ARAŞTIRMA MAKALESİ/ORIGINAL RESEARCH

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Chordomas of the Head and Neck Region

Baş ve Boyun Bölgesi Kordomaları

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ABSTRACT

Introduction: Chordomas are rare, locally aggressive low-grade malignancies that develop from notochordal embryonic residues. They show a dual epithelial-mesenchymal differentiation. Chordomas preferentially occur in the sacrum. The head and neck localization is uncommon. Here we report chordomas of spheno-occipital, and cervical region diagnosed in our department and summarize clinicopathological characteristics of these cases.
Methods: Retrospectively, the cases diagnosed as "chordoma" were reviewed from 2002 to 2021. Clinicopathological features of cases with a tumor at spheno-occipital, and cervical region were assessed.
Results: Of 9 cases (4 males, 5 females) with a mean age of 53,4 (13–88 years), eight cases were diagnosed as conventional chordoma and one case as chondroid chordoma. Mean follow-up was 37 months (3-167 months). Recurrence was detected in 2 cases and distant metastasis was determined in one case.
Discussion and Conclusion: Chordomas are resistant to chemotherapy and radiotherapy. Given the location and invasive nature of these tumors, complete resection is difficult. In the head and neck region, chordomas should be included in the differential diagnosis of tumors especially with myxoid characteristics.
Keywords: chordoma, head and neck, recurrence

ÖZ

Giriş ve Amaç: Kordomalar notokordal embriyonik kalıntılardan gelişen nadir, lokal agresif düşük dereceli malignitelerdir. Dual epitel-mezenkimal farklılaşma gösterirler. Kordomalar daha çok sakrumda görülür. Baş ve boyun lokalizasyonu nadirdir. Burada kliniğimizde tanı konulan sfeno-oksipital ve servikal bölgekordomları sunulmakta, bu olguların klinikopatolojik özellikleri özetlenmektedir.
Yöntem ve Gereçler: Geriye dönük olarak 2002-2021 yılları arasında "kordoma" tanısı alan olgular gözden geçirildi. Sfenooksipital ve servikal bölgede tümörlü olguların klinikopatolojik özellikleri değerlendirildi.
Bulgular: Dokuz vaka (4 erkek, 5 kadın) bulundu. Yaş ortalaması 53,4 (13-88 yıl) olup sekiz vaka konvansiyonel kordoma ve bir vaka kondroid kordoma tanılıydı. Ortalama takip süresi 37 aydı (3-167 ay). İki olguda rekürrens, bir olguda uzak metastaz tespit edildi.
Tartışma ve Sonuç: Kordomalar kemoterapi ve radyoterapiye dirençlidir. Bu tümörlerin yeri ve invaziv doğası göz önüne alındığında, tam rezeksiyon zordur. Baş boyun bölgesinde özellikle miksoid tümörlerde, kordomalar ayırıcı tanıya dahil edilmelidir.
Anahtar Kelimeler: kordoma, baş ve boyun, rekürrens

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INTRODUCTION

Chordomas are rare primary bone tumors (1). They arise from notochord residues and show dual (mesenchymal and epithelial) differentiation (2). Although the most common location of the tumor is the sacrum (50-60%), the skull base, cervical vertebrae and thoracolumbar vertebrae are also frequently involved (2). They account for 1.4% of all primary malignant bone tumors, 0.4% of all intracranial tumors, and 0.2% of spinal tumors (3,4). The average age of the cases is 58.5 (3). In the head and neck region, they are diagnosed almost a decade earlier. Primary chordomas originating from extraaxial soft tissue can also be seen rarely (5).

Surgical resection has been the first choice of treatment for many years due to resistance to chemotherapy and radiotherapy. It has been reported that total resection prolongs overall survival and decreases local recurrence. Modern radiation application technologies such as high-dose image-guided stereotactic body radiotherapy and proton and carbon ion therapy can be an alternative to the surgical approach (6).

Clinical and biological behavior varies according to the localization of the tumor (7). Chordomas are characterized by a high local recurrence rate. The 5-, 10-, and 15-year recurrence rate is 30%, 46%, and 57%, respectively. These tumors can recur very late and require a long-term follow-up (4). Nonetheless, distant metastases have been reported in 30% of patients (8). Lung, liver, bone, lymph node and subcutaneous tissue are tissues and organs where chordoma metastasesmay be seen (9).

A differential diagnosis includes many tumors, such as chondrosarcomas, meningiomas, myoepitheliomas, myoepithelial carcinomas, gliomas, and metastatic carcinomas.

Although no grading has been proposed by the WHO for chordomas, a retrospective series of 111 patients showed that the presence of prominent nucleoli and a high mitotic index (≥3/10HPF) significantly correlate with a worse progression free survival (10). The presence of necrosis and apoptosis significantly correlated with the overall survival. Furthermore, the poorly differentiated subtype was associated with a worse progression free survival (10). In contrast, other histopathologic parameters, such as chondroid subtype, abundance of the myxoid matrix, nuclear pleomorphism, fibrous septa, inflammatory cells, or hemorrhage did not correlate with the prognosis. A loss of SMARCB1/ INI1/BAF47 expression is also a significant independent prognostic factor (11).
In this study, we aimed to review the clinical and histopathological features of head and neck chordomas diagnosed in our department.

MATERIALS AND METHODS

Chordoma cases diagnosed in our department between January 2002 and 2021 were scanned from our archive. Cases of chordoma localized in the head and neck were included in the study. The histopathological features of the tumors were reviewed and thepresence of recurrence was investigated.

RESULTS

Nine cases were identified. Four of the cases are male and 5 are female. The averageage of the patients at the time of diagnosis is 53,4 (13-88). The complaints of the patients were headache, dizziness, visual impairment, shoulder and neck pain, and neck swelling. One patient has atypical symptoms such as nasal obstruction and postnasal discharge depending on the location of the tumor. The demographic characteristics of thepatients are listed in Table 1. Surgical ap-

proach was applied to all patients. However, macroscopic tumor residue remained in five patients. Tumor size ranges from 1,3 to 7,5 cm. In histopathological examination, 7 out of 9 cases have a similar microscopic appearance. In these cases, it is seen that cells with oval to round nucleus, prominent nucleolus, eosinophilic cytoplasm form clusters and cords, and these neoplastic cell cords are separated by thin fibrous bands (Figure 1). In addition, giant cells with vacuolized cytoplasm called physaliferous are also noteworthy (Figure 2). These cases were diagnosed as"conventional chordoma". In one case, the matrix is cartilaginous and areas of necrosis are observed with increased cellularity and mitotic activity. This case was interpreted as "chondroid chordoma" (Figure 3). The last case have conventional chordoma features with high grade undifferentiated pleomorphic sarcoma areas and this case was diagnosed as "dedifferentiated chordoma". Vimentin was positive in all cases. EMA (epithelial membrane antigen) showed diffuse staining in 6 cases and focal staining in 2 cases. S100 protein was positive in 6 out of 9 cases. Staining was observed with cytokeratin in all cases except chondroid chordoma. All of the cases are CEA negative and the Ki-67 proliferation index varies between 1-5%.

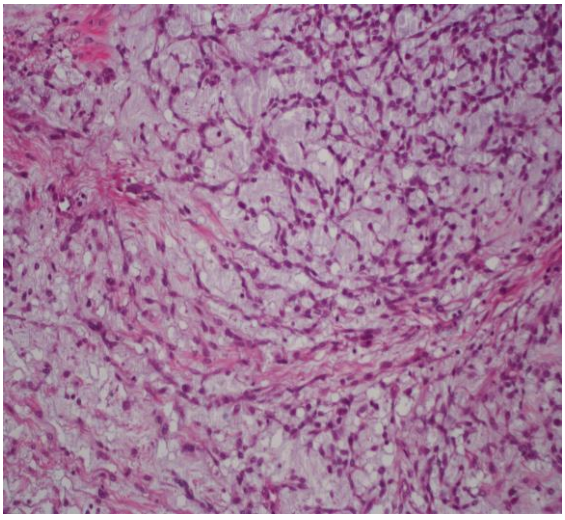

Figure 1: Tumor cells forming cords are observed on the myxoid background (H&E x200)

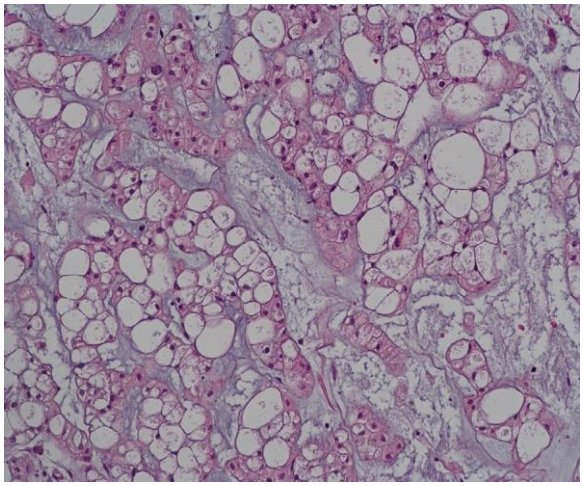

Figure 2: Physaliferous cells with large vacuolized cytoplasm are present (H&E x200)

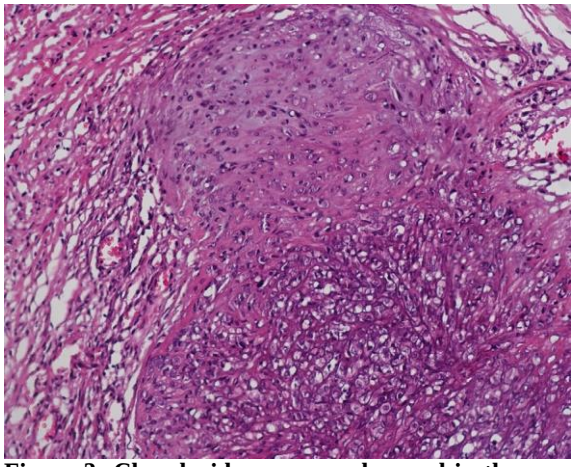

Figure 3: Chondroid areas are observed in the chondroid chordoma case (H&E x10

After surgery, RT was applied to 3 patients, Radiotherapy and KT were applied to one patient. No additional medical treatment was done to four patients. Additional treatment information was not available for one patient. The average follow-up period of the patients is 37 (3-167) months. During this period, local recurrence was detected in the clivus and cervical vertebra in two patients at 17 and 19 months, respectively (2nd and 5th cases). One of these patients was treated with RT after surgery and the other was among those who did not receive additional treatment. Metastasis was detected in the 6th rib at the time of diagnosis in 6th patient with nasopharyngeal chordoma. The 1st

Table 1: Demographics of Patients with Chordoma of Head and Neck

Case	Gender	Age	Complaint	Radiological imaging	Subtype of chordoma	Tumor site	Dimension (cm)	Additional treatment	Follow-up (months)	Outcome
1	M	54	Headache	Mass surrounding the optic nerve, attached to the internal carotid artery.	Conventional	Suprasellar	3	RT and KT	30	Exitus
2	M	52	Headache	Locally invasive tumoral lesion above the clivus	Conventional	Clival	1,3	RT	167	Recur at 17th month
3	M	13	Headache, blindness	NA	Chondroid	Meningeal	3,5	-	35	No recurrence
4	F	50	Neck pain	NA	Conventional	C4-C6	4,5	-	23	No recurrence
5	F	49	Dizziness, shoulder pain	Lobule contoured mass with intraspinal and extraforaminal extension, filling right lateral vertebra corpus, pedicles, right neural foramen	Conventional	C2-C3	3,5	-	26	Recur at 19th month
6	F	75	Nasal obstruction	Mass in the posterior nasopharynx extending into the sphenoid sinus	Conventional	Nasopharygeal	2,5	RT	6	No recurrence
7	M	45	Neck and back pain	Mass lesion in the vertebral corpus. Destructive soft tissue mass compatible with metastasis in the right 6th rib	Dedifferantiated	C4	3,2	NA	4	Exitus at 4th month
8	F	55	Neck swelling	Low-density, lobulated contoured mass destroying C2-4 vertebrae, surrounding the vertebral artery, extending into the retropharyngeal space and nasal foramen, narrowing the laryngeal air column.	Conventional	C1-5	7,5	Patient refused treatment	3	No recurrence
9	F	88	Neck swelling, hand numbness	Mass in heterogeneous inner echo associated with C1-5. Compression on vascular and muscle structures at supraclavicular level 3-4	Conventional	C4-7	7	RT	6	No recurrence

F: Female, M: Male, C: Cervical vertebrae, NA: Not available.

patient, with suprasellar mass, and the 7th patient with dedicated chordoma died at the end of 30 months and 4 months due to tumor.

DISCUSSION

Chordomas, which are rare tumors, constitute 3-4% of primary malignant bone tumors. Its incidence increases with age and peaks in the fifth and sixth decades of life (4,12). The histopathological appearance of the tumor and physaliferous cells were first described by Wirchow and Luscka in 1857 (13). More than half of the tumors are located in the sacrococcygeal region. Skull base (25-35%), cervical vertebra (10%), and thoracolumbar region are other locations of the tumor (14). In our study, 2 cases were located in the sellar region, 1 case in the meninges, 5 cases in the cervical vertebra and 1 case in the nasopharynx. Nasopharyngeal chordoma is extremely rare

in the literature (15). Chordomas of the nasopharyngeal area represent a major challenge in terms of effective treatment due to the relative inaccessibility of the region, tumor involvement of critical neurovascular structures and invasive growth to the skull base, predisposing the tumor to local recurrence and early metastasis (16). The nasopharynx is not a usual site for chordoma. It accounts for only 0.2% of all nasopharyngeal tumors. It is thought that nasopharyngeal chordoma originates from the medial basal canal of the clivus, which is the cephalic outlet of the notochord. To our knowledge, only 21 nasopharyngeal chordomas have been reported in the literature (17,18)

The most common symptom in chordomas is pain. However, for chordomas located in the skull base, symptoms related with the optic nerve and pituitary gland can be observed due to compression (4). Ouyang et al. reported that the most common symptom was headache (19). Although dizziness, shoulder pain and visual impairment were observed in our study, the most common symptom was headache. In one of our cases, the tumor was located in the nasopharynx, and the patient had complaints of nasal obstruction and nasal discharge. Oronasopharyngeal chordomas may cause secondary symptoms such as nasal obstruction due to mass effect, and dyspnea and dysphonia. Symptoms such as mucosal ulceration and nasal bleeding are uncommon symptoms due to their submucosal localization and slow growth (15). There are also studies emphasizing that female gender affects the prognosis negatively (20). Makhdoomi et al. stated that gender has no effect on prognosis (2). Although 5 of the cases in our study were female and 4 were male, the only patient with metastasis was male.

Radiologically, chordomas do not have a specific feature in CT and MRI examinations. However, it can be seen on CT as a soft tissue mass that has formed lytic lesions in the bone. Intratumoral calcifications may accompany this lesion. In MR imaging, theyappear as a mass lesion with hypointense character in T1-weighted images and as hy- perintense in T2-weighted images and dest- ructive in character. Chondroid chordomas may not appear as bright as conventional chordomas on T2-weighted sections. Radiologically, the differential diagnosis includes metastases, chondrosarcoma, other primary bone tumors, multiple myeloma and lymphomas (2,21).

Macroscopically, chordomas are lobulated and soft in consistency. Section surface is myxoid / gelatinous and may include chondroid areas. It may resemble the macroscopic appearance of mucinous adenocarcinoma or chondrosarcoma (4). Microscopic examination shows cells with vacuolized cytoplasm forming cords and nests separated by fibrous septa in a myxoid matrix. Tumor cells are called physaliferous cells because of their foamy, vacuolized cytoplasmic appearance. Vacuolizated clear cytoplasm may cause confusion with lipomatous tumors. In addition to physaliferous cells, oval and round shaped cells with indistinct basophilic cytoplasm are also observed. Mitotic figures are rare and atypical mitosis is not expected. Necrosis is common.

Chordomas are divided in three histological types as conventional, chondroid and dedifferentiated. Focal or diffuse hyaline and chondromyxoid differentiation is observed in the matrix in chondroid chordomas. Dedifferentiated chordomas are biphasic tumors with spindle cell or pleomorphic sarcoma features as well as conventional chordoma. Dedifferentiated chordoma should be considered in the presence of a rapidly growing mass in a patient diagnosed with conventional chordoma. Dedifferentiated chordomas can manifest

with metastases. Its response rates to chemotherapy or radiotherapy are low. Immunohistochemically, tumor cells are stained positively with EMA, keratin and S100 protein. Keratin positivity is especially important in differentiation from chondrosarcoma (4). Of our nine cases, 1 was classified as chondroid and 1 as dedifferentiated chordoma. Chondroid chordoma is the youngest case in our series and is located in the meninges. Chondrosarcoma was considered in the histopathological differential diagnosis because of cellular pleomorphism and mitosis. A diagnosis of chondroid chordoma was made with the uncommon presence of cellular pleomorphism and immunohistochemical findings.

The patient did not receive any additional treatment and there were no signs of recurrence in the 167 moths follow-up. A case of differentiated chordoma presented with shoulder pain and radiological MRI showed a mass in the C4 vertebra. Simultaneously, a tumoral lesion consistent with metastasis was detected on the 6th rib of the patient. Microscopic examination of the surgical excision material revealed the presence of solid, sometimes trabecular clear cells and spindle-like cells. Nucleolar prominence and frequent mitosis have attracted attention. The case was diagnosed as dedifferentiated chordoma. Additional treatment could not be planned for the patient due to poor general condition. The patient died 4 months after diagnosis.

Chordomas are rare malignant tumors of the head and neck region, with a high propensity for local recurrence, even many years after primary treatment. It is believed to have developed from the notochord residue. These tumors are resistant to chemotherapy and radiotherapy. Total excision is difficult due to their localization and invasive nature. The correct histopathological diagnosis is crucial in terms of appropriate treatment and follow-up of patients. In head and neck region, chordomas should be taken into differential diagnosis especially in myxoid tumors.

Authors' contributions: E.E. designed the study, collected the data, performed analysis and wrote the paper

Conflict of Interest: There is no conflict of interest.

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Informed Consent: This study was conducted with a retrospective design.

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