Multifarious Histological Patterns in Solid Multicystic Ameloblastoma: A Rare Presentation

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Abstract:
The jaws are host to a wide variety of cysts and tumors, contributed largely by the tissues involved in tooth formation. Ameloblastoma, the second most common odontogenic tumor is usually a benign, locally aggressive neoplasm of enamel organ type tissue, which does not undergo differentiation to the point of enamel formation. It commonly manifests as a slow-growing, locally invasive neoplasm, located intraorally showing few or no clinical signs in early stages which may gradually result in facial deformity, loose teeth, pathological fracture, and pain due to secondary infection or impingement on peripheral nerves. This tumor shows a male predilection and mandible (ramus area) is affected more commonly than the maxilla. These tumors also tend to show wide morphological variations. We report a case of solid multicystic ameloblastoma (SMA) in a 27-year-old male patient who presented with the complaint of pain and a slow growing swelling in the lower right posterior region of the jaw since 3 months. Hemimandibulectomy was done and the resected specimen, when subjected to histopathological examination, confirmed the diagnosis of SMA showing a mix of histological patterns comprising of follicular, plexiform along with the uncommon granular type. This case report also reviews various mixed histopathologic patterns seen in SMA.

Key Words: Ameloblastoma, granular ameloblastoma, mixed histological variants, odontogenic tumors

Introduction
The process of odontogenesis is highly co-ordinated and complex and relies on several instructive and permissive cellular interactions that result in the initiation and generation of tooth.1 The epithelial remnants of odontogenesis when triggered by unknown mechanisms results in its proliferation and formation of pathological entities such as odontogenic cysts and tumors.2

Ameloblastomas are tumors of odontogenic epithelial origin arising from a developing enamel organ or its remnants, epithelial lining of an odontogenic cyst, or from the basal cells of the oral mucosa.3 These are slow-growing, locally invasive, benign neoplasm of the enamel organ - type tissue which does not undergo differentiation to the point of enamel formation.4 The cells constituting the tumor remain at the cap/bell stage of tooth development.5

Ameloblastoma is the second most common benign epithelial odontogenic tumor after odontomas.6 Based on clinicoradiographic features, histopathology, behavioral, and prognostic aspects, ameloblastomas have four variants, namely, solid multicystic ameloblastoma (SMA), unicystic, peripheral, and desmoplastic ameloblastoma.7 The first known case of ameloblastoma was reported by Cusack in the year 1827.8 The first detailed description of SMA was given by Broca in the year 1868.9 Malassez proposed the name “epithelium adamantin” or “adamantinoma” in the year 1884.10 Since enamel is not a product of this tumor, the term “adamantinoma” was considered a misnomer and was changed to “ameloblastoma” in the year 1930 by Ivey and Churchill.11,12

SMA clinically manifests as a slow-growing, locally invasive neoplasm, located intraorally showing few or no clinical signs in early stages. Gradually, it may result in facial deformity, loose teeth, pathological fracture, and pain due to secondary infection or impingement on peripheral nerves. This tumor shows a male predilection and mandible (ramus area) is affected more commonly than the maxilla. Radiographically, ameloblastomas show considerable variation and may appear as unicellular or multicellular radiolucencies (honeycomb/soap bubble appearance).12 Microscopically, the WHO defines SMA as “A polymorphic neoplasm consisting of proliferating odontogenic epithelium, which usually has a follicular or plexiform pattern, lying in a fibrous stroma.” Other uncommon patterns of SMA seen are acanthomatous, granular cell, desmoplastic, basal cell, clear cell, keratoameloblastoma (KA) and papilliferous KA, hemangiomatous, and mucous cell differentiation in SMA.7

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Sometimes, ameloblastomas show a mixed pattern of follicular and plexiform in a single tumor. However, the presentation of granular histological type along with these patterns is infrequent. We report a case of such an occasional tumor.

**Case Report**

A 27-year-old male patient reported to the Department of Oral Medicine and Radiology, Kalinga Institute of Dental Sciences, with the complaint of pain and a slow growing swelling in the lower right posterior region of the jaw since 3 months. The patient first experienced pain and swelling in the lower right back teeth region around 2 months back for which he visited a private clinic where he underwent extraction of 47, 48. The patient was then relieved of pain and swelling. Around 1½ months post-extraction, the patient again started experiencing pain and discomfort in the same region for which he visited the same private clinic and was then referred by the clinician to college for further evaluation. At the time of reporting to the college, he was suffering from dull, intermittent pain along with the presence of a swelling in the right mandibular posterior area. Past medical, personal, and family history of the patient were not contributory. General physical examination of the patient was unremarkable.

Extra oral examination of the patient revealed facial asymmetry due to the presence of a solitary, diffuse swelling on the right side of the face extending from the parasympysis to condylar area involving the angle and body of the mandible (Figure 1). The swelling was roughly ovoid in shape, measuring 5 cm × 4 cm approximately. The surface of the swelling was smooth, and margins were ill defined. No visible pulsations or secondary changes were seen. The swelling was non-tender, hard in consistency, non-reducible, and non-compressible. A solitary, non-tender, mobile right submandibular node was palpable which was firm in consistency.

On intraoral examination, a diffuse swelling was seen in the posterior aspect of the right buccal mucosa, extending along the ascending ramus of mandible to the upper right vestibular area. Wound dehiscence was seen distal to 46 (Figure 2). The swelling was firm in consistency, tender on palpation, and compressible.

Clinical findings were suggestive of odontogenic keratocyst (OKC) of the right mandible. Aspiration biopsy yielded blood tinged, thick, yellowish, cheesy material. Protein estimation of fluid revealed a value of 5.8 g/100 ml. Orthopantomograph revealed a large multilocular radiolucency in the right mandible extending from the body to condylar region (Figure 3). Incisional biopsy was performed under local anesthesia with adrenaline. On microscopic examination, the hematoxylin and eosin stained section showed ameloblastic follicles with tall columnar cells at the periphery with reversal of polarity and stellate reticulum like cells in the center undergoing cystic degeneration (Figure 4). The connective tissue stroma was fibrous in nature. Thus, a histopathological diagnosis of “follicular ameloblastoma” was given.

Hemimandibulectomy was performed (Figure 5), and reconstruction was done using iliac crest graft (Figure 6). The resected specimen was subjected to histopathological
examination showed areas of follicular variant with foci of
cystic degeneration along with areas representing plexiform
and granular variant, thereby confirming the diagnosis of
“SMA” (Figures 7-9). The patient is under follow-up without
any evidence of recurrence (Figure 10).

Discussion

Reichart and Philipsen defined SMA as “A polymorphic
neoplasm consisting of proliferating odontogenic
epithelium, usually occurring in two main patterns. In the
follicular type of growth, the tumor consists of enamel
organ like islands or follicles of epithelial cells while
in the plexiform type the epithelium forms continuous
anastomosing strands. In both types, the epithelial tumor
components are embedded in a mature, connective tissue
stroma. In general, a tumor shows one or other pattern
throughout. However, not infrequently both patterns are
present in the same tumor.”

Bachman et al. reported a case of a 28-year-old male patient
with a large ameloblastoma in the left mandible which
presented with typical radiographic features of variably sized
radiolucent loculations. Histologically, the tumor showed
plexiform and follicular mixed pattern. The tumor was treated
with partial resection of the mandible.13
Hertog et al. examined all cases of intraosseous benign ameloblastomas treated between 1970 and 2010 in a single institution to establish a possible correlation between the histopathological aspects and demographical data, clinical parameters, and treatment outcome. They found seven cases of SMA showing mixed follicular and plexiform pattern. Mean age of diagnosis was 34.1 years with a mandibular predilection. Four female and three male patients were affected. Enucleation was performed for six out of seven patients, and recurrence was seen in three cases.14

Gautam et al. reported a case of a 30-year-old male patient with unicystic ameloblastoma in the left maxillary region involving the nasal cavity and orbit. Microscopically, the tumor showed mixed plexiform and follicular pattern with superimposed infection. The patient was treated with total maxillectomy followed by prosthetic reconstruction.15

Bajpai and Pardhe reported a case of a peripheral ameloblastoma in a 44-year-old female patient in the right maxilla which histopathologically showed combined features of granular cell, plexiform, acanthomatous, follicular, and desmoplastic ameloblastoma.16

Figuerido et al. reported a case of a 20-year-old female patient with an ameloblastoma in the angle and ramus region of the mandible, which radiographically appeared as a unilocular radiolucency mimicking a dentigerous cyst or unicystic ameloblastoma but showed features of both acanthomatous and plexiform pattern of an SMA histologically. Partial right hemimandibulectomy was done for the patient.17

Literature reveals that follicular and plexiform patterns are the most commonly seen patterns in mixed histologic variants in SMA. However, our case here is unique as areas of follicular, plexiform along with less commonly encountered granular variants were seen. Histopathology of follicular area showed islands consisting of a central mass of polyhedral cells, or loosely connected angular cells resembling stellate reticulum, surrounded by a layer of columnar cells resembling inner enamel epithelium. Cystic degeneration had occurred within these follicles as a result of stromal degeneration. Plexiform area showed epithelium arranged as anastomosing strands forming a network bound by a layer of columnar cells and centrally placed stellate reticulum like cells. Granular pattern revealed extensive granular transformation of the central stellate reticulum like cells and quite often, the peripheral cells also.18,19 The granular cells were cuboidal, columnar, or rounded, and the cytoplasm was filled with acidophilic granules, which have ultrastructurally been identified as lysosomal aggregates.7,20-23 Granularity is attributed to increased apoptotic cell death and associated phagocytosis by neighboring neoplastic cells.7 The granular cells are periodic acid-Schiff positive and diastase resistant.20 These cells have also been found to be positive for antichymotrypsin, antitrypsin, keratins, acid phosphatase, and negative for vimentin, S 100, and neuron specific enolase.20,24,25

Histological variant of SMA does not seem to have any significance on clinical management or prognosis.7 Pathologists may choose not to report the histologic pattern for this reason.13 Granular cell ameloblastoma was considered to have a more aggressive behavior, which was correlated with enhanced DNA synthesis and presence of carcinoembryonic antigen within more mature cells or within cystic spaces.26 However, this concept is not accepted anymore. Current evidence suggests that the clear cell variant is more aggressive due to its locally destructive growth and ability for both nodal and distant metastases.7

The designation of conventional, unicystic, peripheral, or desmoplastic types is not to be confused with the histologic pattern since these descriptions have considerable impact on the patients treatment and prognosis.13 SMA requires radical surgical excision while unicystic ameloblastomas can be treated by conservative surgical enucleation.7 Literature indicates that
the cystic variant is less aggressive. However, if infiltration from the epithelial cyst lining into the cyst wall is demonstrated, treatment should be performed aggressively like that of SMA. Peripheral ameloblastomas should be treated conservatively. In our case, histopathology confirmed SMA and hence aggressive treatment in the form of hemimandibulectomy was done, and reconstruction was done using iliac crest graft.

Protein estimation of the fluid obtained from aspiration biopsy could guide in the diagnosis of cysts and tumors before surgery and will help a lot to determine surgical procedures for preventing the future recurrence of the cyst or tumor. According to Hamidreza et al, if the amount of soluble proteins in cyst fluid is higher than 5 g/100 ml, the cyst may be a radicular cyst, follicular cyst, fissural cyst, or tumor-like ameloblastoma, but if this amount is lower than 4 g/100 ml, it may be an OKC. In our case, the protein content was found to be 5.8 g/100 ml and hence was in accordance with the mentioned study.

According to Gardner, the characteristic slow growth of SMA is significant and it may take years before recurrence becomes evident. Recurrences may occur 5-10 years after surgery due to the persistence of the original tumor which was not resected or due to actual recurrence of new neoplastic cells. Hence, it is essential that follow-up must be done for at least 10 years and preferably more. In our case, the patient was followed up for a year, without any evidence of recurrence.

Conclusion
Factors to be considered while designing therapy of ameloblastoma include the location of lesion, extent of expansion, presence of sound uninvolved cortical bone, and the clinical and radiologic classification of tumor into SMA, unicystic, desmoplastic, or peripheral type. Ameloblastomas show a lot of histological variations; however, it does not seem to have any significance on clinical management or prognosis. Successful treatment renders an acceptable prognosis, causing minimal disfigurement. Due to its high recurrence rate, long-term follow-up for at least a period of 10-years should be done.

References