Desmoplastic Ameloblastoma (a Hybrid Variant): Report of a Case and Review of the Literature

Ismail Yazdi DMD*, Maryam Seyedmajidi DMD**, Ramin Foroughi DMD**

Desmoplastic ameloblastoma is a rare variant of ameloblastoma with special histologic and radiographic features and anatomic distribution which differs from those in the classic type of ameloblastoma. The purpose of this article is to assist the dental community in better understanding of this variation of odontogenic tumor. We present a patient with desmoplastic and conventional variant of ameloblastoma (hybrid lesion) localized in the anterior portion of the mandible. The tumor was expansive and painless. The radiographic finding showed an ill-defined mixed (radiopaque/radiolucent) lesion between roots of the lower left canine and the lateral incisor. Marginal resection was performed. Follow-up examination one year later revealed no recurrence of the tumor. Desmoplastic variant of ameloblastoma tends to infiltrate between bone trabeculae. Curettage leaves islands of the tumor within bone, which later manifest as recurrences. Therefore, for big lesions en bloc excision is the most widely used treatment to avoid recurrence.

Keywords: Ameloblastoma • anterior • desmoplastic • jaw • odontogenic tumor

Introduction

Ameloblastoma is a benign epithelial odontogenic tumor that usually exhibits aggressive behavior. It expands severely to the cortical bones and may have a high recurrence rate. It also may cause mobility and displacement of the teeth, as well as root resorption. Some researchers and clinicians have considered ameloblastoma as a low-grade malignant tumor. Malignant ameloblastomas and ameloblastic carcinomas are known variants. This tumor occurs most frequently in the posterior mandible, and usually appears as a well-demarcated unilocular or multilocular radiolucent lesion that can be associated with a crown of a nonerupted tooth. The margins of this lesion, however, often show irregular scalloping. The neoplasm extends through cancellous bone, but usually is confined by compact bone such as the inferior border and ascending ramus of the mandible. These sites seem to act as effective barriers that delay spreading of the tumor for some time. Desmoplastic ameloblastoma (DA) does not have these characteristics and is a variant that was initially documented in the literature in 1984 by Eversole et al. DA has a marked predilection to occur in the anterior regions of the jaws, particularly the maxilla. Radiographically, this type seldom suggests ameloblastoma and usually resembles to a fibro-osseous lesion because of its mixed radiolucent and radiopaque appearance. The mixed radiographic appearance is due to osseous metaplasia within the dense fibrous septa that characterizes the lesion, and it is not because of the production of a mineralized product by the tumor.

Histopathologically, ameloblastoma exhibits proliferating odontogenic epithelium within a background of fibrous stroma. The epithelium is characterized by prominent palisading of the basal cell nuclei (i.e., reverse polarization) and by vacuolization of the cytoplasm of the basal cells. Within the epithelial islands, stellate reticulum-like areas may be noted. Foci of squamous-like...
changes, granular cells, clear cells, and basaloid cells, as well as follicular, cystic, and plexiform patterns, give clues to the histologic variants of this lesion. Some of the variations in histologic patterns appear not to have significant bearing on prognosis. Desmoplastic variant is an unusual type of ameloblastoma with special histologic and radiographic features. It is also more complicated to be treated because of its tendency for penetrating the surrounding bone. Recurrence of solid type ameloblastoma may take place in the first two years, but some recur after four to five or more years following initial surgery; therefore, patients need to be followed up longer.\textsuperscript{5}

In one study, immunolocalization of transforming growth factor beta (TGF-\(\beta\)), one of the most potent local factors for modulating extracellular matrix formation, was observed in DA in order to study its participation in the stromal desmoplasia. Seven cases of DA, including a hybrid lesion, were studied together with ten cases of ordinary follicular and plexiform ameloblastomas as the control. In contrast to ordinary ameloblastomas, marked immune-expression was observed in all DAs but one. In the hybrid lesion, TGF-\(\beta\) was not expressed in the area of follicular ameloblastoma but in that of DA. These results show that TGF-\(\beta\) produced by tumor cells of DA plays a role in the desmoplastic matrix formation.\textsuperscript{6}

A unique case of DA is reported by Kawai et al. Biopsy specimens from the anterior portion of the lesion displayed typical histologic features of the desmoplastic variant of ameloblastoma. However, those from the posterior portion disclosed a large cystic formation. Oxytalan fibers were identified in the stromal tissue of the tumor, which suggested that the tumor arose from the epithelial rests of Malassez in the periodontal membrane of the related tooth.\textsuperscript{7}

Till date, 150 cases of DA have been reported in Japanese, Chinese, Malaysian, Western, African, and Indian populations.\textsuperscript{8} The first detailed report on the desmoplastic variant of ameloblastoma in the English literature was given by Eversole et al. in 1984 who called it an 'ameloblastoma with pronounced desmoplasia.'\textsuperscript{4} However, Takigawa et al.\textsuperscript{9} and Uji et al.\textsuperscript{10} were the early ones to draw attention to this unusual variant, characterized by extensive stromal desmoplasia with small compressed nests and strands of odontogenic epithelium. Radiographically, this variant exhibited no features of conventional ameloblastoma. In 2001, Philipsen et al. reviewed the 100 cases of DA reported in the literature from Japanese, Western, Chinese, Malaysian, Black, and Indian populations from 1984 through 2001.\textsuperscript{11} A further 50 cases have been reported since then.\textsuperscript{8, 12–26} The growing knowledge regarding the clinico-radiographic presentation and pathology of DAs has led to its categorization as a distinct variant of ameloblastoma in the World Health Organization (WHO) classification of odontogenic tumors in 2003. Other variants are solid multicystic ameloblastoma (SMA), unicystic ameloblastoma, and peripheral extraosseous ameloblastoma.\textsuperscript{27}

In this article, we present the clinico-pathologic features of a case of DA in Iran.

**Case Report**

A 48-year-old woman visited an oral and maxillofacial surgeon for evaluation and treatment of an expansile lesion of the anterior mandible that extended from the left canine to the left lateral incisor area. The lesion had been present for four months. The patient’s medical history revealed nothing significant.

The patient reported a history of a slowly enlarging anterior mandibular mass, without bleeding, pain, or sensory changes. The clinical examination revealed buccal cortical expansion of the anterior mandible. The intraoral examination disclosed a large, hard, nontender mass of the anterior mandible, covered by an intact overlying mucosa. No lymphadenopathy or fistulae were present. The involved teeth were vital and exhibited no mobility. Periapical radiography showed a mixed lesion of the mandible with poorly-defined borders mimicking fibro-osseous lesions (Figure 1). The differential diagnosis included focal cement-osseous dysplasia, cemento-
ossifying fibroma, and odontogenic tumors.

The oral surgeon administered a local anesthetic agent and performed an excisional biopsy by marginal resection. A piece of cream-gray elastic soft tissue with the size of 0.7×0.5×0.4 cm in formalin was received. Histologically, irregular odontogenic islands with a stretched-out 'kite-tail' appearance were seen in a dense desmoplastic stroma. Tumor elements were present between bone trabeculae. The peripheral layer of the epithelial islands and the inner core were made up of flattened cells and spindle-shaped, respectively. Odontogenic epithelium in the form of follicles, which is typical for SMA, and irregular stretched-out epithelial islands were observed in a desmoplastic background. This was categorized as 'hybrid' variant of DA (Figures 2 and 3). Collagen fibers of the stroma stained by van Gieson were demonstrated desmoplasia (Figure 4). The diagnosis was DA. The patient’s postoperative course was uneventful. Postoperative radiography and a clinical follow-up examination one year later disclosed no recurrence or residual tumor.

Discussion

DA exhibits important differences in anatomic distribution, histologic appearance, and radiographic findings compared with other types of ameloblastoma. However, age and sex distributions do not differ from those seen in patients with other types of ameloblastoma.7

Approximately half of the desmoplastic lesions are located in the maxilla, and the vast majority of them occur in the anterior or premolar portion of the jaws. In contrast unicystic or classic types of ameloblastoma are usually found in the posterior area of the mandible. Maxillary lesions are more insidious than mandibular tumors owing to the proximity of vital structures and the maxillary sinus. Also, the very thin cortical bone of the maxilla forms a weak barrier for the spread of tumors. Consequently, maxillary ameloblastomas may be able to spread earlier and more quickly than mandibular neoplasms.7

The radiographic appearance of this neoplasm usually indicates a mixed radiolucent/radiopaque lesion. Approximately half of these lesions have diffuse borders in the radiography28 and look similar to a fibro-osseous lesion or malignant tumor. The lamina dura also is involved.29 The radiographic appearance may indicate that this tumor is more aggressive than other variants of ameloblastoma.30

Waldron and El Mofty31 described the histologic appearance of DA as small ovoid islands and narrow cords of odontogenic epithelium widely separated by dense, moderately cellular, fibrous, and connective tissue. Although columnar cells with reverse polarity within the epithelial islands are present, they are not the dominant feature. Spicules of mature lamellar bone trabeculae have been reported in intimate contact with the tumor, and invasion has been

Figure 2. Odontogenic epithelium in the form of follicles typical of solid multicystic ameloblastoma and the irregular stretched-out epithelial islands and osseous metaplasia (osteoplasia) in a desmoplastic background (hematoxylin-eosin stain, ×40).

Figure 3. Irregular odontogenic islands with a stretched-out kite-tail appearance in a dense desmoplastic stroma (hematoxylin-eosin stain, ×40).

Figure 4. Collagen fibers stained by van Gieson were demonstrated desmoplasia (van Gieson stain, ×100).
demonstrated. This histologic finding may indicate the potential for local invasion, and accounts for the diffuse radiographic imaging.

DA may exhibit a more aggressive behavior than other types of ameloblastoma. Various facts about this lesion may suggest aggressiveness:

- A potential to grow to a large size;\(^3^1\)
- The common location in the maxilla that may produce an early invasion to adjacent structures;
- The diffuse radiographic appearance and the histologic finding of bone invasion.\(^3^1\)

Finally, it is almost impossible to find the exact interface of the lesion with normal bone, making it especially difficult to be treated surgically.\(^3^2\)

Even after two decades of the first report of DA, the cause for this peculiar histologic appearance is still unclear. Compared with the SMAs, various immunohistochemical studies have reported DA tumor cells as showing variable expression of S-100 protein and desmin,\(^3^3\) marked immunorepression of TGF-β,\(^3^4\) high expression of caspase-3 and Fas,\(^1^3\) decreased expression of CK19,\(^2^6\) and high expression of p63.\(^3^5\) Compared with the stroma of SMA, the desmoplastic stroma of DA has been reported to show a strong positive reaction for collagen type VI (ruling out the scar tissue),\(^3^6\) immunonegativity for tenascin, and strong immunopositive reaction for fibronectin and type I collagen.\(^3^7\)

Desmoplasia of the stromal connective tissue in DA can be argued to be a maturation of SMA, as similar dense collagenization is seen during maturation of longstanding tumors. This argument can be supported by the existence of 'hybrid' tumors, wherein the follicles were present in a desmoplastic background. But the lesser frequency of DA in the posterior mandible compared with SMA is then unanswered. Firstly, it is probable that the location of the tumor can influence the maturity of the lesion and, hence, the tumors in the anterior jaws may mature sooner than those occurring in the posterior mandible. Of significance in this context is the higher frequency of SMA in the anterior jaws in Blacks, indicating the possible racial influence in the site predilection of ameloblastomas. It is also possible that the majority of these ameloblastomas could turn out to desmoplastic variants if a careful histologic review is carried out. Secondly, DA might not actually be a rare entity. Many hybrid lesions may have been misclassified, since the presence of typical ameloblastic islands in some areas could have warranted a diagnosis of SMA.\(^8\)

The biologic behavior of DA is still not fully understood. This lesion will remain an enigma until researchers pursue more definitive tumor analysis techniques and aggressive follow-up and tracking in many more cases.

References

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