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Research Article

# Skull Bone Tumors: A Seven Year Retrospective Study in Tertiary Care Centre

**Supriya Prasad[1], Jayasree K[1]*, Sindhu Nair P[1], Sreejith Nair[2], Priyakumari T[3] and Venugopal M[4]**

*[1]Division of Pathology, Regional Cancer Centre, Thiruvananthapuram, India*
*[2]Division of Medical Oncology, Regional Cancer Centre, Thiruvananthapuram, India*
*[3]Division of Pediatric Oncology, Regional Cancer Centre, Thiruvananthapuram, India*
*[4]Division of Imageology, Regional Cancer Centre, Thiruvananthapuram, India*

***Corresponding Author:** Jayasree K, Division of Pathology, Regional Cancer Centre, Thiruvananthapuram, India.

**Received:** May 29, 2021; **Published:** July 28, 2021

## Abstract

**Introduction:** Primary skull bone tumors are very rare and account for less than 1% of all bone tumors. They include a spectrum of lesions, which may be benign or malignant.

**Objective:** These tumors have not been reported systematically in literature, as majority of the published studies are single case reports. Hence, through this study we aim to evaluate the spectrum of benign and malignant tumours of skull bones in different age groups and locations.

**Materials and Methods:** This a retrospective study. A total of 29 cases over a period of seven years from 1st January 2011 to 31st December 2017 are included in this study.

**Results and Conclusion:** There were a total of 29 cases of the primary bone tumors of the skull, over a period of 7 years. The mean age of the patients was 25.4 years with slight female predilection. Majority of the patients were adults, but a substantial number (n = 12) were in the pediatric age group. Malignant cases constituted approximately 90% of cases. The most common tumor was osteosarcoma, with predominance in the pediatric population and located in the calvarial bones. Among the adults the most common tumor was chordoma followed by chondrosarcoma. A multidisciplinary approach involving the treating physician, the radiologist and the pathologist is advocated for proper typing and management of these tumors.

***Keywords:*** *Skull; Bone; Tumors; Malignant*

## Introduction

Skull bones are different from the remainder of the bones where most of the skull bones - like frontal, parietal and nasal bones undergo intra-membranous ossification [1]. Whereas some other cranial bones like sphenoid, occiput, petrous part of temporal and base of the skull undergo endochondral ossification and have complex anatomy [2]. Primary skull bone tumors are very rare, accounting for fewer than 1% of all bone tumors [3]. They include a spectrum of lesions, which can be benign or malignant. These tumors have not been reported systematically in literature, because the majority of the published studies are either on individual tumors or as single case reports. Skull bone tumors are a definite entity because they include multiple subtypes and need a multidisciplinary approach. Malignant tumors are more common than benign tumors of skull bones [1,2]. Commonest malignant tumors reported within the skull is chordoma, while commonest benign tumour is osteoma. Tumors are most often located at the skull base, of which clivus is the commonest location [3]. Overall benign tumors are extremely rare in skull base and tumors of the vault bones also are infrequent. In this retrospective analysis,

the spectrum of extra gnathic skull bone tumors is studied to document the various tumors encountered in a tertiary care cancer center and their clinic-pathological features.

## Materials and Methods

This is a retrospective study conducted in the Division of Pathology, Regional Cancer Centre, Trivandrum from 1st January 2011 to 31st December 2017. All cases of primary bone tumors of extra gnathic skull bones over a period of seven years were retrieved and their clinical, radiological, and pathological features were analysed from the case files and by viewing the H&E-stained slides and relevant immunohistochemical slides. All cases of metastasis and hematological malignancies within the skull bones were excluded.

## Results

There were 29 cases of primary skull bone tumors over a period of seven years. The mean age of the patients was 25.4 years, and the age range was 1 to 59 years. There was a slight female preponderance with 14 males and 15 female patients. Even though the bulk of the patients (n = 17) were adults, but a considerable number (n = 12) belong the pediatric age (Table 1). Malignant tumors predominated both within the adults (Figure 1) and the pediatric age group (Figure 2) (n = 26, 16 adults and 10 pediatric). One pediatric case was in the intermediate category. There were two benign tumors, one each within the adult and pediatric cases. The tumors in temporal bone presented with a deviation of angle of the mouth and in the frontal bone with proptosis. The Tumors within the base of the skull presented with diplopia, deviation of septum, and squint.

| | Number of Cases (%) | Median Age (Years) | Male: Female | Most Common Site |
|---|---|---|---|---|
| **Malignant** | | | | |
| Osteosarcoma | 10 (34.3) | 15.1 | 5:5 | Calvarium |
| Chordoma | 9 (31.0) | 40.2 | 4:5 | Clivus |
| Chondrosarcoma | 6 (20.7) | 27.3 | 3:3 | Sphenoid |
| Ewing Sarcoma | 1 (3.5) | 1.5 | Male | Calvarium |
| **Intermediate** | | | | |
| Giant Cell Tumor | 1 (3.5) | 13 | Female | Clivus |
| **Benign** | | | | |
| Aneurysmal Bone Cyst | 1 (3.5) | 13 | Female | Sphenoid |
| Chondroblastoma | 1 (3.5) | 27 | Male | Calvarium |

***Table 1:*** *Distribution of the cases according to the nature of the disease, age group and site predilection.*

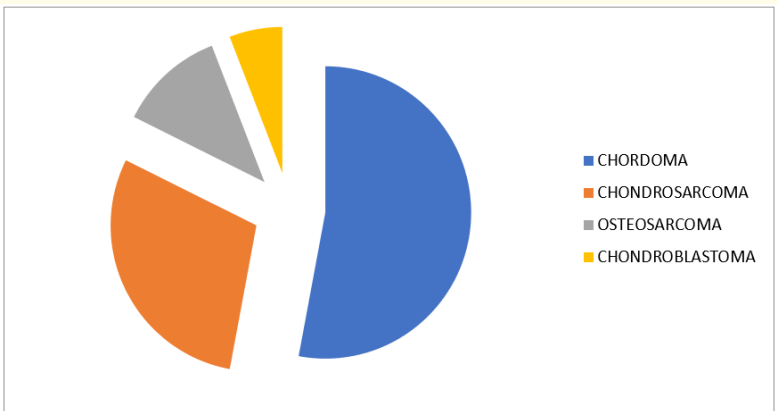


***Figure 1:*** *Skull bone tumors in the adult age group.*

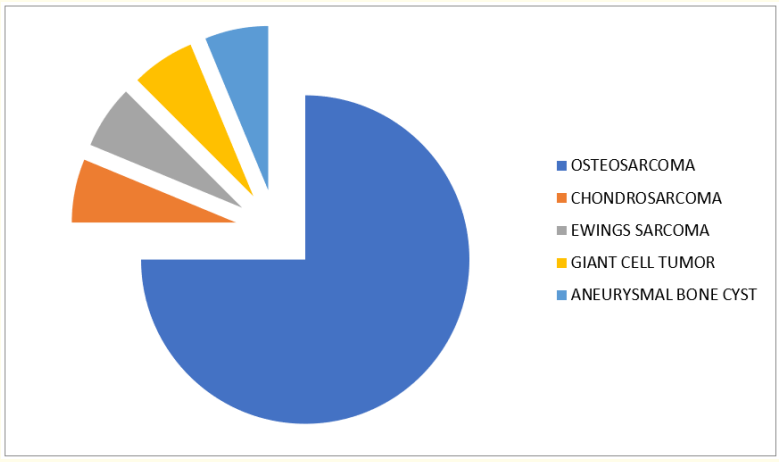


***Figure 2:*** *Skull bone tumors in the pediatric age group.*

There were 10 cases of osteosarcoma, which was the commonest category. Out of those 10 cases, 8 were within the pediatric age group and two were adults. The median age was 15 years; the youngest patient was one year old at the time of diagnosis while the oldest was 37 years old. There were an equal number of males and females. The second commonest tumor was chordoma; all the adults, with a median age of 40.2 years, the youngest being 25 years and the oldest was 59 years. Clivus was the most common location for the chordoma. Chondrosarcoma constituted six cases. The median age of the patients was 27.6 years. Most of them were conventional chondrosarcomas, mostly in adults with exception of one case of mesenchymal chondrosarcoma in an eight-year-old child. Sphenoid was the most common location for chondrosarcomas. Among other tumors, there was one case of Ewing sarcoma within the malignant category, one case of giant cell tumor within the intermediate category and one case each of aneurysmal bone cyst and chondroblastoma within the benign category. Aneurysmal bone cyst and giant cell tumors were seen in the base of the skull. Chondroblastoma was seen in adults, while Ewing sarcoma, giant cell tumor, and aneurysmal bone cyst were seen within the pediatric age. The symptoms of those tumors were associated with the location of the presentation. Tumors within the base of the skull presented with diplopia, deviation of septum, and squint.

## Discussion

Skull bone tumors are uncommon entities. The diagnoses of those tumors are difficult due to technical difficulties of surgical removal because of their location. However, the advances in the field of radiology and neurosurgery have led to a rise in the diagnoses of these tumors [3]. Chordoma and osteoma are the most common malignant and benign tumor respectively, reported within the largest case series from India [3]. The flat bones of the face, calvarial bones, and the clavicles undergo intramembranous ossification while bones at the base of the skull undergo endochondral ossification [1]. Hence, chondroid tumors are more common in the base of the skull while osteogenic tumors are more common in the calvarial bones.

Osteogenic sarcoma of the skull bones is a highly malignant disease demanding aggressive therapy. More than half of all osteosarcomas occur within the long bones of the limbs; most lesions within the head and neck arise from the mandible and less frequently, the from maxilla in patients in the third and fourth decades of life (about a decade later than the appendicular skeleton) [4]. In our study, the foremost common skull bone tumor was osteosarcoma (Table 2) 10 cases comprising about 34% of our cases of skull bone tumors. So far about 150 cases of skull bone osteosarcomas are reported in the literature [5-8]. In previous studies, osteomas were the most common osteoid

producing tumor of the skull bone [3]. However, this being a tertiary care cancer hospital, there are fewer benign cases in our study. Eight out of ten patients of osteosarcomas were within the pediatric age with equal male and female predilection. Review of literature also supports the very fact that the bulk of the cases are in the second decade of life. In the present study, there were two pediatric patients with multicentric osteosarcomas with skull bone being one of the sites. A 13-year-old girl, who had frontal bone osteosarcoma was diagnosed with bilateral retinoblastoma at 1 year of age. Patients with hereditary retinoblastomas are well known to have a high risk of developing osteosarcoma especially after radiotherapy [9]. Eight out of ten cases were high-grade osteosarcomas including one case of giant cell-rich osteosarcoma. Giant cell rich osteosarcoma often causes diagnostic problem because of its similarity with giant cell tumor or aneurysmal bone cyst. The presence of atypical mitosis and focal tumor osteoid helped in the diagnosis (Figure 3). The remaining two were low-grade diseases. The low-grade osteosarcoma had diagnostic difficulty due to bland looking cells. Permeation of bony trabeculae along with radiological findings helped in diagnosis. Other spindle cell neoplasms like nerve sheath tumor and desmoplastic fibroma were in the differential diagnoses especially in mastoid bone.

| | Age (years) | Sex | Site | Histology | Grade |
|---|---|---|---|---|---|
| 1 | 1 | Male | Sellar region | Chondroblastic | High |
| 2 | 7 | Male | Frontal | Fibroblastic | High |
| 3 | 12 | Male | Temporal, multicentric | Fibroblastic | High |
| 4 | 12 | Female | Parietal, multicentric | Chondroblastic | High |
| 5 | 13 | Male | Mastoid | Fibroblastic | High |
| 6 | 13 | Female | Orbit | Fibroblastic | High |
| 7 | 15 | Male | Occiput | Osteoblastic | Low |
| 8 | 15 | Female | Clivus | Giant cell rich | High |
| 9 | 26 | Female | Frontal | Fibroblastic | High |
| 10 | 37 | Female | Temporal | Osteoblastic | Low |

***Table 2:*** *Distribution of osteosarcomas according to age, sex, site and type.*

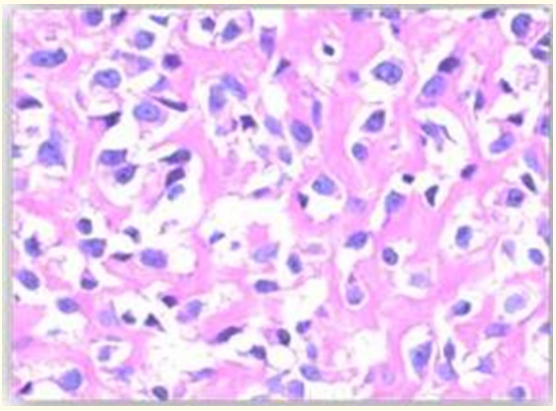

***Figure 3:*** *HE, 40X. Photomicrograph of a high-grade osteosarcoma with osteoid formation.*

The commonest tumor in adults were chordomas (n = 9), (Table 3) with site predilection for clivus. They comprised 30% of the entire cases. The median age was 40.2 years with a slight female predominance. Review of literature also showed chordoma as the most common malignant neoplasm with a predilection for clivus [3]. Four out of nine cases were chondroid chordomas (Figure 5) and rest were conventional chordomas. Grossly, chordomas are grey to bluish-white tumors with a glistening appearance, which frequently shows a pseudo capsule. Microscopically, they have a lobular architecture with densely packed spindle-shaped cells and multivacuolated (physaliphorous) (Figure 4) epithelioid tumor cells in clusters and groups. Physaliphorous cells are loosely packed and are embedded in a complex stromal matrix [3]. The most common differential diagnosis in cases of chondroid chordoma is chondrosarcoma; however, they were differentiated from chondrosarcomas by immunohistochemistry AE1/AE3 (Pan Cytokeratin) and S100. Cytokeratin was positive in all chordomas (Figure 6) whereas chondrosarcomas were positive for S100 and negative for AE1/AE3. Brachyury is a more specific marker for chordoma and helps to differentiate from chondrosarcomas in difficult cases especially chondroid chordomas and poorly differentiated chordomas. Poorly differentiated and dedifferentiated chordomas were not present in this study. EMA can also be used for chordoma diagnosis [3]. Chordoma is a rare tumor arising from the remnants of the notochord. The most common site the sacrum, followed by the skull base (30%) where clivus is the predominant site of origin [11,12]. Skull base chordomas are seen in patients who are almost a decade younger than those with sacral chordomas [11].

| | Number of cases (%) | Median Age (years) | Male:Female |
|---|---|---|---|
| Conventional | 5 (55%) | 37 | 1:4 |
| Chondroid | 4 (45%) | 44.25 | 3:1 |

***Table 3:*** *Distribution and types of chordomas.*

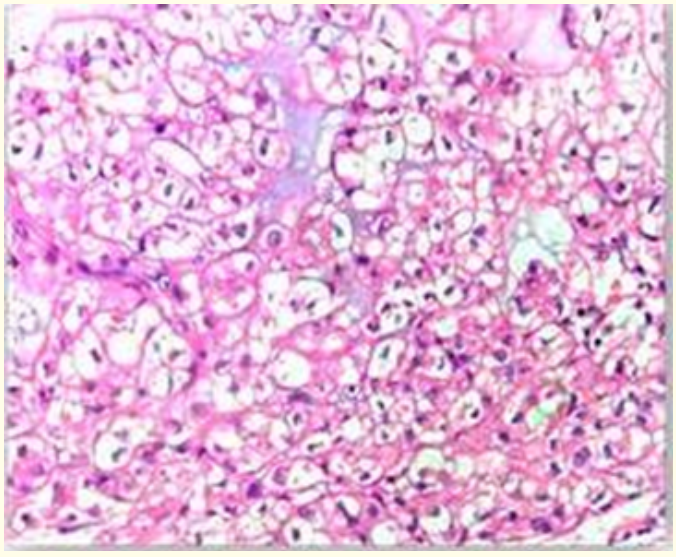

***Figure 4:*** *HE, 400X. Conventional chordoma with numerous "physaliphorous" cells.*

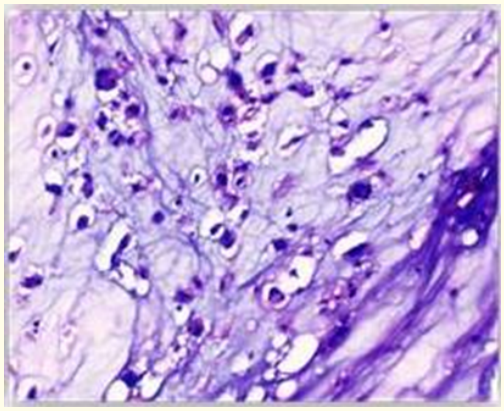

***Figure 5:*** *HE, 400X. Chondroid chordoma with areas of hyaline cartilage.*

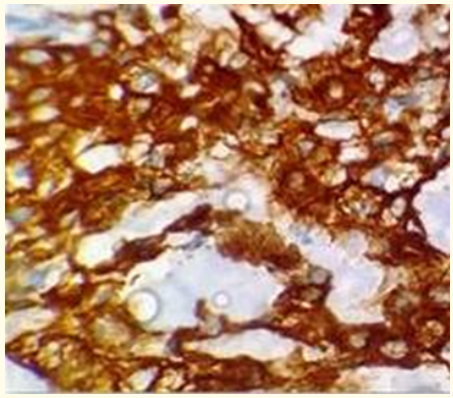

***Figure 6:*** *IHC, 400X. AE1/AE3 (Pancytokeratin) positivity in chordoma.*

Approximately 20% (n = 6) of our cases were chondrosarcomas with site predilection for the base of the skull (Table 4). Two cases were seen in the temporal bone. Five cases were conventional chondrosarcomas. The mean age of the patients was 27.6 years. The youngest case was an eight-year-old girl with mesenchymal chondrosarcoma (Figure 7). Chondrosarcomas are classified as conventional, mesenchymal, clear cell, and dedifferentiated types. Conventional chondrosarcoma is the commonest subtype. Mesenchymal chondrosarcomas commonly arise from the meninges of the skull bone [1]. Chondrosarcoma accounts for 0.15% of all the intracranial tumors [14,15]. The WHO grading system consists of three categories: grade I (well-differentiated), grade II (moderately differentiated), and grade III (poorly differentiated), and therefore the biological behavior of those tumors is characterized by subsequent compression or invasion of local structures [15]. Endochondral ossification is seen at the base of the skull and hence chondrosarcoma of skull bone occurs mostly at this site [1]. The mesenchymal chondrosarcomas have a poorer prognosis and are known to occur in younger population in comparison to the conventional chondrosarcomas [15,16].

| | Age (years) | Sex | Site | Histology |
|---|---|---|---|---|
| 1 | 8 | Female | Sphenoid | Mesenchymal chondrosarcoma |
| 2 | 21 | Male | Clivus | Conventional chondrosarcoma |
| 3 | 24 | Female | Clivus | Conventional chondrosarcoma |
| 4 | 28 | Male | Temporal | Conventional chondrosarcoma |
| 5 | 33 | Male | Temporal | Mesenchymal chondrosarcoma |
| 6 | 52 | Female | Sphenoid | Mesenchymal chondrosarcoma |

***Table 4:*** *Distribution and types of chondrosarcomas.*

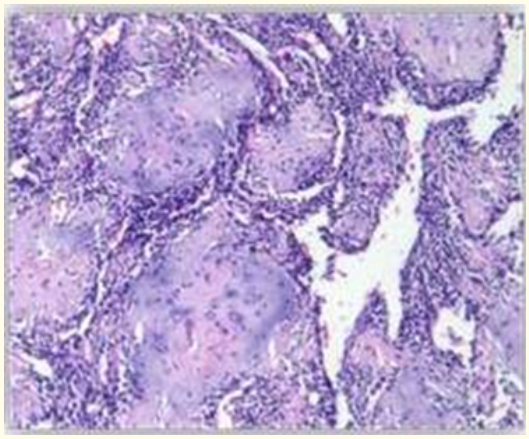

***Figure 7:*** *HE, 400X. Mesenchymal chondrosarcoma composed of small round cells admixed with lobules of hyaline cartilage.*

Among other tumors, we had one case of Ewing Sarcoma in a one and a half-year-old male child in the temporal bone. Ewing Sarcoma is a malignant neoplasm that shows neuroectodermal differentiation and is characterized by recurrent balanced translocations involving the EWSR1 gene on chromosome 22. It usually occurs in patients younger than 20 years and involves the diaphysis of long bones. The skull and vertebrae are involved only occasionally. It is positive for FLI-1 and has strong membranous positivity for CD99. NKX2.2 is a novel marker for Ewing Sarcoma which is more specific. However, molecular testing for EWSR1 gene rearrangement may be necessary to rule out other close differentials like mesenchymal chondrosarcoma, small cell osteosarcomas and other small round cell sarcomas where immunohistochemistry might not help [3,17] (Figure 8).

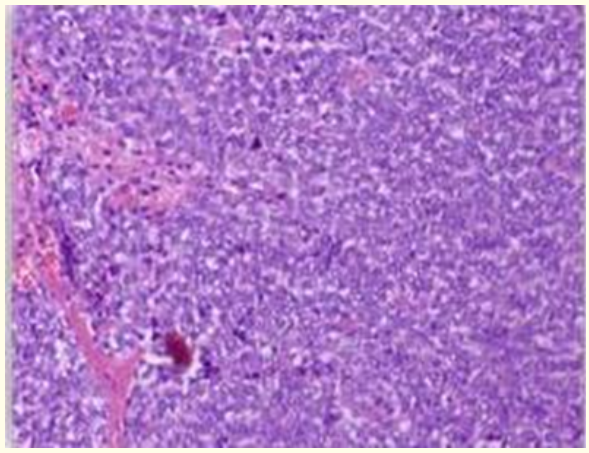

***Figure 8:*** *HE, 400X. Ewing's sarcoma showing malignant small round cells.*

In our study, we had a couple of other rare tumors like giant cell tumor (GCT), aneurysmal bone cyst (ABC), and chondroblastoma. Approximately 1% of GCTs affect the bones of the skull and face, with the sphenoid being the foremost common location [3,11]. Aneurysmal bone cyst may be a differential of giant cell tumor and may be distinguished from the latter by the distribution of the giant cells along the walls of vascular channels. Both our cases of ABC and GCT were found in the base of the skull and seen in adolescent females. Chondroblastoma was found in an adult male in the petrous a part of the temporal bone. It recurred thrice. The temporal bone is a preferred site for chondroblastoma. It may be mistaken for giant cell tumor. But the stromal cells of chondroblastomas are round to oval with abundant cytoplasm and vesicular convoluted nuclei resembling Langerhans cell nuclei. Temporal bone chondroblastomas frequently show pigment laden macrophages as seen in our case.

## Conclusion

Primary bone tumors of skull are rare. With recent advances in neurosurgery, we pathologists are becoming exposed to more number of skull tumors which were considered inaccessible till the recent past. A multidisciplinary approach involving the treating physician, the radiologist, and the pathologist is advocated for accurate diagnosis and ultimately for the best possible treatment. Judicious and selective use of immunohistochemistry helps to reach a selected diagnosis in certain cases like chordoma and Ewing Sarcoma. The spectrum of skull bone tumors, with morphological variations and site-specific predilection should be known.

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