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An extensive nodular lesion involving hard palate and nasal turbinate

Q1 Sanpreet Singh Sachdev, BDS,[a] Tabita Joy Chettiankandy, MDS,[a] Prajwalit Prakash Kende, MDS,[a] Rajiv S. Desai, MDS,[b] Sagar S. Vaishampayan, MDS,[c] and Sandesh Suryawanshi, BDS[a]

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CLINICAL PRESENTATION

A 38-year-old man was referred to our institute for the examination of asymptomatic swelling on the right posterolateral aspect of the hard palate. The patient noticed the swelling 2 months before when it increased to its present size and was perceived during tongue movement. The patient's medical, social, and dental history were nonsignificant. To the best of his knowledge, he was not allergic to any medication and did not undergo any prior surgery. He did not consume tobacco products or have a history of any parafunctional habit or trauma.

Extraoral facial examination revealed no gross facial deformity or asymmetry. The submental, submandibular, and cervical lymph nodes were normal in size and consistency and nontender on palpation. On intraoral examination, an ovoid expansile nodular lesion, approximately 3 × 2 cm in size, extending from the right maxillary first premolar to the second molar anteroposteriorly and from the midline of the palate to the buccal vestibule involving the right maxillary alveolar bone, was noted (Figure 1). In addition, obliteration of the buccal vestibule was noted. Buccoversion of both the involved maxillary molars involved in the lesion was noted without mobility of the teeth. The swelling was non-fluctuant and slightly firm on palpation and fixed to underlying structures. When pressure was applied, blanching was noted without any associated tenderness. An erythematous area was visible on the posterior aspect of the lesion.

Radiographic findings

Multislice spiral computed tomography revealed a well-defined, mixed lesion involving the right side of the hard palate that was associated with a mildly enhancing soft tissue component (Figure 2A-C). The dimensions of the lesion were 18 × 16 × 14 mm. The lesion superiorly extended into the right side of the nasal cavity and abutted the inferior turbinate. The lesion mesiodistally extended from the palatal cortex of the right maxillary molar teeth to the midline. The interior of the lesion exhibited multiple hyperdense foci that were suggestive of calcified bodies. Multiple areas of destruction were observed in the floor of the right maxillary sinus and the right-side floor of the nasal cavity. The floor of the right maxillary sinus exhibited a soft tissue density similar to that of the lesion. Mucosal thickening was observed in the medial walls of the maxillary sinus bilaterally. To visualize the exact extent of the lesion with a better soft tissue contrast, magnetic resonance imaging (MRI) was performed.

On MRI, the mass appeared to be hyperintense and isointense on T1- and T2-weighted images, respectively. The mass extended from the palatal cortex of the right molar region, crossing the midline and extending to the left hard palate region (Figure 2D and E). The posterior extent of the lesion was visualized up to the soft palate. A soft tissue mass of the similar intensity was noted over the left side of the hard palate and bilaterally in the floor of the maxillary sinus. An incidental finding of the altered signal intensity (isointense and hyperintense on T1- and T2-weighted images, respectively) along the medial wall of the maxillary sinuses on both the sides was suggestive of mucosal thickening due to secondary inflammation.

DIFFERENTIAL DIAGNOSIS

A surgeon would speculate a submucosal nodular swelling on the hard palate to be a minor salivary gland neoplasm owing to its tendency to frequently occur as painless swelling at the same site.[1,2] Pleomorphic adenoma (PA) is the most common minor salivary gland neoplasm, with the palatal area being its most common site of occurrence. PA usually occurs as a well-defined mass with firm consistency without any associated

[a]Department of Oral Pathology and Microbiology, Government Dental College and Hospital, Mumbai, India.
[b]Department of Oral Pathology, Nair Hospital and Dental College, Mumbai, India.
[c]Department of Oral and Maxillofacial Surgery, MGM Dental College, Navi Mumbai, India.
Q2 Corresponding author: Sanpreet Singh Sachdev Dr. E-mail address: Sunpreetss@yahoo.in

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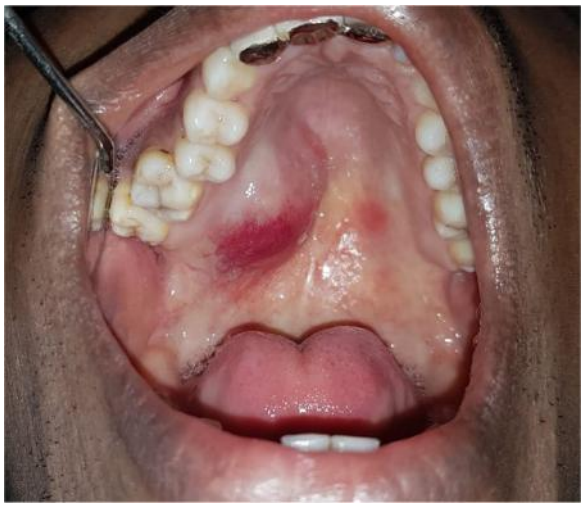

Fig. 1. Intraoral erythematous nodular lesion on the hard palate.

symptoms, similar to the present lesion. Due to the slow-growing nature of PA, deep-seated lesions may become extensive before they become symptomatic.[2] Similar to the present case, larger PAs can exhibit heterogeneous enhancement with small regions of calcification.[3] Therefore, PA was considered in the differential diagnosis.

The extensive involvement in the present case raised suspicion for a malignant lesion. Mucoepidermoid carcinoma (MEC) is among the most common malignant minor salivary gland neoplasms. MEC tends to occur as an asymptomatic, reddish, slow-growing swelling involving the hard and soft palate regions.[1] Calcifications are conventionally considered to rarely occur in malignant salivary gland neoplasms and are often associated with high-grade tumors. Calcifications, occurring in approximately 20% of MECs, may not be a rare finding.[4] These calcifications might originate from the precipitation of mucous secretion by neoplastic cells.[3] Therefore, MEC was included as a differential diagnosis for the present case. Other malignant salivary gland neoplasms, such as adenoid cystic carcinoma and polymorphous adenocarcinoma, frequently occur in the

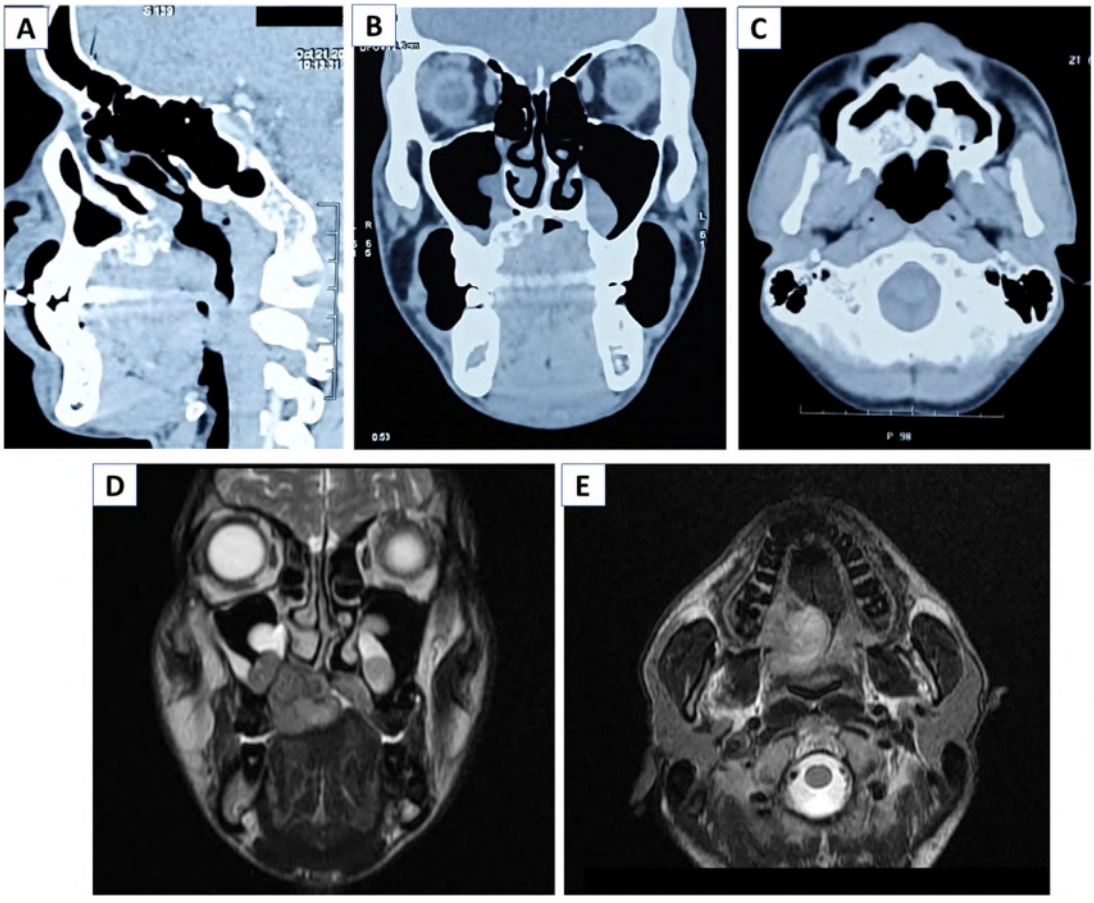

Fig. 2. Multislice spiral CT scan of head and neck showing a mixed lesion involving the hard palate in **(A)** sagittal view, **(B)** coronal view (note the mucosal thickening of medial wall of maxillary sinuses on both the sides), and **(C)** axial view; **(D)** T2-weighted image of coronal section showing hyperintense lesion involving the right side of hard palate and its extent in the floor of right and left maxillary sinuses; **(E)** T2-weighted image of axial section shows hyperintense lesion extending to the soft palate area.

palate. However, these entities rarely exhibit focal calcifications and were therefore more unlikely than PA or MEC in the present case.

Apart from salivary gland neoplasms, lymphoma was a strong consideration in the differential diagnosis of the present case, given the clinical appearance and location. Lymphoma is the second most common malignant tumor noted in the oral cavity, surpassed only by oral squamous cell carcinoma. However, oral lymphomas are considerably rare, accounting for 3.5% of intraoral malignant neoplasms. Most oral lymphomas comprise extranodal non-Hodgkin lymphoma (NHL), whereas only 1% to 4% of Hodgkin lymphomas occur at extranodal sites. The common intraoral sites of the occurrence of NHL include the tonsils, palate, tongue, floor of the mouth, and salivary glands.[5] Extranodal NHL occurring on the palate can have a clinical presentation of an ulcerated or nonulcerated, asymptomatic, erythematous mass. Radiographically, such NHLs often appear as a lytic radiolucent lesion involving the hard palate.[5,6] Although NHLs are usually soft on palpation and do not exhibit areas of calcification, ruling them out would warrant definite investigations such as biopsy and histopathologic examination.

Malignant tumors of hard tissues, such as osteosarcoma (OS) and chondrosarcoma (CS), can occur as extensively destructive lesions with focal calcified structures. Although uncommon, approximately 10% of OS occur in the jaws, with a male predilection.[7] Development of OS in the long bones has been correlated with rapid bone growth occurring during puberty. However, the OS of the jaws differ from that of the long bones in terms of the time of onset, lower metastatic spread, and better survival. Differences in embryogenesis, molecular or genetic pathways involved, and the tumor microenvironment have been implicated to account for these differences.[8] The incidence of gnathic OS peaks from the third to fifth decades of life, which is 1 or 2 decades after adolescence. The mean age of occurrence in patients with gnathic OS was reported to approximately 30 to 35 years.[8] Swelling is the most common presentation in the cases of OS, whereas pain, paresthesia, and ulceration are noted less commonly.[9]

CS typically occurs as painless swelling in the long bones and rarely in the jaws. CS occurs mainly from the second to fifth decades of life, with peak occurrence in the third decade of life. Certain variants of CS, such as mesenchymal chondrosarcoma (MCS), exhibit a propensity to occur in the jaws.[9] Gnathic CS is usually more prevalent in the maxillary jaw, whereas MCS exhibits relatively more even distribution of occurrence in both the jaws.[10,11] Approximately two-thirds of MCS occur as intraosseous lesions, predominantly in the axial skeleton.[12] In most cases, radiography reveals a well-defined soft tissue mass, often with irregular radiopaque foci due to the presence of calcification or cartilaginous areas.[10] Computed tomography typically reveals aggressive bone destruction with a large associated soft tissue mass and chondroid mineralization.[12] CS occurring in the maxilla can have a clinical and radiographic presentation, as noted in the present case. Therefore, CS was considered in the differential diagnosis but only after the more common entities.

Ewing sarcoma (EWS) is another possibility considering the destructive lesion, although it has a predilection to occur in the mandible and in patients aged <30 years.[10] Areas of cortical destruction leading to communication between the intra- and extraskeletal components of the tumor are frequent in EWS. Furthermore, EWS was reported to involve the jaws in approximately 8% of cases.[13] The enhancement pattern is highly variable, and MRI features are nonspecific, resembling those of other aggressive soft tissue sarcomas. Calcifications are rarely noted in approximately 7% to 9% of cases.[14] Incisional biopsy and its histopathologic examination are warranted to exclude EWS from the differential diagnosis.

Histopathologic findings

An incisional biopsy specimen from the central submucosal region of the tumor was obtained to visualize the deeply situated epicenter of the lesion. Gross examination of the specimen revealed a grayish, fleshy mass with few brownish areas and small whitish foci. The specimen was firm in consistency, and the cut surface exhibited a gritty surface texture.

The histopathologic picture in hematoxylin and eosin−stained sections exhibited a hypercellular connective tissue stroma with a predominant population of round or angulated to spindle-shaped basaloid cells with scant cytoplasm arranged in sheets and nests (Figure 3A). In addition, the cells assumed a pseudoalveolar growth pattern in some areas, with dense collagenous bundles intervening the clusters of cells (Figure 3B). Few abrupt areas of the cartilage were present adjacent to mesenchymal cellular areas (Figure 4A and B). The cartilaginous tissue was of mature well-differentiated type (Figure 4C).

A neoplastic lesion predominantly composed of round to spindle-shaped cells could be representative of an array of lesions that present with similar patterns such as alveolar rhabdomyosarcoma, lymphoma, or EWS/PNET, wherein the cartilage observed could be a part of reactive formation due to the tumor.[10] The cartilaginous component, although scanty on the microscopic analysis of the specimen, could be a part of the lesion or metaplastic

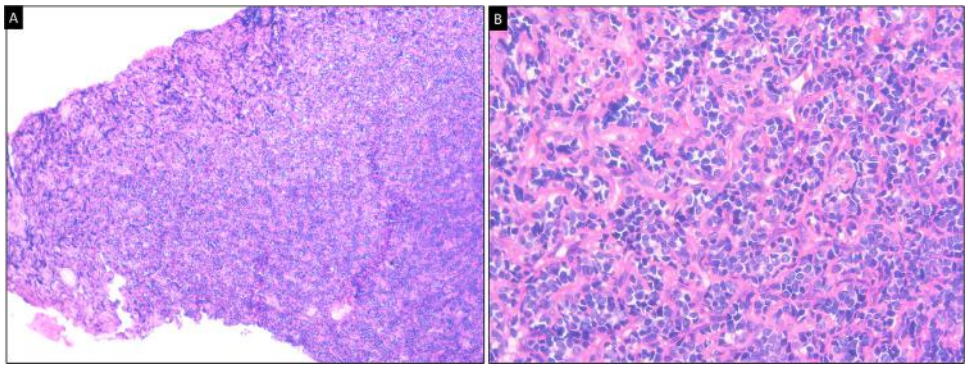

Fig. 3. **(A)** Low power view exhibiting predominant population of basaloid cells proliferating in sheets and nests within the stroma (hematoxylin and eosin stain, × 100); **(B)** dense collagenous bundles intervening clusters of cells exhibiting a pseudo-alveolar arrangement (hematoxylin and eosin stain, × 400). A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM06619.

formation within the tumor. Therefore, OS and MCS were considered in the differential diagnosis.[7,10] Although the presentation was that of a malignant neoplasm, scanty cellular atypia or abnormal mitotic activity was noted. Thus, a benign neoplasm at the more aggressive end of the spectrum, such as myoepithelioma with chondroid areas, which is a tumor known to occur at this site, was considered.

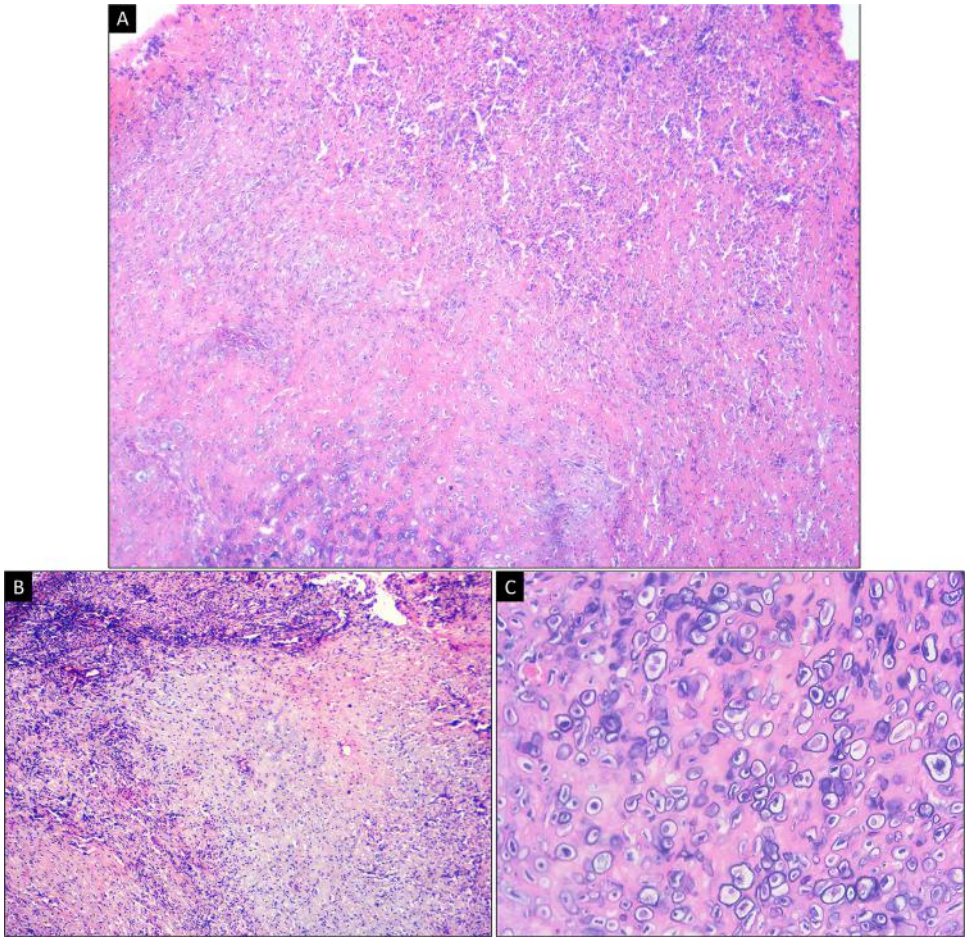

Fig. 4. **(A)** Low power view exhibiting bimorphic lesional tissue comprising of cellular and cartilaginous areas (hematoxylin and eosin stain, × 40). **(B)** Abrupt transition between the primitive cells and cartilaginous area (hematoxylin and eosin stain, × 100). **(C)** Well-differentiated cartilaginous component (hematoxylin and eosin stain, × 400). A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM06618.

Table 1. Immunohistochemical markers analyzed and their results

Sr. No.	*IHC marker assessed*	*Result*	*Inference*
	Cytokeratin AE1/AE3	Negative	Ruled out neoplasms of epithelial origin
	EMA	Negative	
	Calponin	Negative	Ruled out neoplasm of salivary gland origin and myoepithelial cells
	p63	Negative	
	Desmin	Negative	Ruled out rhabdomyosarcoma
	Myogenin	Negative	
	MyoD1	Faint staining in few mesenchymal cells	
	SAT-B2	Negative	Ruled out osteosarcoma
	LCA	Negative	Ruled out lymphoma
	MIC-2	Intense membranous immunoreactivity in mesenchymal cells	Likely to be mesenchymal chondrosarcoma, Ewing sarcoma/PNET, synovial sarcoma
	NKX 2.2	Intense nuclear immunoreactivity in mesenchymal cells	

IHC, immunohistochemistry.

DIAGNOSIS

Immunohistochemistry is an indispensable tool for resolving cases that may be shared by lesions of various origins and for helping to ascertain the exact origin of cells. Relevant immunohistochemistry markers were tested for individual differential diagnoses, and their results are listed in Table 1.

CD99, also known as MIC-2, is a marker commonly employed for diagnosing EWS/PNET. Positive expression of MIC-2 may also be noted in synovial sarcoma, mesenchymal chondrosarcoma, rhabdomyosarcoma, hemangiopericytoma, and certain other mesenchymal tumors.[15] Positive immunoexpression of MIC-2 (Figure 5A) and NKX 2.2 (Figure 5B) narrowed down the probable diagnosis to EWS/PNET and MCS.[16]

A similar expression of CD99 is noted in synovial sarcoma; thus, a lesion devoid of or with the cartilaginous component is indistinguishable among these 3 entities.[10] Negative immunoexpression of cyokeratin AE1/AE3 as well as EMA indicated the absence of epithelial differentiation. Consequently, synovial sarcoma was inferred to be unlikely, although poorly differentiated tumors may be negative for epithelial markers.

Based on clinical, radiographic, histopathologic, and immunohistochemistry findings, the lesion was diagnosed as MCS.

MANAGEMENT

Fluorodeoxyglucose (FDG)-positron emission tomography was performed to determine the presence of any metastatic foci and the treatment protocol. The lesion exhibited increased FDG uptake with an SUV_{max} of 6.4 (upper cutoff = 2.5). No abnormal hypermetabolic foci were detected elsewhere in the brain, neck, thorax, abdomen, and pelvis, although non-FDG−avid small bilateral cervical adenopathy was noted. Ventricles and cerebrospinal fluid spaces in the brain were unremarkable without any mass effect or midline shift. Major vascular structures appeared to be normal. Satisfactory inflation with adequate lung volumes were noted, devoid of any pleural or pericardial effusion.

The patient was referred to a higher treatment care center for further evaluation and treatment, wherein a right infrastructural maxillectomy procedure was performed. Histopathologic examination of the excised specimen predominantly demonstrated the presence of

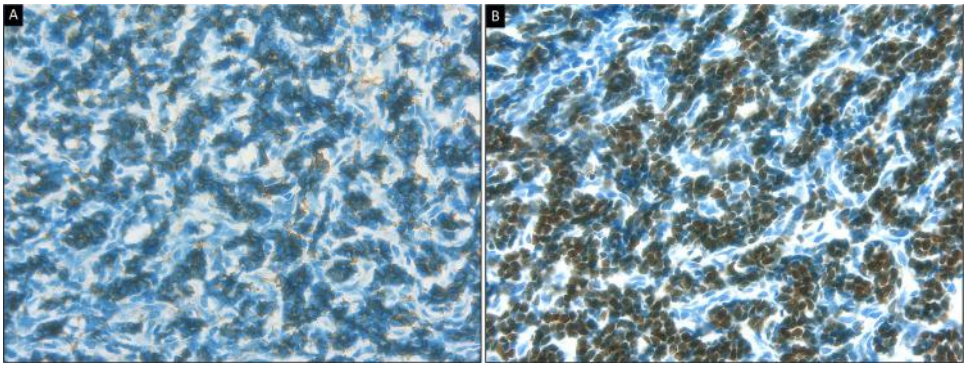

Fig. 5. Mesenchymal cells exhibiting **(A)** intense membranous immunoexpression of MIC-2 (X400), and **(B)** intense nuclear expression of NKX 2.2 (× 400).

monomorphic small round cells with scant cytoplasm arranged in sheets and a pseudoalveolar pattern. Nuclei of the cells were round to angulated with stippled chromatin.

Abrupt poorly circumscribed areas of the well-differentiated hyaline cartilage were noted among the clusters of mesenchymal cells. Prominent thin-walled branching vessels resembling the hemangiopericytoma-like pattern were noted. No significant cellular atypia was observed. Although the absence of the abundant cartilaginous component in the incisional biopsy specimen of the tumor presented diagnostic hurdles, the characteristic histopathologic features of MCS were easily recognizable in the excised tumor specimen, thereby confirming the diagnosis.

The excised specimen was devoid of any lymphatic or vascular emboli. In addition, vascular invasion and necrosis were absent. All margins were free of the tumor, with medial palatal mucosal margin being the closest (1.0 cm from the tumor). The mitotic count for the entire lesion was determined to be 1/10 hpf. Atypical mitotic figures were not identified. Overall, French Fédération Nationale des Centres de Lutte Contre Ie Cancer (FNCLCC) grade II (3 + 1 + 0) was assigned.

Based on the absence of metastatic foci along with an intermediate FNCLCC grade (grade II) assigned for the present case, the prognosis was discerned to be questionable. Accordingly, radical surgery followed by radiotherapy and chemotherapy was inferred to be an appropriate treatment plan for the case. The patient responded well to treatment and showed no evidence of disease after a 12-month follow-up.

DISCUSSION

CS accounts for only 0.1% of neoplasms occurring in the head and neck region. Various histologic variants of CS, such as clear cell, myxoid, dedifferentiated, and mesenchymal, have been described.[17] MCS is a rare variant accounting for less than 10% of all CS cases.

A clinicopathologic study performed by Vencio et al.[18] identified 19 cases of gnathic MCS among more than 40 000 cases of bone tumors on file at the Mayo Clinic, indicating the lesion's rarity.[18] Unlike the other variants of CS, MCS exhibits a marked propensity to occur in the jaws.[19,20]

MCS is a bimorphic tumor consisting of 2 components: a hypercellular undifferentiated mesenchymal component and a well-differentiated cartilaginous component. Primitive mesenchymal cells proliferate in various patterns, including sheets, pseudoalveolar, or pericytoma-like; they have been interpreted as hemangiopericytoma with cartilaginous differentiation in earlier years.[21] Because of its cartilaginous component, MCS has often been regarded as a variant of conventional CS. Preponderance in young adults, particularly in the age group of 15 to 35 years, along with female predilection, differentiates it from other forms of CS.[19,20] MCS is generally perceived as a rapidly enlarging tumor occurring more frequently at intraosseous sites with an aggressive clinical course and a high incidence of metastasis, unlike the extraskeletal counterparts of CS.[17,19]

MCS has a propensity to occur as asymptomatic swelling in the head and neck region, particularly the orbit, craniofacial bones, dura mater, and occipital region or neck; however, reports of the lesion presenting in any possible anatomic site have been published.[10,19] Intraorally, MCS has most frequently been reported to occur in the maxilla, presenting as a radiopaque or mixed mass extensively involving nasal and paranasal sinuses, as noted in our case.[20,22] However, because the maxillary bone develops due to membranous instead of endochondral ossification, the derivation of the tumor has been ascribed to primitive mesenchymal cells or vestigial nests originating from the cartilage tissue of the incisive papilla, nasal capsule, or paraseptal cartilage.[22]

The microscopic picture of MCS is considerably characteristic consisting of the sheets of undifferentiated round to spindle-shaped cells, with an abrupt transition to small, poorly defined areas of the well-differentiated hyaline cartilage that blends with hypercellular areas.[10,17] Varied proportions of solid cellular and richly vascular areas may be noted in different areas of the lesion. Although the histologic features of MCS are characteristic, the lack of the adequate cartilaginous element on incisional biopsy specimens may pose diagnostic problems. Such specimens may closely resemble EWS or poorly differentiated synovial sarcoma, which are also immunohistochemically reactive to MIC-2 and NKX 2.2 antibodies.[16,23] Therefore, resolution among these entities is complicated and warrants meticulous evaluation for the chondroid component.[10]

SOX9 is a transcriptional factor that is considered as the master regulator of chondrogenesis. SOX9 was reported to be expressed in mesenchymal and cartilaginous components in 21 out of 22 cases of MCS by Wehrli et al.; the other small round blue cell tumors were negative for this antigen.[24] Recent studies have identified an association of MCS with *HEY1−NCOA2* gene fusion, which is absent in other types of CS.[25] In the present case, the use of RT-PCR or FISH to detect *HEY1−NCOA2* fusion could have helped differentiate MCS from other entities in the differential diagnosis. The presence of well-differentiated cartilaginous areas, although scant, in our case indicated the probable diagnosis of MCS, which was confirmed later through the histopathologic examination of the excised tumor after surgery.

Another diagnostic pitfall exists in differentiating MCS from spindle cell, alveolar, or sclerosing rhabdomyosarcoma owing to the aberrant expression of MyoD1 in many cases of MCS. In our case, a weak expression of Myo-D1 was noted only in few mesenchymal cells.[26] The *HEY1-NCOA2* fusion might be responsible for activating the pathway of myogenic differentiation and the subsequent expression of MyoD1 in MCS.[10] Negative immunoreactivity of myogenin along with hints of chondroid areas can aid in preventing the possible misinterpretation of the lesion as alveolar rhabdomyosarcoma.

The clinical course of MCS is relatively aggressive, with metastasis reported in a higher percentage of cases compared with extraskeletal CS.[17,19] Metastatic lesions principally occur in the lungs, whereas lymph nodes are less likely metastatic sites. Clinical regression of neoplasms has been reported in several patients, although late metastases have been reported. Extensive studies involving MCS with long-term follow-up have reported a 5-year survival rate of approximately 55% and a 10-year survival rate of 27% (n = 111) to 43% (n = 107).[19,27] Presence of metastatic foci and size of tumor have been identified as predictive factors for survival, although a reliable prognostic correlation with the patient's age or the degree of cellular differentiation is not established.[10,27]

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DECLARATIONS OF INTEREST

none

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REFERENCES

1. Toida M, Shimokawa K, Makita H, et al. Intraoral minor salivary gland tumors: a clinicopathological study of 82 cases. *Int J Oral Maxillofac Surg*. 2005;34:528-532.
2. Almeslet AS. Pleomorphic adenoma: a systematic review. *Int J Clin Pediatr Dent*. 2020;13:284-287.
3. Bavle RM. Microcalcifications in salivary gland tumors. *J Oral Maxillofac Pathol*. 2014;18:2-3.
4. González-Arriagada WA, Santos-Silva AR, Ito FA, Vargas PA, Lopes MA. Calcifications may be a frequent finding in mucoepidermoid carcinomas of the salivary glands: a clinicopathologic study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2011;111:482-485.
5. Silva TD, Ferreira CB, Leite GB, de Menezes Pontes JR, Antunes HS. Oral manifestations of lymphoma: a systematic review. *Ecancermedicalscience*. 2016;10:665.
6. Abdelwahed Hussein MR. Non-Hodgkin's lymphoma of the oral cavity and maxillofacial region: a pathologist viewpoint. *Expert Rev Hematol*. 2018;11:737-748.
7. Krishnamurthy A, Palaniappan R. Osteosarcomas of the head and neck region: a case series with a review of literature. *J Maxillofac Oral Surg*. 2018;17:38-43.
8. Bertin H, Gomez-Brouchet A, Rédini F. Osteosarcoma of the jaws: an overview of the pathophysiological mechanisms. *Crit Rev Oncol Hematol*. 2020;156:103126.
9. ElKordy MA, ElBaradie TS, ElSebai HI, KhairAlla SM, Amin AAE. Osteosarcoma of the jaw: challenges in the diagnosis and treatment. *J Egypt Natl Canc Inst*. 2018;30:7-11.
10. Weiss SW, Goldblum JR, Folpe AL. *Cartilaginous and osseous soft tissue tumors*. Enzinger and Weiss's Soft Tissue Tumors. 7th ed. Canada: Elsevier Health Sciences; 2020:1053-1062. Q5
11. de Souza LL, Pontes FS, Fonseca FP, da Mata Rezende DS, Vasconcelos VCS, Pontes HAR. Chondrosarcoma of the jaw bones: a review of 224 cases reported to date and an analysis of prognostic factors. *Int J Oral Maxillofac Surg*. 2019;48:452-460.
12. Stanbouly D, Litman E, Vasilyeva D, Philipone E. Mesenchymal chondrosarcoma in the maxilla: a case report and literature review. *J Oral Maxillofac Surg*. 2021;79:1706-1711.
13. Margaix-Muñoz M, Bagán J, Poveda-Roda R. Ewing sarcoma of the oral cavity. A review. *J Clin Exp Dent*. 2017;9:e294-e301.
14. Murphey MD, Senchak LT, Mambalam PK, Logie CI, Klassen-Fischer MK, Kransdorf MJ. From the radiologic pathology archives: Ewing sarcoma family of tumors: radiologic-pathologic correlation. *Radiographics*. 2013;33:803-831.
15. Pasello M, Manara MC, Scotlandi K. CD99 at the crossroads of physiology and pathology. *J Cell Commun Signal*. 2018;12:55-68.
16. Yoshida A, Sekine S, Tsuta K, Fukayama M, Furuta K, Tsuda H. NKX2. 2 is a useful immunohistochemical marker for Ewing sarcoma. *Am J Surg Pathol*. 2012;36:993-999.
17. Takata T, Slootweg PJ. Odontogenic and maxillofacial bone tumours. In: El Naggar AK, Chan JK, Grandis JR, Takata T, Slootweg PJ, eds. *WHO Classification of Head and Neck Tumours*, 4th ed., Lyon: France: IARC; 2017:203-232.
18. Vencio EF, Reeve CM, Unni KK, Nascimento AG. Mesenchymal chondrosarcoma of the jaw bones: clinicopathologic study of 19 cases. *Cancer*. 1998;82:2350-2355.
19. Almansoori AA, Kim HY, Kim B, Kim SM, Lee JH. Chondrosarcoma of the jaw: a retrospective series. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2019;128:106-111.
20. Takahashi K, Sato K, Kanazawa H, Wang XL, Kimura T. Mesenchymal chondrosarcoma of the jaw – report of a case and review of 41 cases in the literature. *Head Neck*. 1993;15:459-464.
21. Reeh MJ. Hemangiopericytoma with cartilaginous differentiation involving orbit. *Arch Ophthalmol*. 1966;75:82-83.
22. Choo CS, Wan Abdul Rahman WF, Jaafar H, Ramli RR. Mesenchymal chondrosarcoma of maxilla in paediatric patient. *BMJ Case Rep*. 2019;12:e228969.
23. Shibuya R, Matsuyama A, Nakamoto M, Shiba E, Kasai T, Hisaoka M. The combination of CD99 and NKX2.2, a transcriptional target of EWSR1-FLI1, is highly specific for the diagnosis of Ewing sarcoma. *Virchows Arch*. 2014;465:599-605.
24. Wehrli BM, Huang W, De Crombrugghe B, Ayala AG, Czerniak B. Sox9, a master regulator of chondrogenesis, distinguishes mesenchymal chondrosarcoma from other small blue round cell tumors. *Hum Pathol*. 2003;34:263-269.
25. Wang L, Motoi T, Khanin R, et al. Identification of a novel, recurrent HEY1-NCOA2 fusion in mesenchymal chondrosarcoma based on a genome-wide screen of exon-level expression data. *Genes Chromosomes Cancer*. 2012;51:127-139.

26. Folpe AL, Graham RP, Martinez A, Schembri-Wismayer D, Boland J, Fritchie KJ. Mesenchymal chondrosarcomas showing immunohistochemical evidence of rhabdomyoblastic differentiation: a potential diagnostic pitfall. *Hum Pathol*. 2018;77:28-34.

27. Schneiderman BA, Kliethermes SA, Nystrom LM. Survival in mesenchymal chondrosarcoma varies based on age and tumor location: a survival analysis of the SEER database. *Clin Orthop Relat Res*. 2017;475:799-805.