Chondrosarcoma of the jaw: a retrospective series

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Objectives. Low-grade chondrosarcoma presents with features similar to those of benign lesions, such as chondroma and synovial chondromatosis, increasing the difficulty in reaching an accurate diagnosis preoperatively. In this study, we retrospectively reviewed 10 chondrosarcoma cases and evaluated the diagnostic approaches and management modalities.

Study Design. Ten cases were included in the present study. We evaluated the clinical features, initial diagnosis, histopathology subtype, immunohistologic markers, final diagnosis, and treatment modalities.

Results. Most of the lesions were found in the mandible. Two cases were followed up for 1 month and 4 years, respectively as benign lesions before malignant changes were detected. With regard to chondrosarcoma histopathology subtypes, 6 cases were identified as conventional chondrosarcoma, whereas 4 cases were diagnosed as mesenchymal chondrosarcoma with aggressive behavior; of these, 3 were associated with local recurrence and metastasis. The immunohistologic markers showed no specificity for chondrosarcoma.

Conclusions. Distinguishing low-grade chondrosarcoma, particularly in the temporomandibular joint, from benign lesions, such as chondroma or synovial chondromatosis, remains difficult. Currently, the correlation between clinical, radiographic, and histologic features accompanied by close follow-up is extremely important for patients diagnosed with chondrogenic lesions. Postoperative radiotherapy seems to be beneficial in patients with positive surgical margins. (Oral Surg Oral Med Oral Pathol Oral Radiol 2019;128:106−111)

Chondrosarcoma is a malignant tumor in which the tumor cells produce cartilage.[1] Chondrosarcoma of the jaw and facial bones is uncommon and represents 5% to 12% of chondrosarcoma cases. There are few reported studies on this condition, and its clinical behavior varies widely. A review of the literature revealed 13 case series of chondrosarcoma in the head and neck.[1−13] The progression of this disease is slow (0.5−12 months), and the symptoms are related to the site of origin. The most commonly affected sites are the sinonasal area, the maxilla, and the mandible. Its prognosis seems to be related to the early establishment of a diagnosis, histopathologic subtype, early treatment intervention, and resectability. Adjunctive management modalities are still controversial, but surgery alone or surgery with postoperative radiotherapy was the most frequently reported approach. The disease tends to recur locally but may metastasize on rare occasions. The average 5-year survival rate was 65.5%. Another review of temporomandibular joint (TMJ) case reports since 1997 has also been performed.[14−31] In that review, it was found that TMJ chondrosarcoma usually presents clinically with swelling, pain, or trismus. The symptom duration ranged between 2 and 48 months. Significant difficulty in reaching a preoperative diagnosis is common, even with the aid of computed tomography (CT), magnetic resonance imaging (MRI), and fine-needle aspiration biopsy. The condition is usually misdiagnosed as synovial chondromatosis, pleomorphic adenoma, myxoma, or osteochondroma. Treatment of TMJ chondrosarcoma is also challenging because of the proximity of vital structures, such as the facial nerve, parotid gland, skull base, and internal carotid artery. Surgery was the most commonly reported treatment modality, and the length of follow-up ranged from 7 months to 27 years. On the basis of these reports, which showed its rarity; variable behavior; similarity to benign lesions, such as synovial chondromatosis; difficulty in reaching a diagnosis; and controversy in treatment, our purpose was to retrospectively evaluate the diagnostic process and management modalities for patients diagnosed with and treated for chondrosarcoma at our institute.

MATERIALS AND METHODS

During the period 2000−2018, of the patients seen at the Seoul National University Dental Hospital, 10 were included in this study. Clinical features, initial diagnosis, histopathology subtype, immunohistologic markers, and treatment modalities were all evaluated. The initial diagnosis, which was based on CT and/or MRI along with

Statement of Clinical Relevance

This study reviewed 10 cases of chondrosarcoma of various grades with regard to their management modalities and prognosis. The review revealed cases with difficulties in diagnosis and the development of chondrosarcoma from longstanding benign lesions.

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incisional biopsy, was compared with the final diagnosis, which was based on the histopathology of the excised mass. We also analyzed the treatment modalities and survival outcomes. Data analysis was carried out by using the Statistical Package for the Social Sciences software, v. 23 (SPSS Inc., Chicago, IL). Institutional review board exemption for the study was obtained (IRB No. ERI19015).

RESULTS

Demographic data

Nine patients presented to our hospital with various chief complaints related to undiagnosed chondrosarcoma, and 1 patient was referred with an established diagnosis of chondrosarcoma. Patient age ranged from 20 to 72 years (mean age 48.3 years). All 10 patients included in the study were females. The common complaints were swelling (60%) and, to a lesser degree, pain (30%). Other symptoms were nasal obstruction, trismus, and headache. The primary site of chondrosarcoma was the mandible in 80% of cases (8 cases: 5 condyle, 1 ramus, 1 body of the mandible, 1 masticatory space), and in 20% of the cases, the lesions were located in the maxilla (2 cases: 1 posterior maxilla and 1 hard palate) (Table I).

Diagnosis

The initial preoperative chondrosarcoma diagnosis was made with the aid of CT and/or MRI and confirmed by incisional biopsy and histopathologic analysis. In case number 1, the initial incisional biopsy specimen showed absence of neoplastic tissue; when the biopsy was repeated 1 month later, it revealed chondrosarcoma tissue. Case number 10 demonstrated growth of a chondrosarcoma within a previously diagnosed benign lesion after a long period. Four years of follow-up with MRI and fine-needle aspiration biopsy showed a synovial cyst. After a later increase in size of almost 1 cm, an incisional biopsy was performed, and histopathology revealed a chondrosarcoma. In the 8 remaining cases, the preoperative diagnosis was in accordance with the postoperative diagnosis.

Of 6 conventional chondrosarcoma cases, 2 cases were grade I and 3 cases were grade II, and in 1 case, the grade was not specified. Four cases were mesenchymal chondrosarcoma, and recurrence or metastasis occurred in 3 of them. The mean tumor stage was T1 N0 M0. With regard to immunohistochemical markers, both types of chondrosarcomas showed a strong positive reaction to vimentin (9 cases) and a variable positive reaction to Ki-67 (7 cases). CD68 was positive in conventional chondrosarcoma (4 cases; see Table I).

Treatment

En block excision with a safety margin was performed in most of the cases (80%). The types of excision procedures for mandibular lesions ranged from condylectomy and partial mandibulectomy to hemimandibulectomy. Three patients underwent neck dissection, but no cervical lymph node metastases were found. Radiotherapy was applied as a main therapy in 1 case with lung metastasis and as an adjunctive therapy in 4 cases where the resection margin was positive or close. Two of these 4 cases received chemotherapy as well. Most cases underwent immediate reconstruction with one or more of the following: reconstruction plate, artificial condyle prosthesis, and free vascularized flap (free forearm flap, free fibula flap, free serratus anterior flap, and free latissimus dorsi flap) (Table II).

Survival

The follow-up period ranged from 1 to 8 years (mean 5.1 years). Of the 10 patients, 1 patient was lost to follow-up; 1 died as a result of the disease within 1 year because of metastasis to the lung; 2 remained alive with evidence of the disease; and 6 patients remained alive without evidence of the disease. Within the determined follow-up period, local recurrence was found in 1 patient. Distant metastases were present in 3 patients (the lung in 2 cases and the femur in 1 case). The disease-free survival rate was 60%, and the overall survival rate was 80% (Figure 1; see Table II).

DISCUSSION

In our study, the age range of patients with chondrosarcoma was consistent with that reported by other studies—that is, the disease occurrence being more common in the third to fifth decades of life.[8,10] There was no gender predilection; the disease showed a predilection for both sexes in various studies, even though we found a female predilection in our study.[8,10] Most studies reported a greater incidence in the maxilla than in the mandible.[1,8,9] However, Garrington et al.[10] and Ajagbe et al.[11] reported a higher prevalence of chondrosarcoma in the mandible than in the maxilla. In the mandible, the tumors were reported most commonly in the body and ramus, less commonly in the coronoid process, and rarely in the condyle.[10,11] However, in the present study, the mandibular condyle was found to be the most commonly involved site. Chondrosarcoma may present with a wide variation of clinical manifestations, depending on the site of origin. Painless swelling was the most commonly reported complaint.[8–11]

Some of the previous studies identified factors and conditions that may contribute to tumor formation, including multiple hereditary exostoses, Ollier disease, Maffucci syndrome, Paget disease, chondromyxoid fibroma, previous irradiation, previous trauma,

Table I. Clinical and pathologic features

Case No. /age/ sex	Symptoms	Site	Preoperative dx	Postoperative dx	Grade	Stage	Histochemical markers
1/72/F	Headache, dizziness	Lt Mn condyle	InB: No evidence of neoplasia 1-mo F/U: CT & InB: Chondrosarcoma	Chondrosarcoma	NA	NA	NA
2/63/F	Palatal swelling	Hard palate	MRI & InB: Chondrosarcoma	Mesenchymal Chondrosarcoma		NA	Vimentin, Ki-67 (10%−∼25%), CD56
3/54/F	Facial swelling, pain	Rt Mn condyle	MRI & InB: Chondrosarcoma	Chondrosarcoma	I	T1 Nx M0	Vimentin, CD68, Ki-67 (1%)
4/25/F	Nasal obstruction	Right posterior Mx	CT & InB: Chondrosarcoma	Mesenchymal Chondrosarcoma		T1 Nx M0	Vimentin, Ki-67 (1%), smooth muscle actin (SMA), desmin, CD99, S-100
5/44/F	Preauricular swelling, trismus	Lt Mn condyle	CT & InB: Chondrosarcoma	Chondrosarcoma	II	T1 Nx M0	Vimentin, CD68, Ki-67 (10%−20%), S-100
6/40/F	Facial swelling	Rt. Mn. ramus	CT & InB: Chondrosarcoma	Chondrosarcoma	II	T1 Nx M0	Vimentin, CD68, Ki-67 (30%−50%), S100
7/39/F	Referred case	Lt Mn body	CT & InB: Chondrosarcoma	Mesenchymal chondrosarcoma		T1 Nx M0	Vimentin, SMA, desmin, CD34
8/20/F	Facial swelling	Rt. masticatory space	MRI & InB: Chondrosarcoma	Mesenchymal Chondrosarcoma		NA	Vimentin, CD99, S-100
9/62/F	Facial swelling, pain, trismus	Rt Mn condyle	CT & InB: Chondrosarcoma	Chondrosarcoma	II	T1 Nx M0	Vimentin, Ki-67 (15%−20%), S-100
10/64/F	Preauricular pain, trismus	Rt Mn condyle	*4 yr F/U MRI: Synovial cyst, Aspiration: absence of malignant cells *4 yr 2 mo F/U Punch biopsy: hyperplastic cartilage chip *4 yr 3 mo F/U CT & InB: Chondrosarcoma	Chondrosarcoma	I	T1 Nx M0	Vimentin, CD68, Ki-67 (5%), S-100

CT, computed tomography; *F/U,* follow-up; *InB,* incisional biopsy; *Lt,* left; *M,* male; *Mn,* mandible; *MRI,* magnetic resonance imaging; *Mx,* maxilla; *NA,* not available; *Rt,* right.

Table II. Present study treatment outcomes

Case No.	Main therapy	Adjunctive therapy	Resection margin	Recurrence	Metastasis	Reconstruction	Outcomes	Follow-up (yr)
1	InB of condyle		-	NA	NA	-	-	LFU
2	RT	RT	-	NA	Lung	-	DOD	1
3	Condylectomy, parotidectomy		Clear	No	No	*Immediate:* LD muscle flap, facial nerve repair, metal condyle prosthesis, reconstruction plate *Late:* Forehead lift	A, NED	8
4	Maxillectomy	RT + CHT	Involved	No	No	*Immediate:* Free forearm flap, orbital floor reconstruction *Late:* Free fibular flap	A, NED	6.75
5	Partial mandibulectomy, Lt zygoma resection	RT	Involved	No	No	*Immediate:* Metal condyle prosthesis), serratus free flap	A, NED	5.75
6	Hemimandibulectomy, ND		Clear	No	No	*Immediate:* Free fibular flap, sural nerve graft for lingual nerve	A, NED	5.25
7	Hemimandibulectomy, ND		Clear	Yes	Lung	*Immediate:* Reconstruction plate *Delayed:* Fibular free flap	A,WD	5
8	Partial mandibulectomy, ND	RT + CHT	Close	No	Femur	*Immediate:* Reconstruction plate	A, WD	5.25
9	Partial mandibulectomy		Clear	No	No	*Immediate:* Serratus anterior free flap, reconstruction plate, artificial TMJ prosthesis	A, NED	5
10	Partial mandibulectomy	RT	Involved	No	No	*Immediate:* LD free flap, facial nerve reanastomosis, artificial TMJ prosthesis	A, NED	4

A, alive; *CHT,* chemotherapy; *DOD,* died as a result of disease; *F/U,* follow-up; *InB,* incisional biopsy; *LD,* latissimus dorsi; *LFU,* lost to follow-up; *NA,* not available; *ND,* neck dissection; *NED,* no evidence of disease; *RT,* radiotherapy; *TMJ,* temporomandibular joint; *WD,* with disease.

previous benign tumor, and family members with a history of malignant bone tumors.[1,10] In this study, patient 10 developed a chondrosarcoma in a longstanding synovial cyst. Davis et al. reported that of 30 patients with synovial chondromatosis, 3 developed chondrosarcoma after 26 years, 10 years, and 6 months, representing a relative malignant risk of 5%.[32]

Conventional chondrosarcoma comprises the common subtype with 90% of cases, while the other variants account for the remaining 10%. In the present study, 60% of patients were diagnosed with conventional chondrosarcoma, and 40% had mesenchymal chondrosarcoma. Evans et al.[33] classified conventional chondrosarcomas into 3 grades (I, II, and III) according to mitotic rate, cellularity, and nuclear size. Generally, grade I tumors account for approximately 60% of tumors, grade II tumors for just over 30%, and Grade III for fewer than 10%. Most authors consider grade I tumors as low-grade tumors and grade II and III tumors as high-grade tumors. Mesenchymal chondrosarcoma, which is considered a high-grade tumor, shows a biphasic pattern that is composed of undifferentiated small round cells within a hyaline cartilage matrix. In our study, 4 cases had mesenchymal chondrosarcoma. These tumors showed aggressive behavior; 3 of the 4 cases were associated with local recurrence and metastasis.

Identification of low-grade chondrosarcoma arising in the TMJ from synovial chondromatosis is extremely difficult. As shown by CT or MRI, both lesions exhibit common features of an intraarticular soft tissue mass, cartilaginous mineralization, and bone erosions, with no specific features to distinguish synovial chondromatosis from low-grade chondrosarcoma.[22,29,31,34] Synovial chondromatosis and low-grade chondrosarcoma share common histologic features, so the misidentification of either lesion is a common occurrence. Both lesions demonstrate clusters of chondrocytes with nuclear atypia and hyperchromaticity in the synovial connective tissue. The degree of cellularity and nuclear atypia are similar in both lesions.[35] Bertoni et al. reported the following histologic features to help in the diagnosis of malignancy: "loss of the 'clustering' growth pattern typical of synovial chondromatosis,

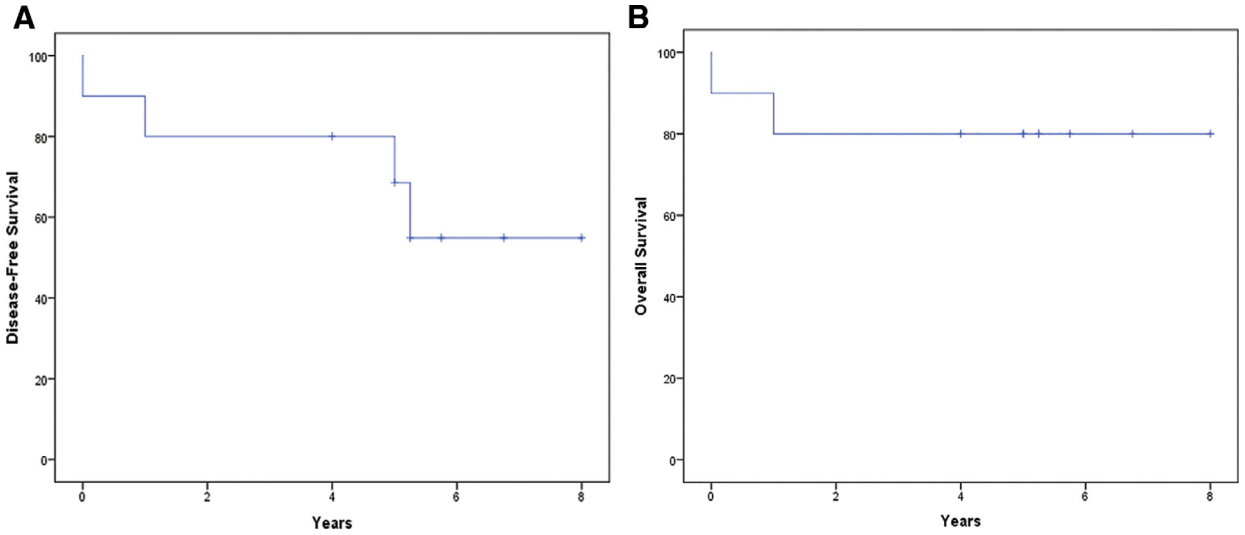

Fig. 1. Kaplan-Meier curves showing the survival rates of patients with chondrosarcoma. **A,** Disease-free survival was 60%. **B,** Overall survival rate over 8 years was 80%.

myxoid change in the matrix, areas of necrosis, and spindling at the periphery of chondroid lobules."[36] However, few of these features would be present in the early stages of chondrosarcoma, and they might be focal.[35] Synovial chondromatosis shows a positive reaction to vimentin, Ki-67, and CD68 immunohistochemical markers.[37] In the present study, chondrosarcoma also exhibited a positive reaction to these markers. Chondrosarcoma may express a wide variety of histochemical markers. All chondrosarcomas, irrespective of cell type, are strongly positive for vimentin.[38,39] Ki-67 immunostaining as a proliferation marker has been investigated in different tumors. In chondrosarcoma, Ki-67 expression is reported to correlate with the histologic grade, recurrence rate, and likelihood of metastasis.[40] In a study of clear cell chondrosarcoma, expression of CD68 was found in coexisting histiocytes and osteoclasts.[41] Although these markers are helpful in the diagnosis of chondrosarcoma, they are not specific for it.

Surgery is considered the main treatment modality. En block resection with a clear histologic margin is the most common approach to prevent local recurrence. Neck dissection is not routinely performed because of the rarity of lymph node metastasis.[5] Although several previous reports have suggested a lack of benefit from radiotherapy,[11] other reports have emphasized the role of adjunctive radiotherapy in eradicating residual microscopic disease in cases with positive postoperative resection margins.[8] In the present study, 4 patients with positive and close margins received postoperative radiotherapy, and no local recurrence was found in their later follow-up visits. Because of the limited number of reports in the literature supporting the benefit of chemotherapy, it was only applied in combination with surgery and radiotherapy for controlling tumors of high grade, rapid local recurrence, or increased potential of metastasis.[11]

Head and neck chondrosarcoma series have reported a 5-year survival rate ranging from 32% to 91.9%.[6,10] The most common causes of death were local recurrence and direct extension to nearby structures. The local recurrence rate was reported to range from 7% to 71% (see Table I).[6,9] The incidence of distant metastasis is less common. When it occurs, the lung, brain, and vertebrae have been reported to be the main sites of metastasis.[2,6,10,13] Also, studies have reported several prognostic factors, such as an early established definitive diagnosis, primary location of the tumor, tumor size, histologic subtype and grade, and resectability.[3,10]

CONCLUSIONS

The distinction of low-grade chondrosarcoma, particularly in the TMJ, arising from benign lesions, such as chondroma or synovial chondromatosis, remains difficult. It would be of great benefit to identify a specific immunohistologic marker for chondrosarcoma. Currently, the correlation of clinical, radiographic, and histologic features, accompanied by close follow-up, is extremely important in the management of patients diagnosed with chondrogenic lesions. Postoperative radiotherapy seems to be beneficial in patients with positive surgical margins.

DISCLOSURE

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