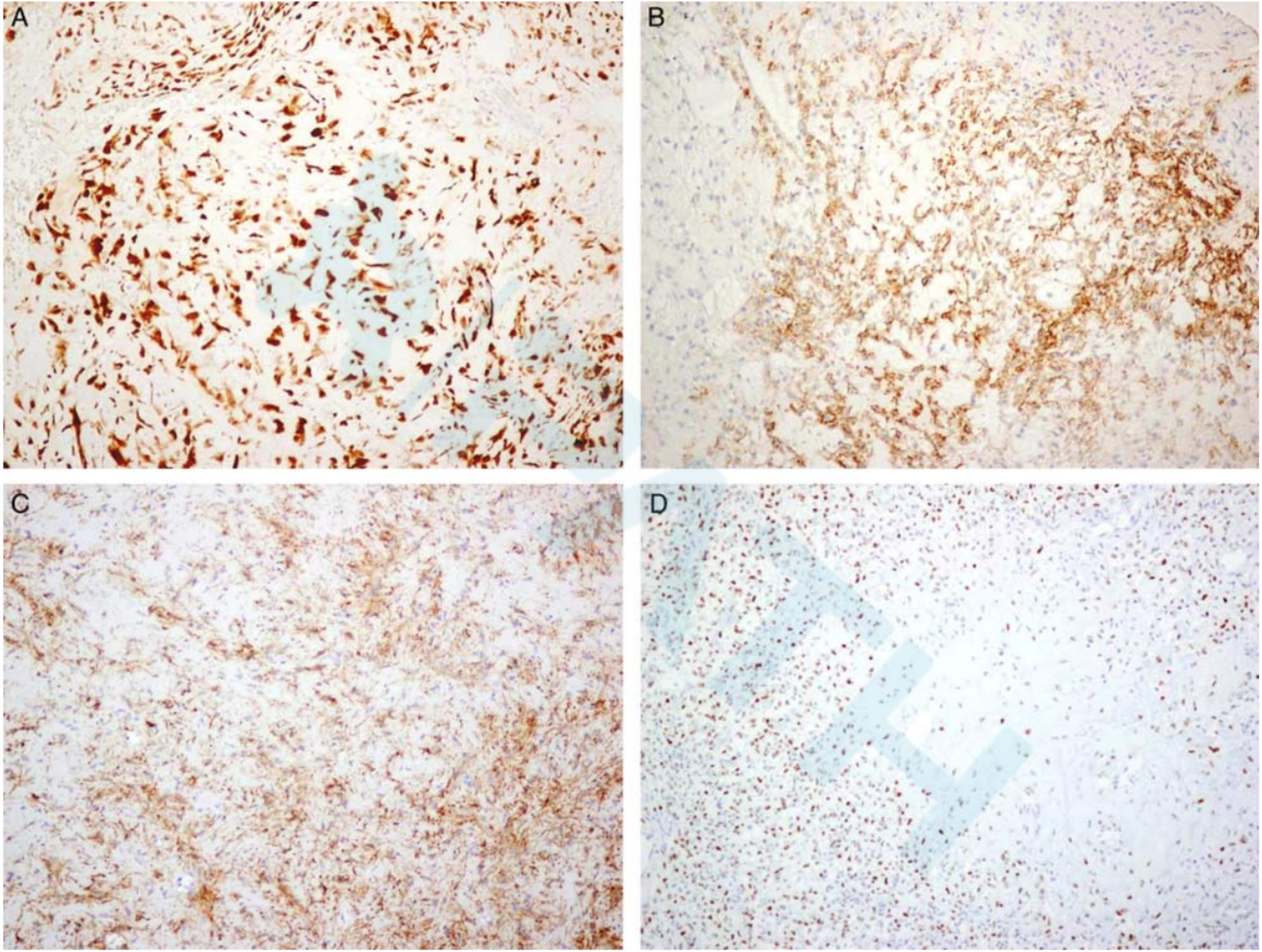


FIGURE 4. Although craniofacial CMF rarely stains with any markers, occasional positivity may be seen for S-100 (A), EMA (B), or SATB2 (D). C, SMA staining was routinely observed.

DISCUSSION

- Clinically, craniofacial CMF presents slightly later in life than peripherally occurring tumors (average age of occurrence, 44.3 vs. 31.1 y, respectively)
- On the basis of radiologic, craniofacial CMFs arise in the more usual intraosseous space, they show uncharacteristically destructive appearances, a feature often noted in other reports of cranial and skull base CMFs
- Microscopically, craniofacial CMF shows largely overlapping features with tumors occurring in other locations, with few notable exceptions

- CMF arising in craniofacial bones shows typical morphologic features of a lobulated growth pattern of uniform spindled to stellate cells within a variably chondromyxoid to fibrous stroma
- In contrast to its peripheral counterpart
  - calcifications are much more prevalent in craniofacial CMF
  - whereas giant cells and prominent atypia are much less common
- CMF arising in sinonasal locations usually contain a dense vascular network, frequently with rounded hyalinized vessels. This finding may be a useful diagnostic feature

- CMF lacks a distinct immunophenotype, with only occasional positivity for S-100 protein or EMA and consistent staining for SMA
- On the basis of available follow-up data, there is a risk of recurrence in 33% of cases, irrespective of margin status, but no reported instances of metastasis to date

DIFFERENTIAL DIAGNOSIS

- Chondroma
- Chondroblastoma
  - The characteristic cells are uniform, round to polygonal with well-defined cytoplasmic border, clear to slightly basophilic cytoplasm
  - Round to ovoid nucleus(chondroblasts)
  - Chicken wire calcification
- Fibromyxoma
- Low-grade chondrosarcoma
  - The lack of hemangiopericytoma-like vessels
  - The presence of nuclear atypia
  - Immature cartilaginous elements
  - Mutations in IDH1/2

- Osteosarcoma
  - The characteristic “lacy” osteoid
  - MDM2, CDK4(+)
  - SATB2 can be nonspecific
- Chordoma
  - Arising in midline locations
  - The presence of physaliphorous cells
  - immunopositivity for EMA, keratins, brachyury often S-100 protein

- Myoepithelial lesions
  - A variably prominent chondromyxoid and/or hyalinized stroma
  - S-100, EMA, GFAP, cytokeratin
  - Frequent EWSR1 gene rearrangements
- Nasopharyngeal angiofibromas
  - Not exhibit the same lobulated architecture characteristic
  - The stromal cells fail to stain with most markers, including SMA
- Solitary fibrous tumor
  - CD34, CD99, Bcl-2, STAT6
  - NAB2-STAT6 fusion gene

CONCLUSION

- Craniofacial CMF poses diagnostic pitfalls including frequent aggressive radiologic features and lack of a specific immunophenotype
- Tumors may recur, largely due to the difficulty of obtaining clear surgical margins in this anatomic region
- Furthermore, propensity for local destruction and invasion can create significant morbidity

Thank You !