

**CHORDOMA AND CHONDROID TUMORS OF THE SKULL
BASE A CLINICOPATHOLOGICAL STUDY OF 28 CASES**

**DISSERTATION SUBMITTED FOR THE DEGREE OF
DOCTOR OF MEDICINE IN PATHOLOGY**

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Dr. Naina Kataria (Goel).

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INTRODUCTION
AND
HISTORICAL REVIEW

Chordomas and chondroid tumors occurring at the base of the skull pose many clinical and surgical problems. They are comparatively rarer forms of intracranial space occupying lesions.

Clinical interest in cranial chordomas and chondrosarcomas has increased in the last few years. The reasons for this surge in interest appear to be as follows:

1. **High detection rate:** Better diagnosis of cases with the help of Magnetic resonance imaging (MRI). Even with the help of Computerised tomography (CT) scanning it is difficult to detect some of these lesions as they are located in the base of the skull. Unclear delineation of the tumor due to bone artifacts may sometimes lead to difficulties in identification of the tumor.

2. **Better evaluation:** MRI not only helped in clearly defining the extensions of the tumor, but also clarified the relationships to adjoining neural and vascular structures. The relationship of

the tumor to the internal carotid artery, which is crucial while planning and executing the surgical treatment could be clearly seen on MRI.

3. **Better treatment modalities** Advancements in skull base surgical techniques in the last decade has increased the awareness and improved the management efficiency of these relatively difficult neurosurgical problems.

4. Parallel to the improved radiological and neurosurgical enthusiasm in the management of these cases, the pathology of these tumors is also a subject of renewed interest. Immunohistochemical and ultrastructural studies have also helped in differentiating and subclassifying these tumors.

Cranial chordomas are slow growing but locally invasive tumors that usually present between the 3rd and 5th decades of life. Male predominance has been recorded. Chordoma accounts for approximately 1% to 4% of all primary bone neoplasms. The tumor was originally described by Virchow in 1857 who postulated that it was a cartilaginous entity. One year later, Muller proposed a notochordal origin that has largely been accepted and reaffirmed by work of others (3).

Although the sacrum is the most common site of origin, approximately 30% of these tumors occur in the region of the skull

base. More frequent site of presumptive origin at the cranial base is the region of the junction of basisphenoid with basiocciput.

In 1973, Heffelfinger and his colleagues described a histologically biphasic neoplasm that demonstrated both chondroid and chordoid differentiation for which the term 'chondroid chordoma' was coined (25). These tumors occurred almost exclusively in the spheno-occipital region, afflicted younger patients, and had a much better prognosis than typical chordoma. Several studies followed the report of Heffelfinger et al and have supported their conclusion (1,12,24,27,33,36,43,48,50,52,54,58,66,49,62). These studies have offered both histologic (1,12,24,27,33,36,43,48,50,54,58,66,49,62), immunohistochemical (1,12,27,33,36,43,50,52,54,58,66) and electron microscopic evidence (36,43,52,62) of the existence of chondroid chordoma. However, several investigators have questioned the validity of 'chondroid chordoma' as a separate clinicopathologic entity (6,7,40,63). These investigators propose that chondroid chordoma is actually a low grade chondrosarcoma. Further studies continue as regards subclassification of this tumor.

Chordomas of the spheno-occiput region are sometimes distinguished from chondrosarcomas with difficulty. The classification of these neoplasms is controversial. Chordomas and chondrosarcomas are two distinct varieties of tumor but have marked clinical, radiological, surgical and pathological resemblance

(4,23,38,59). However chordomas are of epithelial origin whereas chondrosarcomas originate from the mesenchymal cells.



AIMS AND OBJECTIVES

- 1) To study the clinical, radiological and pathological aspects of the chordoid and chondroid tumors of the base of the skull.
- 2) To determine the relationship of chondroid chordomas to chordomas and chondrosarcomas on the basis of clinical, radiological and conventional histopathological methods as well as to perform an immunohistochemical analysis on selected cases.
- 3) Evaluation of the therapeutic modalities and to assess the prognosis.

MATERIAL AND METHODS

This is a retrospective study of 28 cases of chordomas and chondrosarcomas of the skull base region encountered during a period of 31 years since 1965 (when the neuropathology department was started as a specialised sub-unit) in a large Teaching Hospital in Bombay. Details of clinical and radiological features were obtained from the case records of the neurosurgical unit of the Hospital.

PATHOLOGICAL STUDY:

In all cases multiple bits of surgically removed tumors were received. In 5 cases the surgery was repeated as there was recurrence of the tumors. Autopsy was performed in 3 cases.

HISTOPATHOLOGY:

Sections from the formalin fixed paraffin embedded blocks were prepared and routinely stained with haematoxylin-eosin. Reticulin, Periodic Acid Schiff (PAS) and Alcian Blue stains were also employed wherever necessary. Sections were reviewed to classify the tumors as Chordomas, Chondroid Chordomas or Chondrosarcomas. Any chondroid area in a chordoma qualified it as a chondroid chordoma in accordance with the criteria laid down by

Heffelfinger et al (1973) (25).

Immunohistochemistry: The immunohistochemical studies were carried out in 18 cases. These studies were performed in 3 batches using commercially available staining kits manufactured by Span Diagnostics Ltd. India (2 batches) and Dakopatts Corporation Belgium (1 batch).

These staining kits were designed for demonstration of cell antigens using the Streptavidin-Biotin amplification system by the indirect method.

For each cases, the markers studied were

1) **PanCytokeratin:** Monoclonal antibody to Human PanCytokeratin obtained by fusion of mouse myeloma cells to splenocytes of the mouse immunised with cytoskeleton preparation of human A43/1 carcinoma cell line (Clone C-11-IgG1, Novacastra Lab. U.K., Sigma).

2) **Vimentin:** Monoclonal antibody to Vimentin obtained by fusion of mouse myeloma cells to splenocytes of the mouse immunised with purified calf lens (Clone LN-6-IgM, Novacastra Lab. U.K., Sigma).

The cost of immunohistochemical reagents precluded in using a larger panel of antibodies.

Eighteen tumors were selected for immunohistochemical studies. These included 4 classical chordomas, 9 chondroid chordomas and 5 chondrosarcomas.

The immunohistochemical study was performed as per the following protocol.

Staining protocol using Streptavidin Biotin HRPD complex method:

- 1) Formalin fixed paraffin embedded tissue was cut at 5 microns thickness.
- 2) Mounted on synthetic Epsilon coated slides.
- 3) Deparaffinised with Xylene.
- 4) Rehydrated in graded alcohol.
- 5) All slides placed in a humid chamber to ensure no drying of the sections at any stage.
- 6) Added 2 drops of Endogenous Enzyme blocking Reagent (0.3% hydrogen peroxide in methanol), incubated for 30 minutes.
- 7) Washed twice with Phosphate Buffer solution (PBS) for 10 minutes. Excess PBS drained off.
- 8) Two drops of Non-Specific Binding sites blocking serum (10%

Normal Rabbit serum) added. Incubated for 10 minutes. Excess reagent drained off.

9) The sections were covered with Primary Antibody and incubated for 30 minutes (one batch was incubated overnight at 4 degree centigrade with primary antibody). Repeated step 7.

10). Two drops of Link Antibody (Biotinated anti-mouse Ig) added. Incubated for 30 minutes. Washed thoroughly with PBS. Excess PBS drained.

11). Two drops of Enzyme Conjugate (Streptavidin HRPD Complex) added. Incubated for 30 minutes. Washed twice with PBS. Excess PBS drained.

12). Four drops of Substrate Chromogen (Diamino Benzidine) added. Colour reaction was stopped at 20 minutes.

13) Sections washed thoroughly with deionised water.

14) Counterstained with haematoxylin.

15) Dehydrated, Cleared and Mounted.

Positive control was used for Pancytokeratin using section of a squamous cell carcinoma - skin. Internal positive control of endothelial cell positivity was used as a control for Vimentin.

All incubations were carried out at room temperature except on one of the batches where the incubation with primary antibody was at 4 degree centigrade.

The reaction with primary antibody was considered positive if brown cytoplasmic staining of tumor cells was observed and the intensity was graded (-, +/-, +, ++).

The results of the entire study are presented in a tabular form (Tables 1-11).

RESULTS AND DISCUSSION

The present series of 28 cases is amongst the few large series of these cases reported in the literature. Other large series of chordomas and chondrosarcomas of the skull base are as follows:

Table 1

Author	cases	time period (years)	Institution	Period
Rich et al	48	50	Massachusetts General	1931-1981
Sekhar et al	54	12	Pittsburgh Univ. Hosp.	1982-1994
Heffelfinger	55	61	Mayo Clinic	1910-1971
Present	28	31	Teaching Hospital Bombay	1965-1995

CT scan was introduced in Bombay in 1981. This investigation was significant improvement as regards to the diagnosis of intracranial lesions. The detection rate of chordomas and chondrosarcomas also improved. However, these tumors located in the base of the skull had low detection rate even on CT scanning because a significant number of cases were missed due to the bone artifacts. MRI was introduced in 1988. MRI was used as a principle investigational modality for cranial basal lesions in the Institution since 1992. It was observed that during the period MRI

had picked up an additional 3 cases which were missed on CT scan.

Higher detection rate of chordomas was clearly observed in the present series.

Table 2

Detection rate of chordomas, chondrosarcomas and chondroid chordoma		
Years	Cases	Percentage
1965 - 1970	1	7.14
1970 - 1980	3	10.71
1980 - 1990	9	32.14
1990 - 1996	15	53.57

CLINICAL FEATURES:

Age and sex: Table 3 shows the age distribution. The majority of the cases were in the third decade. The ages ranged from 6 years to 75 years. The mean age at the time of diagnosis was 34.75 years. Male predominance was noted. Eighteen patients were males while 10 were females (Table 4).

Table 3

Age incidence		
Age (in years)	Cases	Percentage
0-10	1	3.57
11-20	4	14.28
21-30	8	28.58
31-40	4	14.28
41-50	6	21.42
51-60	3	10.71
61 and above	2	7.14

Table 4

Sex incidence		
Sex	Cases	Percentage
Male	18	64.28
Female	10	35.72

Site of origin:

Table 5 shows the sites of origin. Mid-clivus was the commonest presumed site of origin or the epicentre of the tumor (82%).

Table 5		
Presumed site of origin of all tumors		
Site of origin	Cases	Percentage
Sella	3	10.71
Lower clivus	2	7.14
Midclivus	23	82.15

Table 6 shows the direction of spread. A large majority of cases showed an eccentric spread (93%).

Table 6		
Direction of spread of tumors		
Direction of Spread	Cases	Percentage
Midline spread	2	7.14
Eccentric spread	26	92.86

Table 7

Clinical features					
Case	Age/sex	Duration of symptoms (months)	cranial nerves affected	other symptoms	histology
1	40/F	2	6,9-12	Quadriparesis	Chordoma
2	46/M	24	5,6,8,9	headache cerebellar signs	Chordoma
3	50/M	48	5,6,8-12	cerebellar signs	Chordoma
4	42/F	12	2-6,8	headache	Chordoma
5	55/M	8	3-6	hemiparesis	Chordoma
6	31/M	6	6(bilat) 9-12	cerebellar signs	Chordoma
7	25/M	12	5,6,9-11	headache	Chordoma
8	57/F	1	5,6,8	cerebellar signs	Chordoma
9	65/F	12	2,3,6	headache	Chordoma
10	6/M	1	2,3	headache	Chordoma
11	50/M	12	3,5,8	Swelling palate difficult breathing	Chondroid Chordoma
12	25/F	2	5,6,8-11	Quadriparesis	Chondroid Chordoma
13	27/M	24	5-12	cerebellar signs	Chondroid Chordoma
14	25/M	6	2-4 (bilat) 6,7,	hemiparesis	Chondroid Chordoma
15	26/F	3	5,6	headache (post-partum)	Chondroid Chordoma
16	25/M	8	3-12	cerebellar	Chondroid Chordoma
17	18/F	4	2-6 bilateral	amenorrhoea	Chondroid Chordoma

18	25/M	2	5,7,9-11	cerebellar	Chondroid Chordoma
19	46/M	6	2-6	epistaxis	Chondroid Chordoma
20	32/M	48	7,9-12	headache	Chondroid Chordoma
21	18/M	6	12	quadriparesis	chondrosarc
22	17/M	8	3,6,9-11	headache	chondrosarc
23	75/F	6	3,6	headache cerebellar sign	chondrosarc
24	35/M	24	3-12	hemiparesis	chondrosarc myxoid
25	52/F	3	9-12	headache	chondrosarc mesenchymal
26	18/M	8	3-12	headache hemiparesis	chondrosarc myxoid
27	30/M	3	Nil	headache neck pain	chondrosarc
28	46/M	24	6,9-12	hemiparesis	chondrosarc

Headache was a frequent presenting symptom seen in 12 patients. The headache was probably secondary to destruction of bone and/or to pressure effects on nerves or adjacent organs. Due to the proximity of a clival chordoma to the sixth nerve, unilateral (20 cases) or bilateral affection (2 cases) of this nerve was commonly seen. Other cranial nerves of the cavernous sinus were affected in 23 cases. The tumor spread was noted to be significantly more frequently on the right side which was observed in 20 cases. Sellar or parasellar chordomas presented with visual deterioration (6 cases), pituitary dysfunction (1 case), a chias-

mal or a cavernous sinus syndrome. Posterior cranial fossa extension resulted in cerebellar signs in 8 patients. Three patients had quadriparesis, while 5 had at least some degree of hemiparesis. Inferior clival extension of the lesion resulted in presentation with twelfth nerve palsy, dysphagia and dysphonia (13 cases). As there was a high incidence of involvement of occipital condyle, occipital pain was also a frequent symptom (4 cases). Symptoms of raised intracranial pressure were noticed in 3 cases only.

Table 8

Summary of major signs and symptoms

Symptoms and Signs	Cases	Percentage
headache	12	42.85
occipital pain	4	14.28
Visual deterioration	6	21.42
sixth nerve affection	22	78.57
other cranial nerves of cavernous sinus	23	82.14
lower cranial nerve affection	13	46.42
cerebellar signs	8	28.57
quadriparesis	3	10.71
hemiparesis	5	17.85
increased intracranial pressure	3	10.71

RADIOLOGICAL FEATURES AND OPERATIVE FINDINGS:

Radiological findings were based on the study of plain X-rays, CT scan and magnetic resonance imaging (MRI) (Figure 1-3).

Plain X-rays and tomography were available for review in 16 cases. Marked bone destruction of the clivus was seen in 8 cases, petrous apex destruction was seen in 4 cases, middle cranial fossa floor destruction was seen in 2 cases, and the sellar floor destruction was seen in 2 cases. Abnormal radio-opacification in the petroclival region was observed 4 cases. In 2 cases the X-rays did not show any abnormality.

CT scan was available in 14 cases. Tumors were usually well visualised and localizable by CT with or without contrast. The tumors were isodense on plain scan with none or only minimal contrast enhancement. Scattered interspersed calcific spots were observed in 8 cases including 5 cases of chondrosarcomas (Figure 1). Two cases moderate hydrocephalus. Destruction of the occipital condyle could clearly be seen in 2 cases.

Magnetic resonance imaging (MRI) features:

MRI scanning was performed in 11 cases. MRI scanning not only delineated the exact site and the extensions of the tumor but also clearly defined the vascular relationship (Figure 3,4). On short TR/TE images (T1 weighted images), both chordoma and chondrosarcoma uniformly had a low to intermediate signal in all

cases. On long TR/ long TE images (T2), the tumors had a very high signal (Figure 4). After Gd-DTPA administration all the soft tissue components of the tumor demonstrated some degree of contrast enhancement. The MRI exactly delineates the location and extent of these neoplasms, relationship of the tumor to neighboring structures such as the brain stem and the pituitary gland and thus played an important role in determining the optimal surgical approaches. The arterial relationships can be determined, and more importantly the displacement of large vessels by the tumor could be distinguished from encasement. The calcific areas in the tumor presenting as low intensity signals can sometimes make identification of the course of the blood vessel (by its flow void) difficult. The information on MRI often renders angiography (Figure 2) and sometimes even CT scanning unnecessary or less useful. In 2 cases the CT scan showed no abnormality so a magnetic resonance imaging (MRI) was performed which showed the basal petroclival tumor.

Relationship to bones: These tumors primarily involved the clivus. The tumors caused bone destruction and spread in an eccentric fashion in the petroclival region (Figure 1-6). The tumor extended by destroying the bone in the vicinity. The tumor was interspersed by normal bony spicules and trabeculae (17 cases). More common pattern of clival involvement was destruction of its one half (14 cases). The petrous bone was frequently destroyed at its apex. In larger lesions a large part of the middle fossa base was involved. The lesion in 7 cases extended along the

clival bone both superiorly and inferiorly. In the present series the occipital condyle was clearly affected in 4 cases. In 2 cases, the lesion primarily involved the inferior part of the clivus and the occipital condyle. The explosive pattern of spread by bony destruction and displacement of soft tissues appears to be a characteristic nature of spread of these tumors. All the above radiological findings were confirmed during surgery.

Relationship to the dura: On reviewing the radiological features and operative records it was observed that in all the patients the tumor was essentially extradural. Although it did appear in 5 cases on radiology that the tumor had invaded the dura, but the operative records suggested that a well defined, although a thinned out dural sheath was present in all cases. In literature, some cases of intradural spread of the tumor has been recorded. The impression from the present study is that the transgression of the dura by these tumors appears to be a rare feature. Surprisingly, however, in the recurrent cases, (following a surgical procedure) intradural and intracavernous sinus spread was a common finding and was seen 3 cases. It appears that the 'unnatural' dural incisions during the surgical procedure was responsible for intradural spread.

Relationship to the cavernous sinus: Russell and Rubenstein (51) mention that intracranial chordomas sometimes 'occupy' the cavernous sinus and spread thence into the middle fossa. In the

present analysis it was observed that the tumor displaces the cavernous sinus on its dome and a thin and stretched dura always prevents the tumor a direct entry into the venous sinuses of the cavernous sinus (Figure 5,6). There are various reports of these tumors invading into the cavernous sinus. However, direct invasion was not recorded in this series. The tumors were classified to have a 'subcavernous sinus extension'. The clinical and functional involvement of the cranial nerves appeared to be secondary to stretch on these nerves rather than direct invasion and involvement.

Relationship to the internal carotid artery: In the present series a peculiar but constant relationship of the internal carotid artery to these tumors was noted. The relationship is shown in the figures 2-6.

MRI scanning not only delineated the exact site and the extensions of the tumor but also clearly defined the vascular relationship. The characteristic petroclival pattern of the tumor displaced the relatively immobile parts of the internal carotid artery in the petrous and precavernous segments along its antero-lateral border (Figures 2-6). In 4 massive tumors, the entire intrapetrous segment of the artery was displaced. At the petrous apex, the fifth nerve was displaced superiorly while the carotid artery was displaced anteriorly. The direction and the site of the displacement of the carotid artery provides additional evidence that the epicenter of origin of these tumors is at the junction of basisphenoid and basiocciput. Complete encasement of

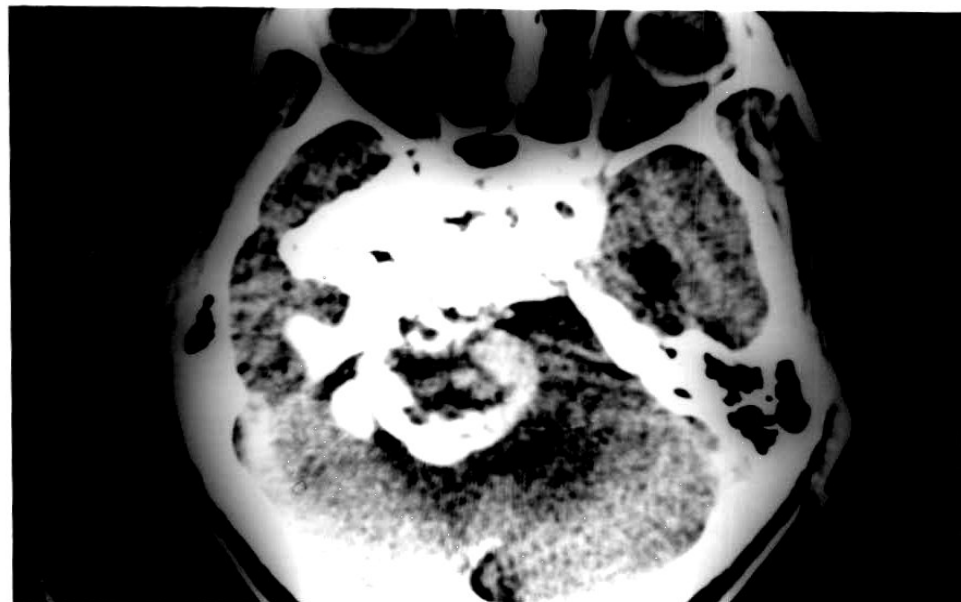


Figure 1: CT scan showing a large petroclival chondrosarcoma. The tumor is largely calcified.

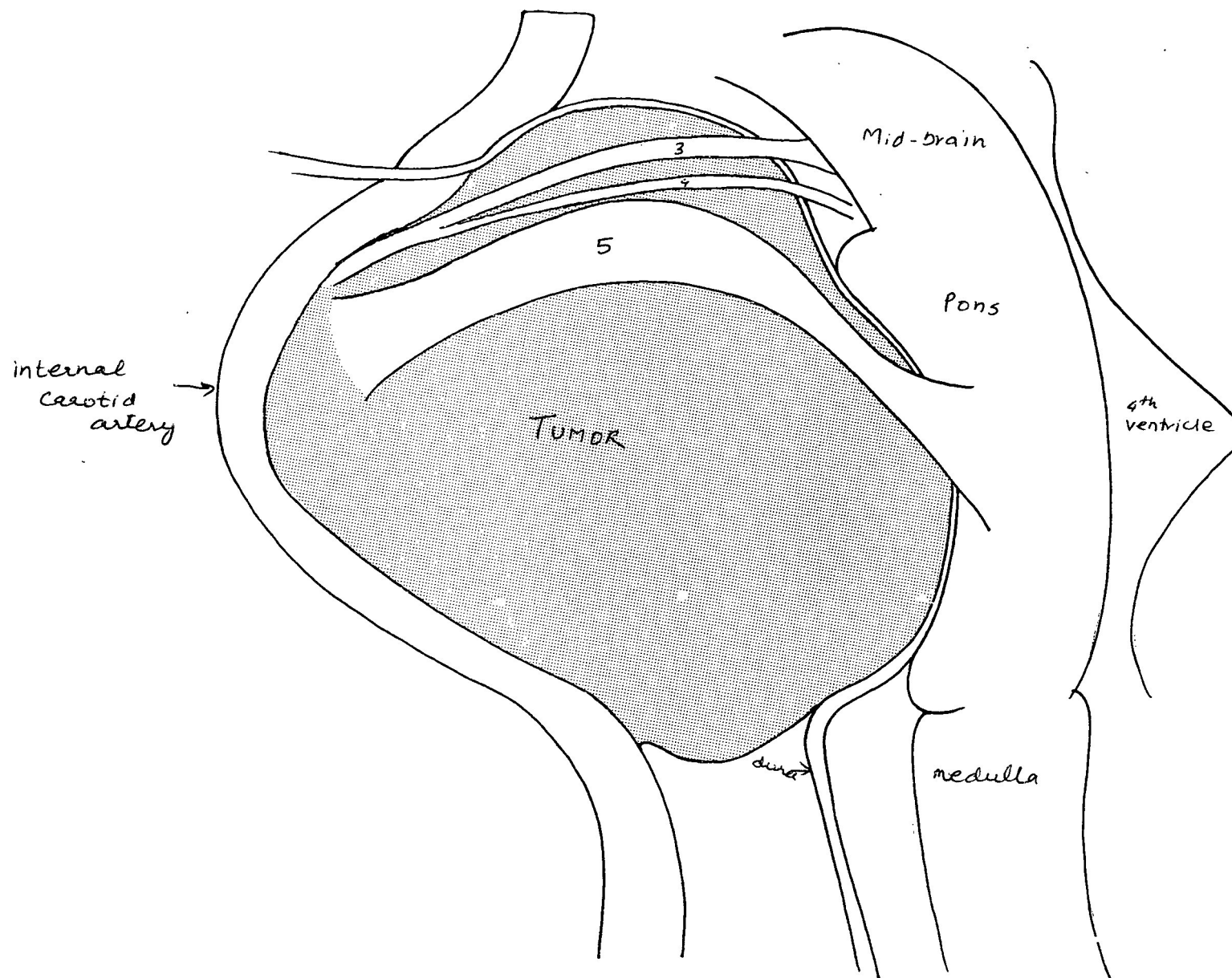


Figure 2: Internal carotid artery angiogram shows that the petrous and cavernous sinus segment of the internal carotid artery is displaced along the anterior border of the tumor (shown in Figure 1).



Figure 3: T-1 weighted MRI shows the large petroclival chordoma. The internal carotid artery is displaced along the anterior border of the tumor.

Figure 5



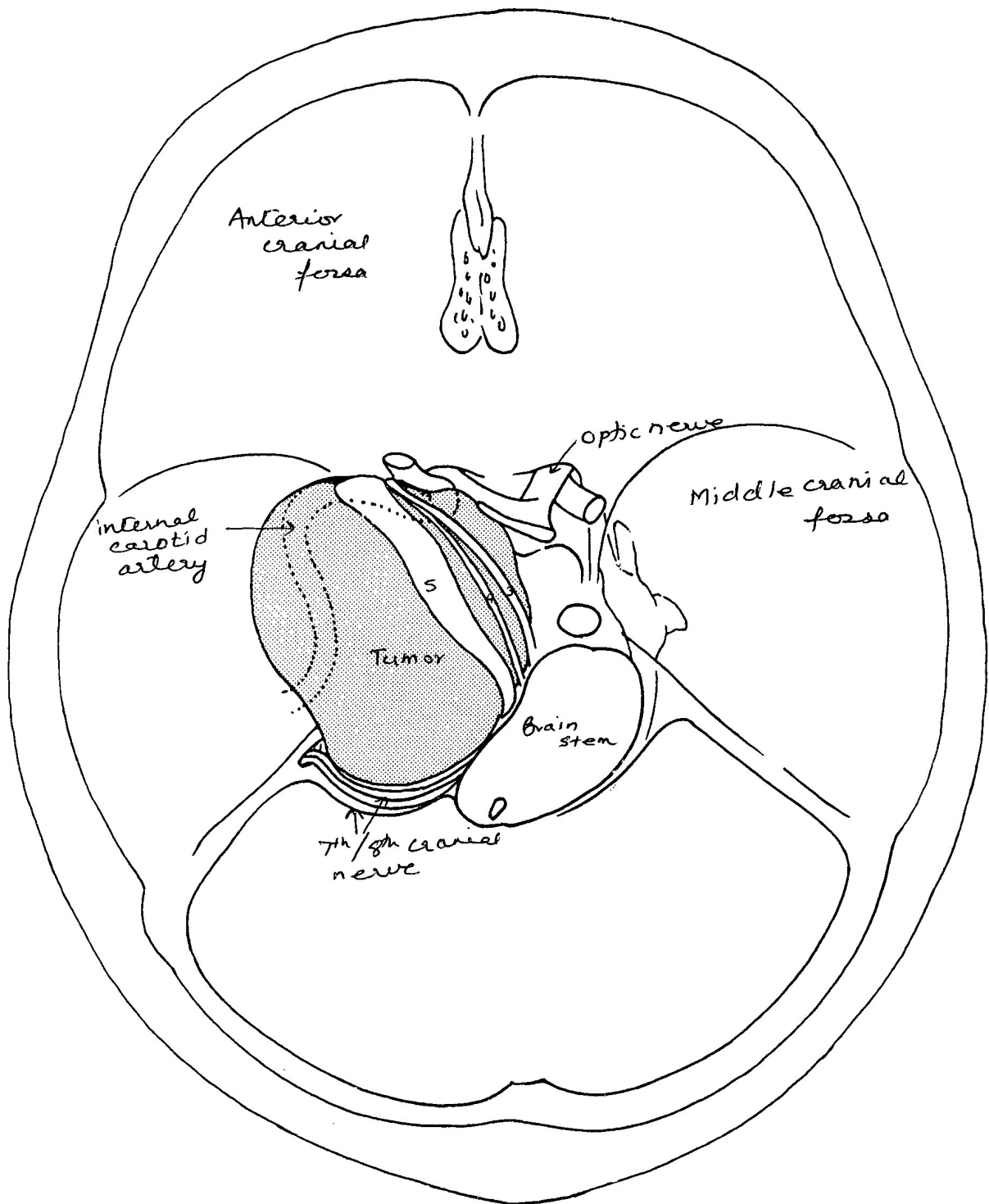


Figure 6

the artery was not seen in any patient despite the massive size of the tumors. Narrowing of the lumen of the vessel was seen in one case and was apparently due to the severe stretch. Myers et al noted vascular encasement by large tumors and observed that in spite of the complete encasement, the lumen of the vessel was not narrowed. Our observations and that of Myers et al (1992) suggest that these tumors are 'capsulated' and grow by expansion and bony destruction that displaces the soft tissues (35). As the tumor grows it pushes the ICA making way for it by destroying the bone. Arterial encasement is a late feature and appears to be secondary to the growth pattern of the tumor, wherein its lobulations surround the artery from its sides.

It appears that a cognisance of this relationship of the tumor to the internal carotid artery could be an important finding that could help in guiding the operation.

In the present study the nature and pattern of growth and of displacement of the carotid artery, cranial nerves and cavernous sinus by chordomas and chondrosarcomas resembled each other.

PATHOLOGY

Gross features:

In the present series the tumors were excised piece meal and were received in multiple bits. The tumors were gelatinous, lobulated, semitranslucent and grayish. Fifteen tumors had a gritty feel incorporating bony bits.

Microscopic features: In the present series on the basis of conventional haematoxylin and eosin staining methods the tumors were classified as follows:

Table 9	
Classification of tumors based on HE stain	
Nature of tumor	Number of cases
Chordoma	10
Chondrosarcoma	8
Chondroid chordoma	10

Chordomas:

Haematoxylin and Eosin staining: All tumors showed multiple lobules of varying sizes separated by intersecting connective tissue septae. The tumor cells were varying in size, from round

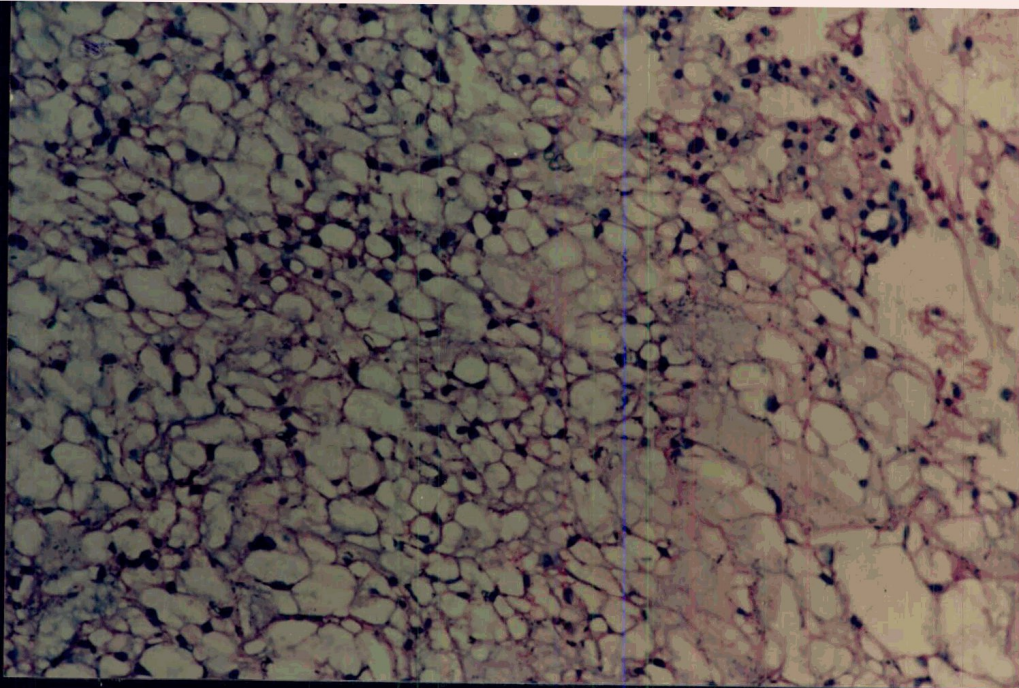


Figure 7: Photomicrograph showing a lobule of chordoma with varying sized cells with clear cytoplasm and inconspicuous round nuclei pushed to the periphery (HE x 250).

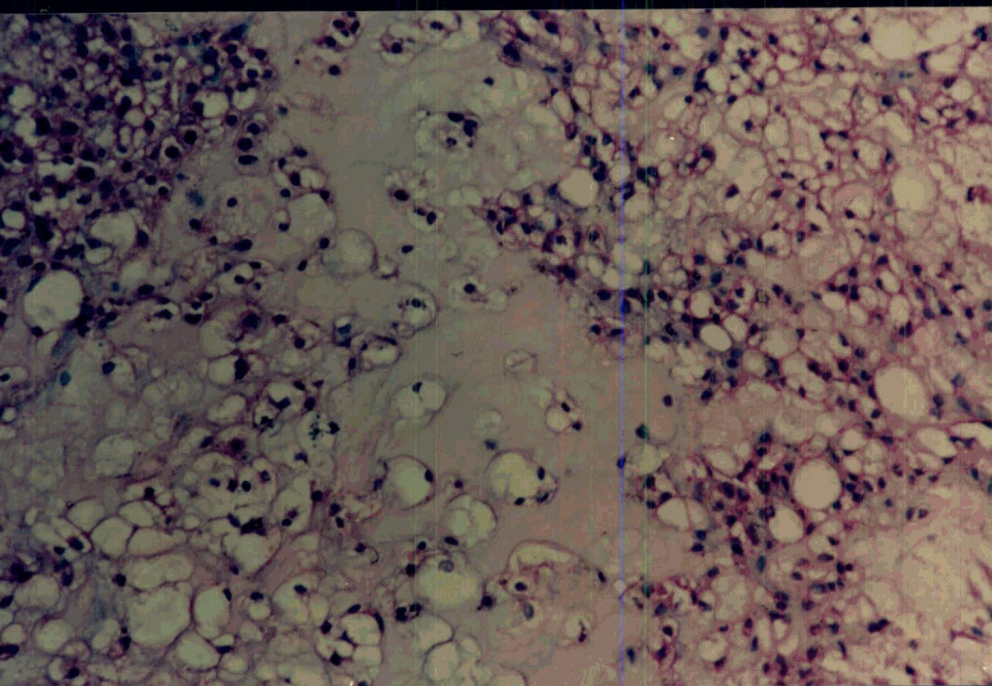


Figure 8: Photomicrograph showing physaliferous ^{cells} surrounded by varying amount of mucin - Chordoma with myxoid change (HE x 250).

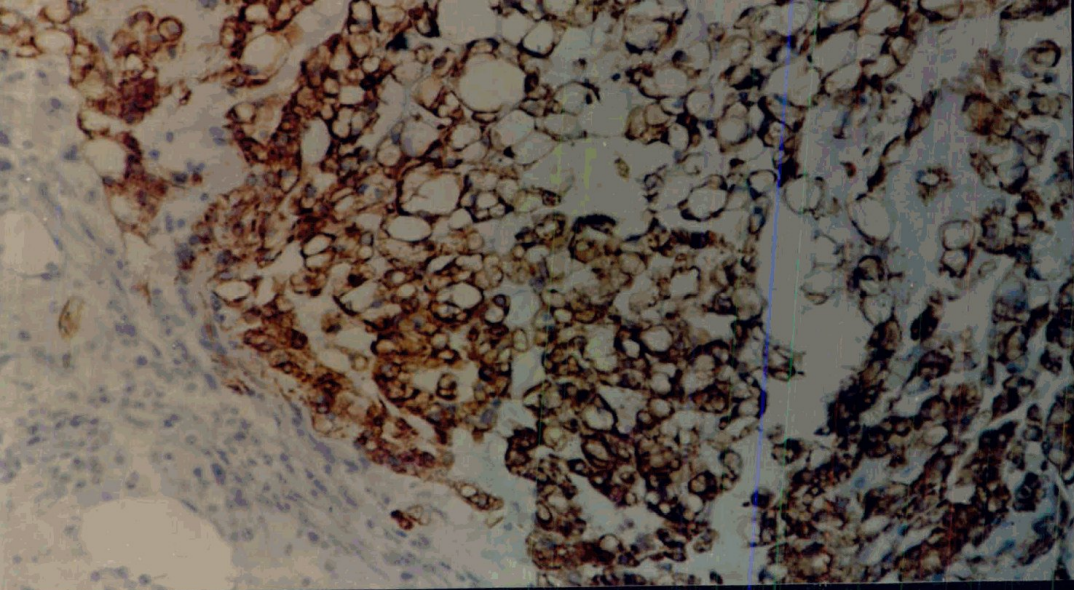


Figure 9: Photomicrograph showing Cytokeratin positive cells in a lobule of chordoma. Lower left corner demonstrates connective tissue septa negative for Cytokeratin - Chordoma (Cytokeratin x 50).

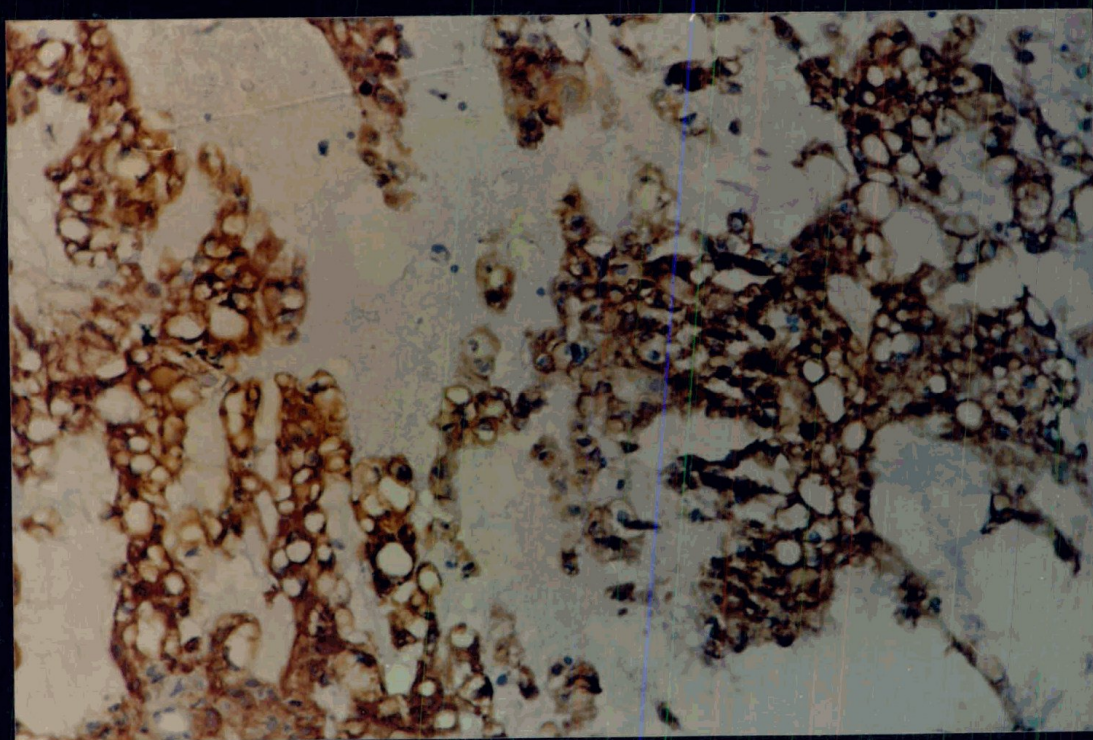


Figure 10: Photomicrograph showing Cytokeratin positivity in physaliferous cells. The mucin is not stained - Chordoma (Cytokeratin x 250).

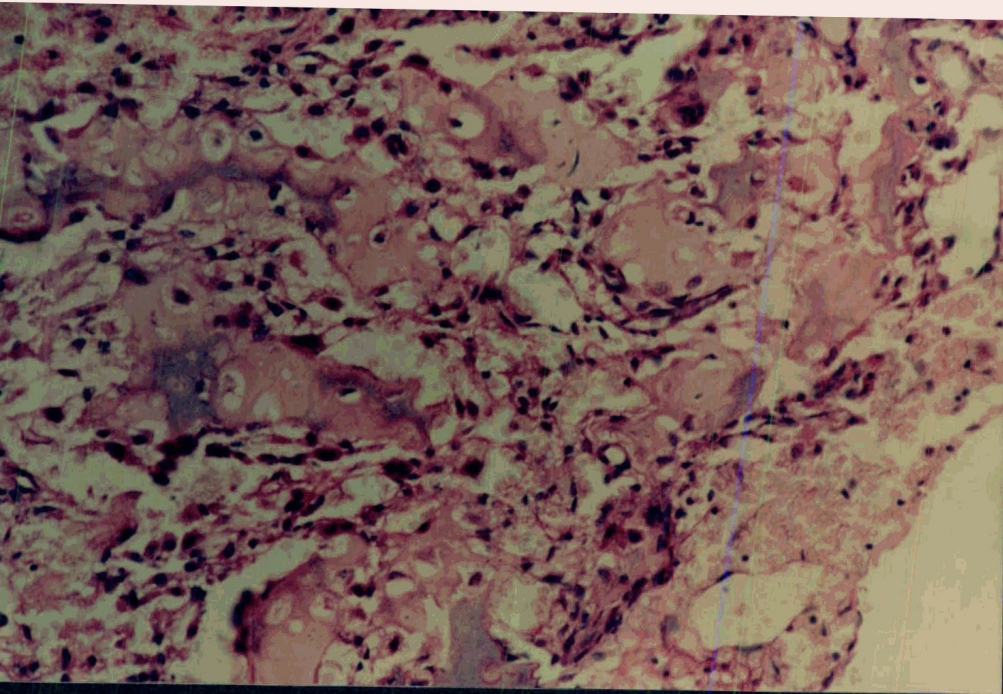


Figure 11: Photomicrograph showing irregular islands of mature and immature cartilage. Low grade Chondrosarcoma (HE x 250).

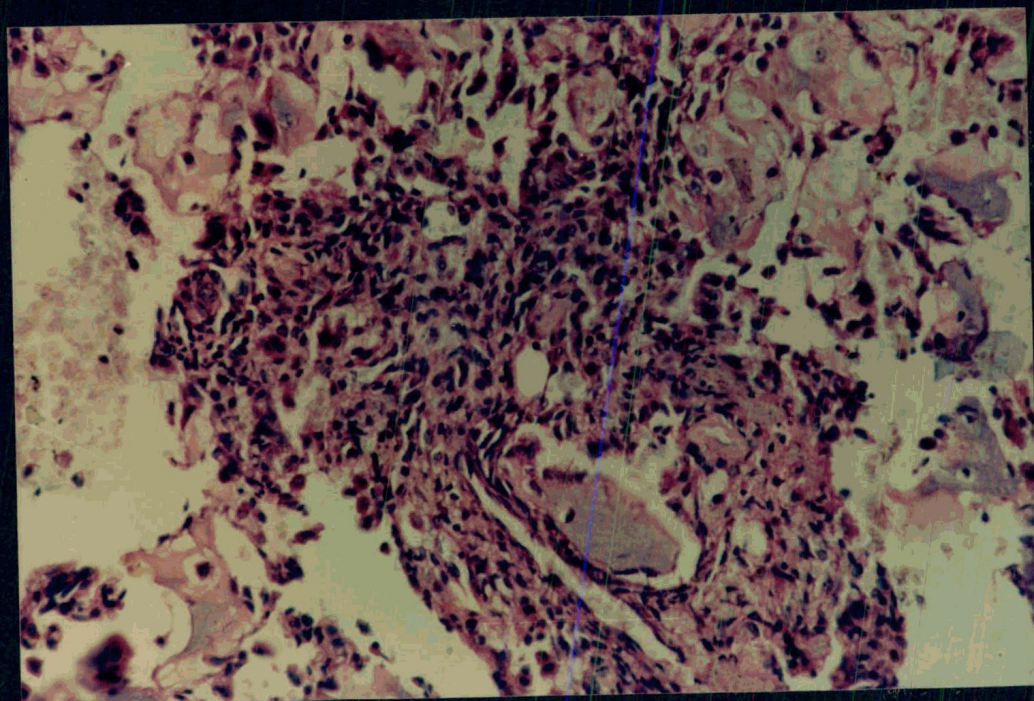


Figure 12: Photomicrograph showing irregular islands of mature and immature cartilage and more cellular area with mild nuclear atypia - Low grade Chondrosarcoma (HE x 250)

to polyhedral. Classical physaliferous cells with clear cytoplasm and small inconspicuous nuclei pushed to the periphery were seen (Figure 7). Three tumors showed stellate cells with single mitoses. The sheets of vacuolated physaliferous cells contained intracytoplasmic mucin, varying from an amount barely visible to a quantity that obviously had ruptured the cells leaving the nuclei, strands of cytoplasm, and adjacent cells surrounded by varying amount of mucin (Figure 8). Cytological atypia was minimal. Mitotic activity was infrequent. Pleomorphism was not striking. Tumor necrosis and vascularity varied but in general it was not significant.

Immunohistochemistry: All chordomas (4/4) were positive for Pancytokeratin (Figure 9,10). Three out of four chordomas also stained for Vimentin.

Chondrosarcomas:

Haematoxylin and Eosin staining: Eight chondrosarcomas studied included 4 classical low grade chondrosarcomas, 3 myxoid chondrosarcomas and 1 mesenchymal chondrosarcoma. These tumors showed varying cellularity (Figure 11) and consisted of irregular islands of mature and immature cartilaginous areas composed of single cells in lacunar spaces surrounded by basophilic hyaline matrix which was a prominent feature in all the cases (Figure 12). The tumors were destroying the surrounding bone and invaded into the normal bony architecture. Mild nuclear atypia characterised by nuclear enlargement was noted. Two cases showed large

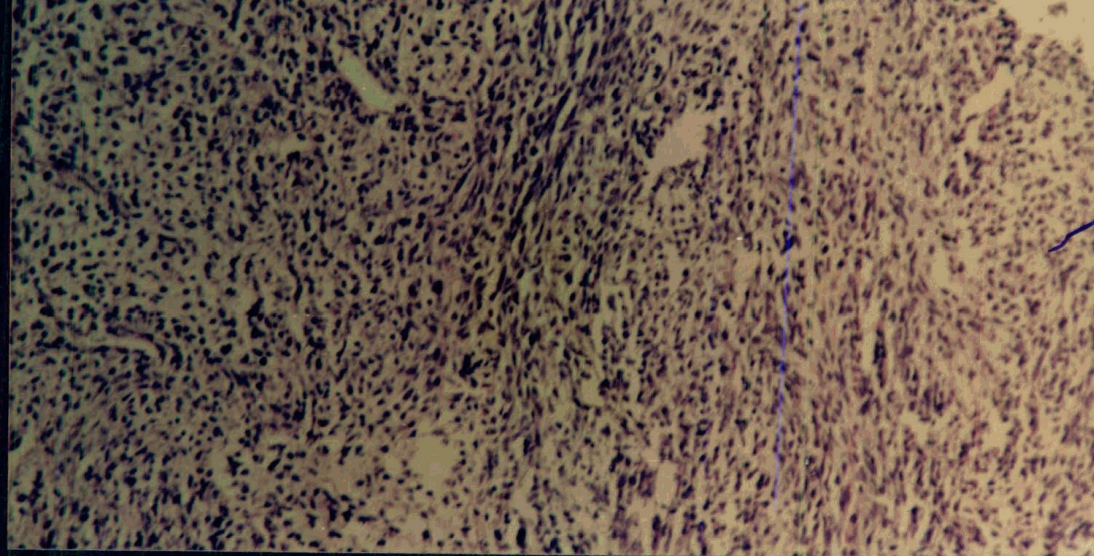


Figure 14: Photomicrograph showing highly cellular tumor with differentiated cells and hyperchromatic nuclei - Mesenchymal Chondrosarcoma (HE x 160).

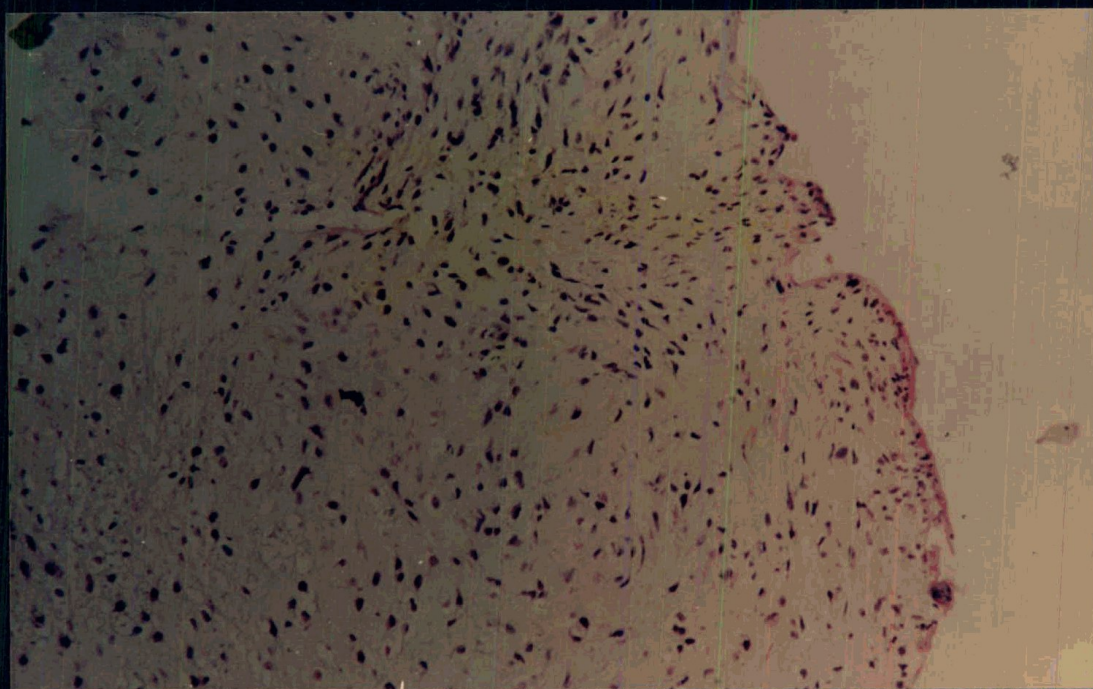


Figure 13: Photomicrograph showing chondroid tissue with cartilaginous cells in myxomatous matrix. Other areas showed highly cellular spindle cell tumor - Mesenchymal Chondrosarcoma (HE x 160).

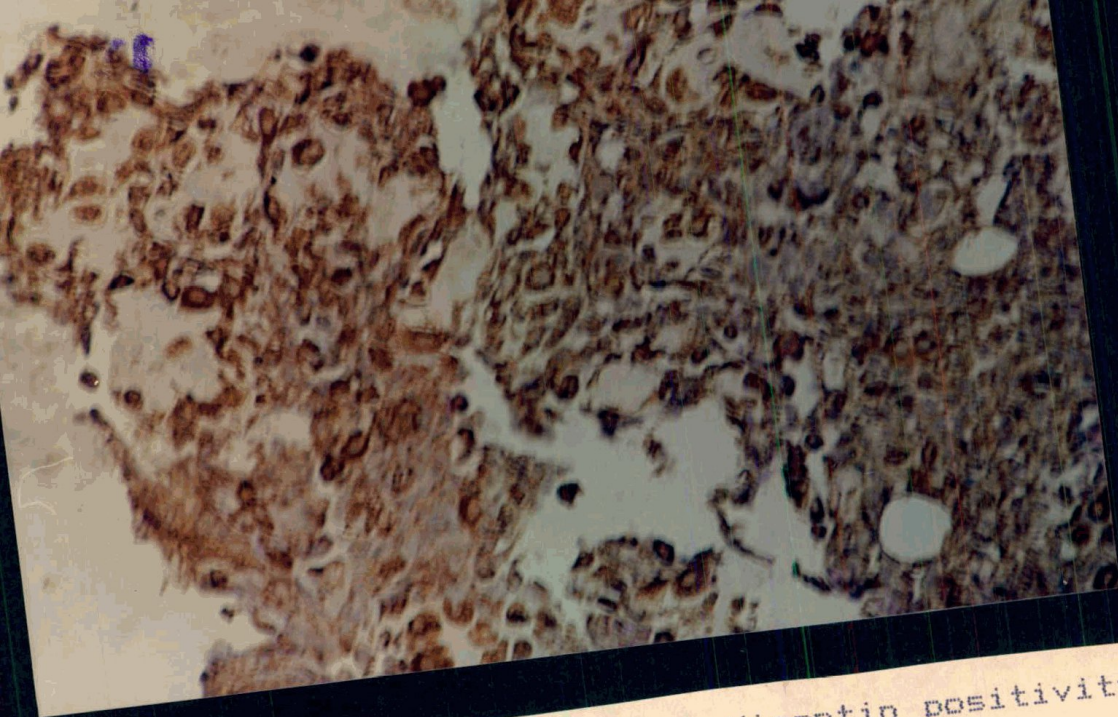


Figure 15: Photomicrograph showing Vimentin positivity in a low-grade Chondrosarcoma (Vimentin x 250).

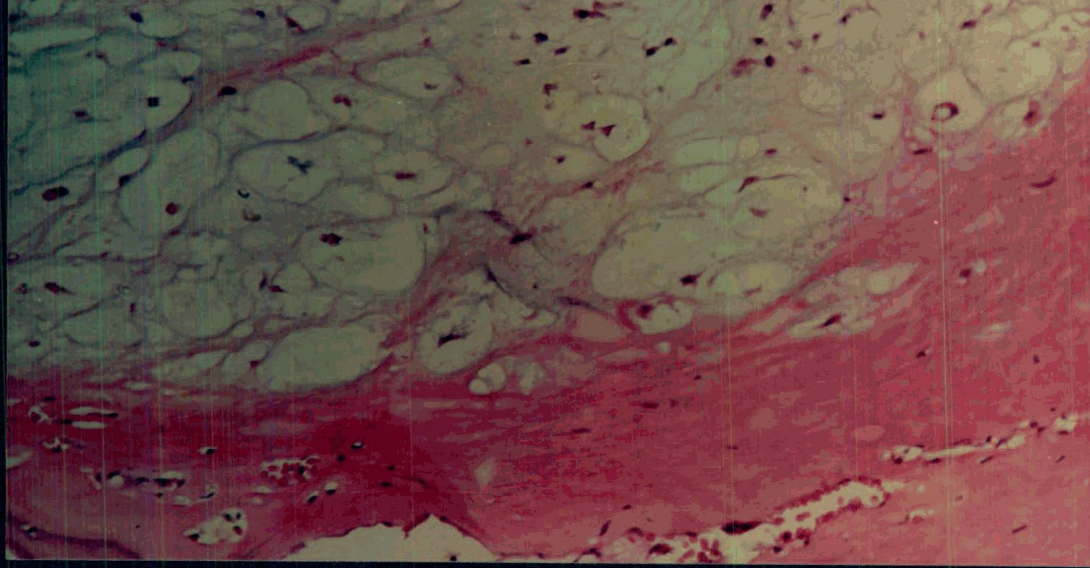


Figure 16: Photomicrograph showing cells with myxoid change originally diagnosed as myxoid chondrosarcoma on haematoxylin/eosin (HEx250).

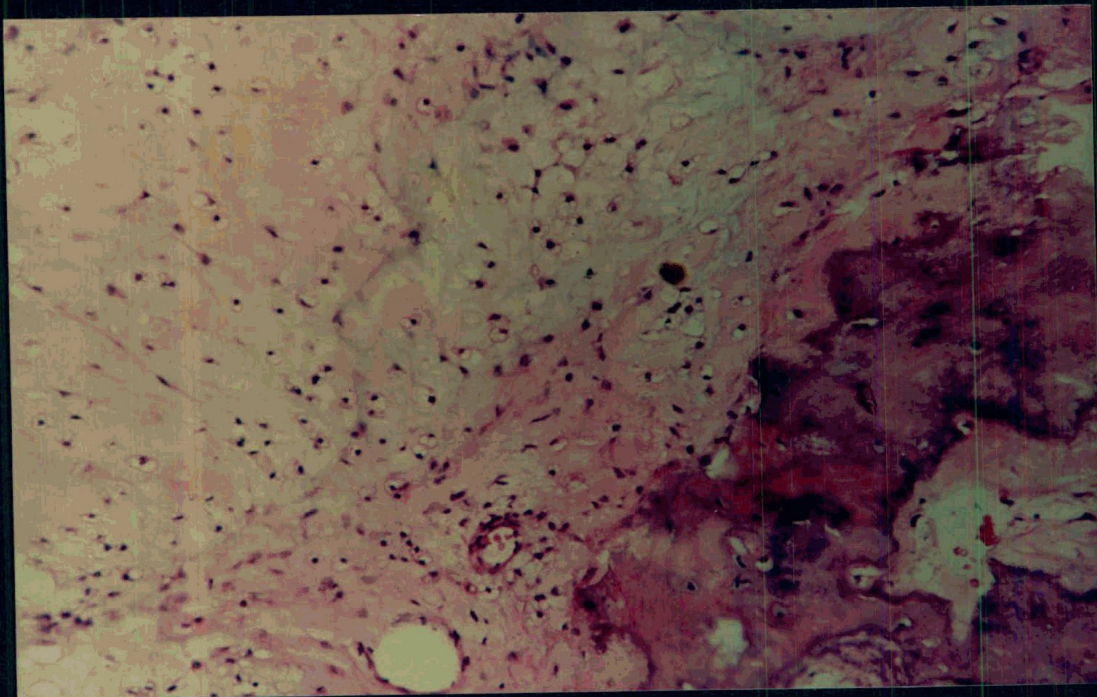


Figure 17: Photomicrograph showing chondroid cells with bony destruction and calcification diagnosed as myxoid Chondrosarcoma on haematoxylin/eosin (HE x 160).

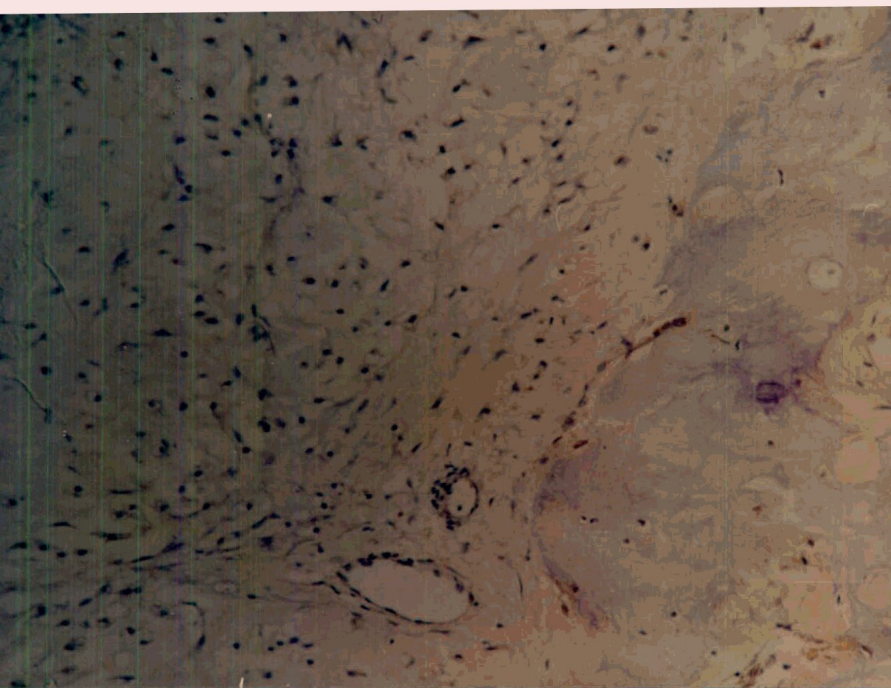


Fig. 18: Photomicrograph demonstrating Vimentin negativity in chondroid areas - Chondroid Chordoma (Vim x 160).

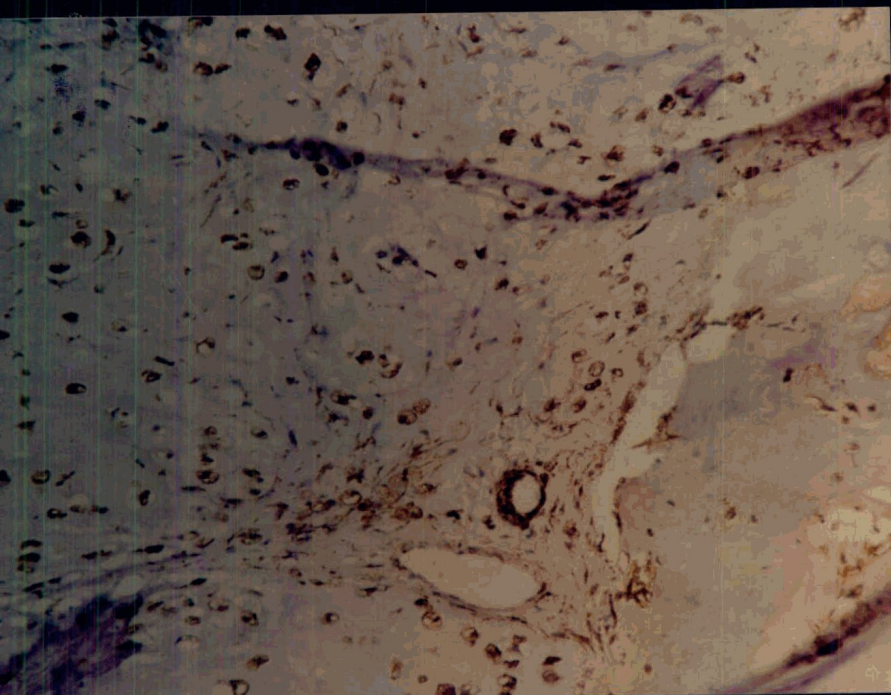


Fig. 19: Photomicrograph showing Cytokeratin positivity in Chondroid areas. Same case as in figures 16,17. Tumor reclassified as Chondroid Chordoma (Cytokeratin x 160).



Fig. 20: Photomicrograph showing Cytokeratin positivity in Chondroid area. Same tumor as above- i.e. Chondroid Chordoma (CK x 160).

hyperchromatic nuclei. Mitotic figures varied. Six of the 8 tumors showed areas of calcification of the hyaline substance. Abundant myxoid change was seen in 5 tumors.

The mesenchymal chondrosarcoma showed a varied appearance in different areas. In some areas the tumor consisted of chondroid tissue with cartilaginous cells in myxomatous matrix (Figure 13). There was no evidence of nuclear atypism or mitosis. In other areas the tumor was highly cellular with spindle shaped cells and oval nuclei arranged in interlacing fascicles (Figure 14). The cells appeared undifferentiated with hyperchromatic nuclei. There were few mitotic figures. Stellate cells with cytoplasmic processes and myxoid stroma was also seen. There were areas of vascular spaces and few foci of spotty calcification. No areas of physaliferous cells or lobular pattern was seen to suggest chordoma.

Immunohistochemistry Immunohistochemistry was performed in 5 chondrosarcomas which included 1 low grade classical chondrosarcoma, 3 myxoid chondrosarcomas and 1 mesenchymal chondrosarcoma. Except for 1 case of myxoid chondrosarcoma, rest of the 4 cases were positive for Vimentin (Figure 15), although the intensity of staining varied in each case. The case of myxoid chondrosarcoma (Figure 16,17) which was negative for Vimentin was positive for Cytokeratin and was thus reclassified as chondroid chordoma (Figure 18,19,20). Remaining 4/5 of the chondrosarcomas were negative for Cytokeratin (Figure 21).

Chondroid chordoma:

Haematoxylin and Eosin staining: Under routine haematoxylin and eosin staining these 10 cases of chondroid chordoma showed a biphasic picture characterised by areas of typical chordoma admixed with areas resembling cartilage. The chordoid areas were composed of cells arranged in lobules, cords and nests, separated by fibrous bands and at places by myxoid stroma. The cells had abundant eosinophilic cytoplasm with many physaliferous cells having vacuolated cytoplasm and small inconspicuous nuclei (Figure 22). The chondroid areas consisted of single cells with larger nuclei and set in a extracellular basophilic matrix with hyaline appearance. Many cells were surrounded by lacunar spaces (Figure 23). In 4 cases the cartilage was sharply demarcated from the surrounding conventional chordoma areas. However, in the remaining cases, the transition was very gradual in that chondroid areas merging imperceptibly into chordoma like areas. The mixture ranged from small foci of chondroid tissue in chordoma type background to tumors where chondroid component dominated. Some of these tumors showed areas of calcifications and sometimes ossification. Cellular pleomorphism was minimal. Most of these tumors appeared relatively avascular. Tumor necrosis was not significant. De-differentiation to a more malignant type of tumor was not seen in any cases.

Immunohistochemistry: Nine chondroid chordomas were subjected to immunohistochemical studies- again using Pan-Cytokeratin and Vimentin. The chordoid as well as chondroid areas in all (9/9)

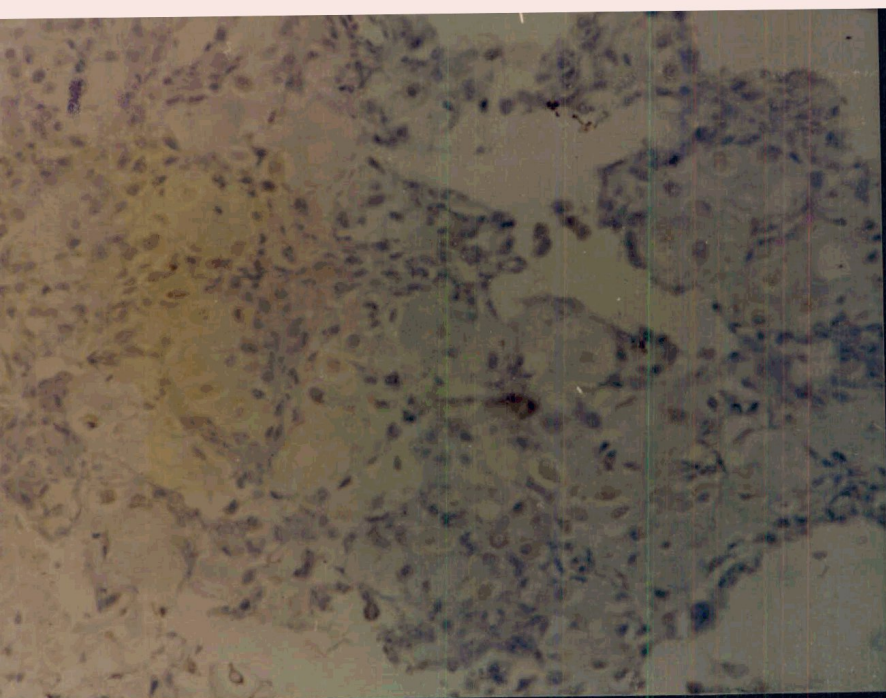


Fig. 21: Photomicrograph demonstrating Cytokeratin negativity in a case of low grade Chondrosarcoma - corresponding HE stained fig. 11 & 12 (CK x 250).

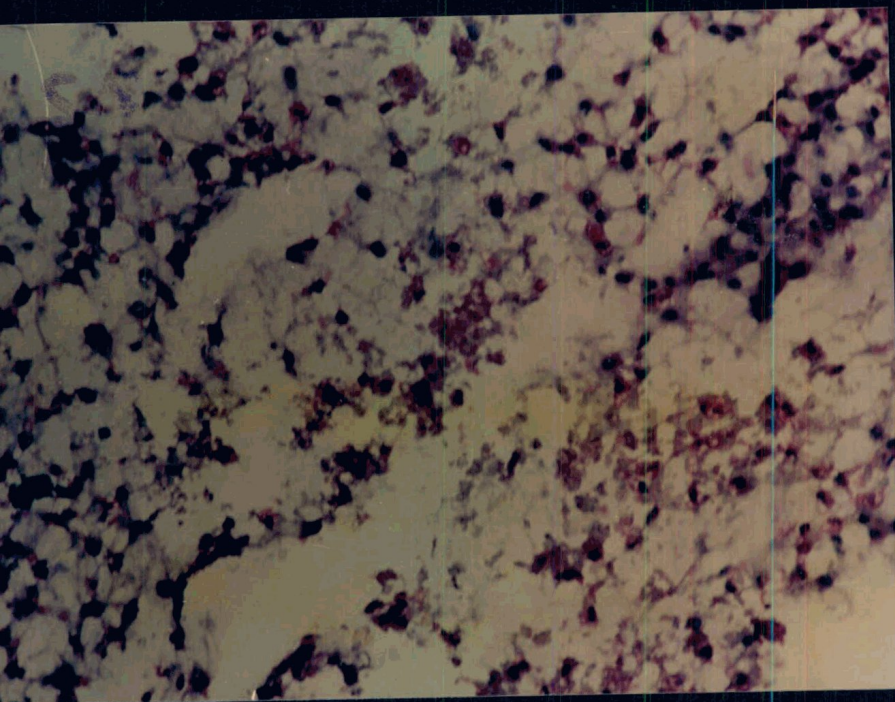


Fig. 22: Photomicrograph showing Chondroid area in Chondroid Chordoma (HE x 250).

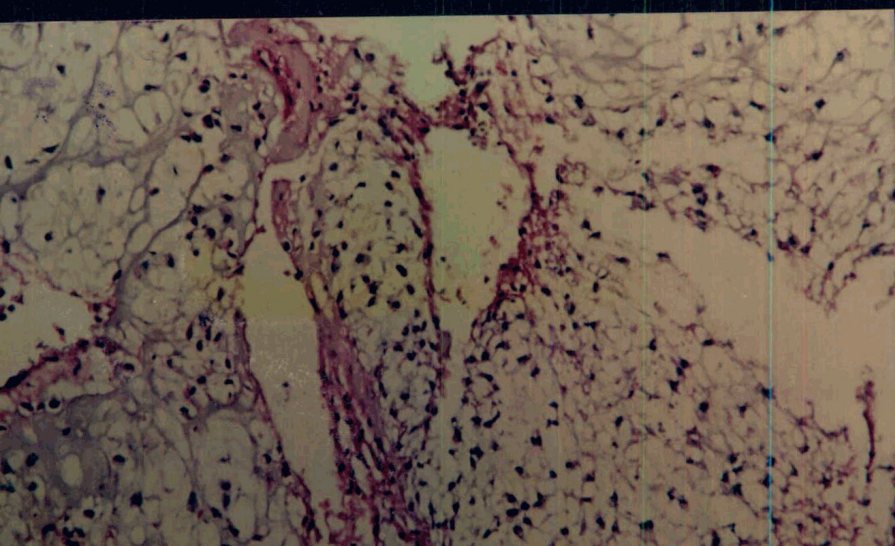


Fig. 23: Photomicrograph showing chordoid and chondroid areas in - same case as Figure 22. (HE x 250).

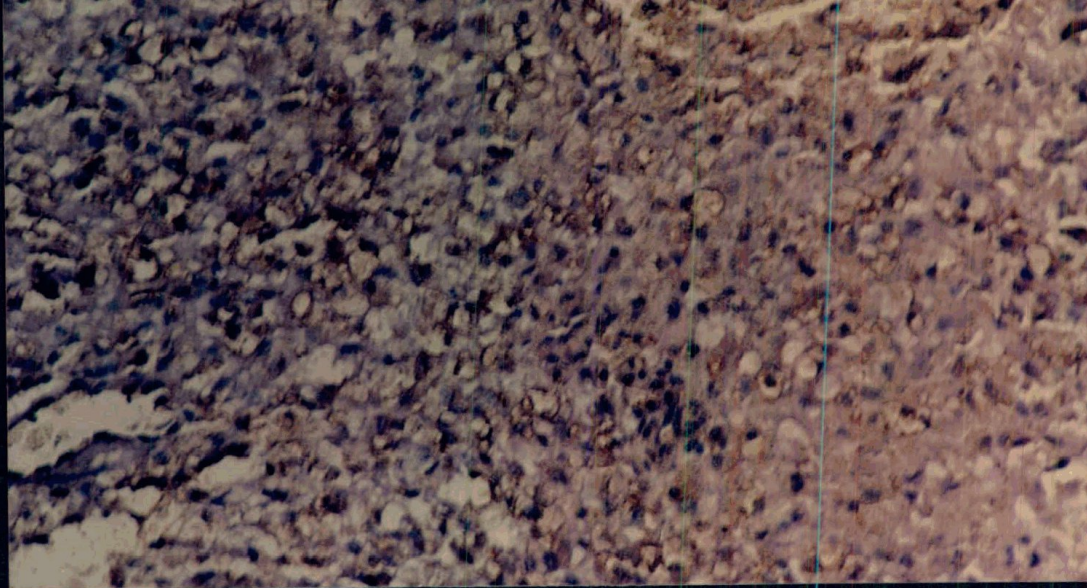


Figure 24: Photomicrograph showing Cytokeratin positivity in a case of Chondroid Chordoma - same case as in Fig. 22 and 23 (CK x 250).

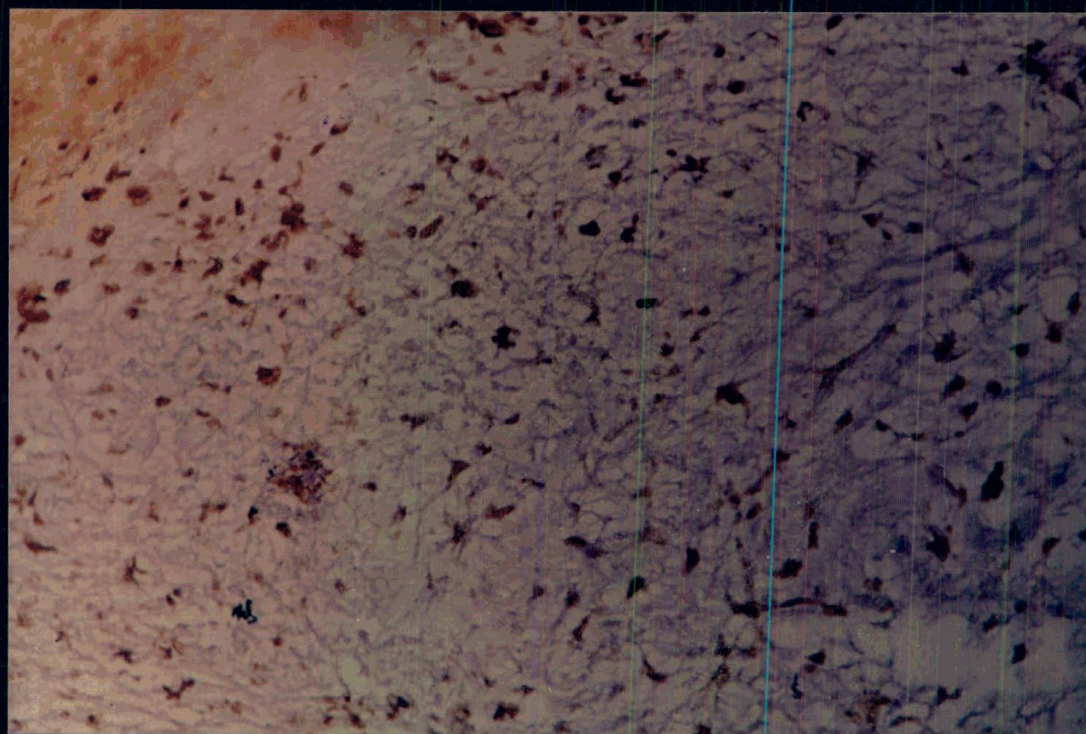


Figure 25: Photomicrograph showing CK positivity in a case of Chondroid Chordoma - same case as in Figures 22-24. (CK x 250)

cases showed positivity for cytokeratin, although the intensity of staining varied (Figure 24,25). 2/9 cases were negative for Vimentin. The staining reaction for Vimentin was inconsistent in 7/9 cases and the background staining could not be completely eliminated due to unexplained technical error despite all precautions. Epithelial marker positivity lends supports to the findings of many recent studies that chondroid chordoma is indeed a variant of chordoma and can be distinguished from chondrosarcomas.

Table 10

Summary of Immunohistochemistry findings in Chordoma, Chondrosarcoma and Chondroid Chordomas of the skull base.

Case	HE based diagnosis	Pancytoker	Vimentin	Revised diagnosis on Immunhisto. study
1	Chordoma	+	+	Chordoma
2	Chordoma	+	+	Chordoma
3	Chordoma	+	-	Chordoma
4	Chordoma	++	+	Chordoma
5	Chondroid chordoma	+	+/-	Chondroid chordoma
6	Chondroid chordoma	+	-	Chondroid chordoma
7	Chondroid chordoma	+	+/-	Chondroid chordoma
8	Chondroid chordoma	++	+/-	Chondroid chordoma
9	Chondroid chordoma	++	+/-	Chondroid chordoma
10	Chondroid chordoma	+	+/-	Chondroid chordoma
11	Chondroid chordoma	+	+/-	Chondroid chordoma
12	Chondroid chordoma	+	+/-	Chondroid chordoma
13	Chondroid chordoma	++	-	Chondroid chordoma
14	Low grade Chondrosarcoma	-	++	Chondrosarcoma
15	Myxoid Chondrosarcoma	-	++	Chondrosarcoma
16	Myxoid Chondrosarcoma	-	+	Chondrosarcoma

17	Myxoid Chondrosarcoma	++	-	Chondroid chordoma
18	Mesenchymal Chondrosarcoma	-	++	Chondrosarcoma

Index: ++ = intense staining, + less intense staining, - Negative
+/- variable and focal positivity

There are other markers such as Epithelial Membrane Antigen (EMA), 5-nucleotidase, S-100, CEA which have been employed by different workers. In the present study these markers could not be used due to the high cost of the primary antibodies.

Differences between chordomas and chondrosarcomas

The classification of these neoplasms is controversial. Chordoma and chondrosarcoma are frequently grouped together because of their clinical, radiological, surgical and histological resemblance (4,23,38,59).

The distinction between chordomas and chondrosarcomas of the skull base is not clearly defined in the literature because of the histological similarities of these tumors in some cases. However, with the introduction of immunohistochemical techniques in the last decade, this distinction has been clarified. While chordomas has an epithelial origin, chondrosarcomas have a mesenchymal cell of origin. These two varieties of tumors have similar sites of origin, nature of spread, radiological features, characters of displacement of structures, and therapeutic prob-

lems. Chondrosarcomas have more cartilaginous content and are therefore more gritty in their feel. Despite subtle differences, the surgical management has generally been reported to be similar (56). With radical resection the ultimate outcome of chondrosarcomas matches with that of chordomas. The chordomas and chondrosarcomas resemble each other in following characters:

1. **Site of origin:** Chordomas arise from notochordal remnants, a tissue ordinarily found in the early stage of the embryo. Therefore this tumor may represent a recapitulation of an embryologic stage, but in a disorganized neoplastic fashion. Chordomas arise more frequently from the region of the junction of basisphenoid with basiocciput. Chondrosarcomas also arise and grow in a similar pattern to chordomas. Although both these varieties of tumors originate around the clivus, a tumor originating from the temporal bone, or from an off-midline epicenter is more likely to be chondrosarcoma.

2. **Radiological parameters:** Chordomas and chondrosarcomas are often easily diagnosed radiologically due to the following features: their specific location; the frequently associated destructive and erosive bone changes; varying amounts of soft tissue component; entrapped bony trabeculae; small dystrophic calcification; areas of necrosis; and recent and old hemorrhages (23,35,39,56,61). Tumor borders are slightly multilobulated and well defined except at sites of marrow invasion and bone destruction. The radiological characters of chordomas and chondrosarcom-

mas are almost similar. A lesion studded with calcific areas is more likely to be a chondrosarcoma.

Chondroid chordoma

In 1973, Heffelfinger et al (25) described a variant of chordoma which in many areas closely resembled a chondrosarcoma and which was, therefore designated as a chondroid chordoma. Histologically, the tumor has areas bearing a close resemblance to a chondrosarcoma and other areas with the features of a classical chordoma. In cases where the chondrosarcomatous components of the tumor predominate, many sections may have to be examined in order to demonstrate the chordomatous features. This variety of chordoma has been recorded to have a better prognosis and is associated with longer survival than the classical chordoma. The tumor occurs in younger patients (mean 35 years) than those with classical chordomas.

The concept of 'chondroid chordoma' has been a subject of much confusion and debate. The concept was first challenged by Brooks and his colleagues (8) on the basis of their immunohistochemical studies. They found (on the basis of their study of 7 cases) failure of these tumors to stain for epithelial markers and an identical staining pattern with chondrosarcomas. They labeled them as 'low grade chondrosarcomas'. Several other investigators also questioned the validity of 'chondroid chordoma' as a separate clinicopathologic entity (6,7,40,63). These investigators agreed that chondroid chordoma is actually a low grade chondrosarcoma.

More recent studies based on electron microscopic and immunohistochemical studies relate these tumor more to chordomas than to chondrosarcomas. On the basis of electron microscopy, ultrastructural features of 'chondroid chordomas' more closely resemble those of classical chordoma (9,18,21,42) and were different from those described in chondrosarcomas. The presence of glycogen, prominent and dilated rough endoplasmic reticulum, and abundant fibrillo-granular matrix is common to all three lesions. Well-formed tonofilament desmosome complexes and rough endoplasmic reticulum mitochondrial complexes are found only in chordoma and chondroid chordoma and not in cartilaginous tumors. Ultrastructurally, chondrosarcoma demonstrated a flocculogranular matrix, glycogen, abundant RER, and scalloped cellular outlines, but lacked desmosomes with tonofilaments.

Immunohistochemically, both the chordoid and chondroid areas of 'chondroid chordoma' had an epithelial phenotype and stained strongly for cytokeratin, EMA, S-100 as well as 5-nucleotidase. In contrast to chondroid chordoma, chondrosarcoma consistently stained for only S-100 protein and was cytokeratin, EMA and 5-nucleotidase negative.

5-nucleotidase, an enzyme that has been described in chordoma but not in chondrosarcoma, was found in both the chordoid and chondroid areas of chondroid chordoma.

Using light microscopy, chondroid chordoma revealed areas that resembled typical chordoma (chondroid areas) and areas that resembled low grade chondrosarcoma (chondroid areas).

These findings indicate that 'chondroid chordomas' is a variant of chordoma with histologic features that may mimic chondrosarcoma. Despite the resemblance of these hyalinized areas to cartilaginous tissue, these tumors retain their epithelial phenotype. Some authors propose that these tumors be classified as 'hyalinised chordomas' rather than 'chondroid chordoma' (28) to clarify their histogenesis and avoid confusion with chondrosarcomas of the base of the skull.

Table 11

Summary of Immunohistochemical profile studies of chondroid chordomas

Study	cases +ve epithelial markers	Conclusion
Bottles (1984)	0/1	Chondroid chordoma does not exist It is a chondrosarcoma variant
Abenzoza (1986)	3/3	Chondroid chordoma is a variant of chordoma
Brooks (1987)	0/7	Chondroid chordoma does not exist It is a chondrosarcoma variant
Salisbury (1987)	2/2	Chondroid chordoma is a variant of chordoma
Meis (1988)	1/3	Chondroid chordoma is distinct from chondrosarcoma
Walker (1991)	0/5	Chondroid chordoma does not exist It is a chondrosarcoma variant

Mitchell (1992)	8/25	Chondroid chordoma exists as a variant of chordoma; epithelial marker-negative examples represent chondrosarcoma
Wojno (1992)	13/13	Chondroid chordoma exists as a variant of chordoma;
Rosenberg (1994)	12/12	Chondroid chordoma exists as a variant of chordoma;
Jeffrey (1995)	5/5	Chondroid chordoma is a variant of chordoma;

Controversy of benign vs. malignant nature of chordoma:

Some reports suggest that the chordomas are of benign nature. Some reports suggest that chordomas are of malignant nature. While there are still other reports which suggest that the tumor is of a low grade malignancy.

Russell and Rubinstein (1989) mention that although these tumors are regionally invasive, and therefore of poor prognosis, most of these tumors are histologically benign (51).

According to Seifert et al (55) chordomas are potentially malignant, whereas Derome and Guiot (15,16) consider them histologically benign tumors. Heffelfinger et al (1973) opine that the main malignant potentials of chordoma lie in its critical locations, its locally aggressive nature, and its extremely high recurrence rate; these account for the almost certain eventual death of the host (25).

Chordomas has been considered by most authors to be a slow-growing, locally aggressive and rarely metastasizing neoplasm with a high incidence of recurrence. Skull base chordoma are reported to metastasize in about 20% (11). On our literature survey no clear pattern of its tendency to metastasize emerges from some large series (11,14,26) and several case reports (10,17,67). Distant metastasis were reported in 43% (22 of 46) of cases reported by Higinbotham et al (26) and in 30% (8 of 27) of those seen by Chambers and Schwinn (11).

Whether the different neoplastic potential is related to various degrees of tumor differentiation is difficult to establish. It seems equally difficult to identify those histologic features which may be indicative of local aggressiveness and of metastatic potential of chordoma.

Chambers and Schwinn (11) reviewed histologic specimens from 23 cases of chordoma with respect to some histologic factors associated with cancer. They concluded that more anaplastic chordomas were more likely to metastasize. Foci of fibrosarcoma were recognized in four cases of metastasizing group. On the other hand, the malignant potential increased in two cases reported by Hefelfinger et al (25) in which a dedifferentiation of chordoma to fibrosarcoma and osteogenic sarcoma was noted. A similar dedifferentiation has also been reported in low-grade chondrosarcoma (13,32).

In the present series there was no incidence of metastasis remote from the primary site.

TREATMENT

Only biopsy of the tumor was taken in 14 cases, subtotal excision of the tumor was performed in 12 cases and radical total excision was carried out in 2 cases. Eighteen patients received post-operative radiation therapy. Five cases were reoperated for recurrences.

Surgical considerations:

Although chordomas and chondrosarcomas were soft, essentially extradural, and relatively avascular lesions, they were difficult to treat surgically because of their proximity to critical neural and vascular structures, depth from the surface and also widespread extension particularly into the adjacent structures such as cavernous sinus, sella, nasopharynx, and hypoglossal canal. These features made the ultimate clinical course 'malignant' and eventually fatal.

The following gross features of the tumor were helpful during surgery on these tumors:

1. Chordomas were usually soft, mucinous and suckable. There were interspersed bony spicules in the tumor which could usually be removed in large pieces. Chondrosarcomas were relatively gritty and had a much larger cartilaginous content.

2. Most of the tumors were relatively avascular.

3. The tumors were extradural in nature with no instance of intradural spread.

4. The tumors grew by displacement of surrounding soft tissues and by destroying the bone. The carotid artery which is in direct relationship with the tumor in its petrous, precavernous and cavernous segments was displaced along the anterior border of the tumor. Sometime this displacement was up to the extent of 3 to 3.5 cms (22).

5. The cavernous sinus involvement was in the nature of displacement rather than invasion. The tumor usually had a sub-cavernous sinus spread. The cranial nerves of the cavernous sinus were displaced on the superior surface of the tumor.

6. Whenever the tumor extended posteriorly into the posterior cranial fossa, the brain tissue, vessels and nerves were more often displaced by the tumor. The tumor being separated from these structures by thinned and stretched out dura.

7. More frequent site of origin of these tumors was in the region of spheno-occipital synchondrosis. From this site the tumor usually spread eccentrically on one side. Midline spread was relatively uncommon and was seen in 2 cases.

The surgery should be aimed towards a radical surgical excision, a factor on which ultimate prognosis and outcome will depend.

Sen et al (1989) suggest removal of about a centimeter of normal bone around the tumor involved bone (56).

Effects of radiation therapy:

Chordomas and Chondrosarcoma were found to be a relatively radiation resistant tumor. Eighteen patients in the present series were subjected to irradiation treatment. In none of the our cases actual tumor size reduction was noted following radiation therapy. Symptomatic improvement in noted in at-least 5 patients following this modality of treatment. Total doses of radiation of 6000-7000 cGy, fractionated at 200 cGy per day, appeared to be required for worthwhile palliation. For tumor eradication it appears that doses in excess of 6500 to 7000 cGy is required, but this can only be achieved in selected circumstances when treatment volumes are small and include minimal amounts of normal tissue. High doses are needed to be effective, indicating a relative radioresistance probably due to the slow growth of the tumor and limited mitotic activity. Since the tumors are slow growing, the effects of radiotherapy will be slower in appearing but will last longer than the effects on faster growing tumors.

Various combinations of chemotherapeutic agents have been attempted without any success.

Effective outcome of these lesions has been reported to depend on

the extent of the surgical resection of the tumor (34,38,39,45,46). The role of radiotherapy for chordomas is not established, but there are reports of successful outcome following this modality of treatment (55,56). Especially in recent years, the value of radiation has been recognized (5,14,26,30,41,47,64,65). Authors of these reports agree that irradiation, though not curative, offers the possibility of significant palliation and regression of the tumor. There are a few reports of rapid regression of the tumor following radiation treatment (3,44,41,60).

In one patient tumor growth and clinical neurological worsening was observed whilst the patient was on radiation therapy. One patient worsened clinically after 2 weeks of radiation therapy. In other patients radiation therapy appeared to have at-least a growth limiting effect.

Therapy and survival:

Extensive surgery combined with radiation has been the management of choice for chordomas, particularly in recent years. The present series of patients were so treated, making it difficult to compare these modes of therapy when used singly. There is no evidence of cure in the sense of survival rates becoming equal to those in the general population. The major object of therapy

appears to be to increase the patient's survival time and to make him productive and comfortable as possible.

Reoperations are relatively difficult as the tumor may spread intradurally through the rents in the dura made during the first operation. Such recurring tumors invade into the cavernous sinus. Some authors have noticed invasion of the chordomas into the cavernous sinus. However, most of these cases were the recurrent variety of tumor. In case radiotherapy has already been given, it results in dissection of the tumor from the surrounding vessels difficult and wrought with danger of injury to adjoining vessels, nerve and brain. In cases with recurrence despite surgery and radiation treatment, reoperation is the only effective mode of treatment and means of palliation.

OUTCOME:

Of the 28 cases, 4 patients died in the immediate post-operative phase.

Six patients died due to tumor growth between 2 months to 4 year period.

Ten patients did not follow up after surgery. In three of these cases, relatives sent letters informing of poor neurological condition of the patient at 6, 8 and 18 months post-operative interval respectively.

No statistically significant difference was observed in the survival periods and outcomes of Chordoma, Chondrosarcoma and Chondroid chordoma as the follow-up period of the cases varied to a marked degree in these cases.

Five patients improved after the tumor resection in their neurological condition and are surviving and well at varying periods. All these patients are back in their preoperative occupation.

Three patients have persistent symptoms and are being observed clinically.

OTHER TECHNICAL STUDIES

Enzyme studies:

Diagnosis is based on morphologic identification of the characteristic physaliferous cells. Although the diagnosis is relatively straightforward when these cells are present, small biopsies of chordomas may occasionally present considerable diagnostic difficulty. The most important differential consideration is chondrosarcoma, but occasionally these lesions may be confused with myxopapillary ependymoma. The enzyme histochemical patterns of the chordomas were different from those seen in fetal notochord remnants, chondrosarcoma, and ependymoma. All of the chordomas were characterized by a strong reaction with 5'-nucleotidase localised on the plasma membranes. This enzyme was not present on the membranes of fetal notochordal remnants, chondrosarcoma, and ependymoma. This reaction pattern is useful in differential diagnosis of chordoma.

The lack of similarity in enzyme histochemical staining between fetal notochord and chordomas is confusing. For years fetal notochordal remnants have been regarded as the source of chordomas (24), and the different histochemical staining pattern between chordomas and the non-neoplastic fetal notochord is noteworthy. There are at-least three possible explanations for this findings. Notochordal tissue may be 5'-nucleotidase positive at a stage of development. Another possibility is that 5'-nucleotidase is expressed only in malignant tumors derived from notochord. A

third possibility is that chordomas are not derived from notochord. It is not possible to state definitively which of these possibilities is correct from the available data, though the first possibility is the most appealing.

Lysozyme has been detected previously in human fetal notochord, normal cartilage, and chondrosarcoma, but not in chordoma. However, in 10% of chordomas were positive for lysozyme in a study conducted by Bottles (1984) (6). This indicates that its absence does not necessarily support the diagnosis of chordoma, and its presence does not exclude it.

Alpha1-Antichymotrypsin has been reported to be present in the low grade chondrosarcoma component of de-differentiated chondrosarcoma in addition to concomitant sarcoma (which is usually a malignant fibrous histiocytoma) (6). Hence, as a marker, it does not independently distinguish chordoma from chondrosarcoma.

Hormone receptors:

Due to the failure of aggressive surgical therapy and radiation therapy in the treatment of chordomas, other types of therapy need to be considered. A decreased male:female ratio of chordomas occurring in the cranium, as well as an increased incidence of "favorable" chondroid chordomas in females suggest hormonal factors may play a role. Multiple studies have addressed the presence of steroid hormone receptors in intracranial tumors. Most of these studies focused on receptor expression by meningiomas. There are only two instances of measurement in chordomas. In a male patient, markedly elevated progesterone (215 fmol/mg) and androgen (712 fmol/mg) were detected^{53,68}. In this patient, there were no progesterone receptors. Estrogen and progesterone receptor levels greater than 10 fmol/mg are considered positive for breast carcinomas. These isolated reports suggest that chordomas express high levels of steroid hormone receptors and may be more amenable to hormonal manipulation than other intracranial tumors.

The demonstration of estrogen and/or progesterone receptors in chordomas may prove to have both prognostic and therapeutic significance. The determination of steroid hormone receptor expression may allow the identification of a subset of patients with more biologically aggressive tumors, thus permitting more aggressive therapy in these patients. Additionally, steroid hormone receptor expression may allow the identification of those patients who are at risk of developing metastases. Differences in

receptor expression between typical chordomas and chondroid chordomas may explain differences in biologic behavior. More importantly, if hormonal dependency can be demonstrated, new therapies may be developed employing anti-hormonal drugs.

Chromosomal analyses

Some studies on cytogenetic analyses chordomas are reported. Tumors showed clonal chromosome abnormalities, including numerical and structural aberrations. The modal chromosome numbers were 36 and 72, respectively. The hypodiploid tumor had a single structural abnormality identified as a $\text{der}(21)\text{t}(1;21)(\text{q}21;\text{q}22)$. The near-triploid tumor had numerous structural rearrangements, including a $\text{der}(21)\text{t}(2;21)(\text{q}11;\text{q}22)$, which involves the same band of chromosome 21 as the translocation in the first tumor. Pro-phasing was a prominent cytogenetic feature of this tumor. The consistent involvement of band 21q22 in translocations in two chordomas suggests a possible specific association of this chromosome region with chordoma. Protooncogenes ETS2 and ERG have been mapped to this chromosome band.

The results of ploidy analysis performed on both classic chordoma and chondroid chordoma by Mitchell et al 1993 were unrevealing. Both exhibited essentially the same proportions of diploid and tetraploid examples. Of interest is occasional finding of aneuploidy in classic chordomas, whereas none of the chondroid tumors were aneuploid. The significance of this finding is unclear in that the behaviour of the aneuploid lesions was similar to that of diploid tumors.

SUMMARY AND CONCLUSIONS

1. Twenty eight chordoid and chondroid tumors encountered at the base of the skull during 31 years from 1965-1995 were studied retrospectively.
2. Male predominance was noted. The lesions occurred more predominantly in the third decade of life.
3. Most chordomas and chondrosarcomas of the skull base arise in the clivus and have an eccentric spread. The spread in our series was significantly more towards the right side.
4. These tumors are essentially extradural. In our entire series none of the tumors had an intradural extension despite the large sizes of the tumors.
5. Grossly, the soft tissues like major vessels and cranial nerves adjoining the tumor are displaced around the tumor.
6. The internal carotid artery, even in its fixed intra-petrous segment is displaced along the anterior border of the tumor in all cases. This finding has not been reported in the literature. As the tumor is located in the depth from the surface, cognisance of the exact relationship of the tumor to the internal carotid artery has significant implications in planning the surgical strategy.

7. The cavernous sinus and its cranial nerves are displaced on the dome of the tumor. Essentially the tumor has a sub-cavernous sinus extension.

8. The functional affection of all the cranial nerves appears to be secondary to their stretch rather than direct invasion and destruction.

9. In the present series the difference in the long term outcome of chordoma, chondroid chordoma and chondrosarcoma was not statistically significant.

10. Most of the surgical resection were either only biopsy or partial resections. The exact correlation between radical total resection and the long term outcome could not be estimated.

11. Chordoma arising in a child was seen to behave in an unusually aggressive form.

12. On routine HE staining chondroid elements could be identified in a significant numbers of chordomas and they show an immunohistochemical profile that is identical to the non-chondroid chordomas. Thus the term Chondroid chordoma should be maintained and strict morphologic and immunohistochemical criteria be routinely used to distinguish it from chondrosarcomas to allow for more studies to determine its prognostic significance.

13. The treatment of chordoma, chondrosarcomas and chondroid chordoma is essentially similar.

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