Granular cell – Peripheral ameloblastoma: a rare variant

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Abstract Ameloblastoma is an epithelial odontogenic tumour of the jaw and exhibits diverse microscopic patterns which occurs either singly or in combination with other patterns. Peripheral ameloblastoma is a rare odontogenic soft tissue tumor, derived from epithelial and/or mesenchymal elements being part of the tooth-forming apparatus. The lesions responsible for approximately 1% to 5% of all cases of ameloblastoma affecting alveolar mucosa and gingiva occurring mainly, in the middle age. This article describes a case of peripheral ameloblastoma affecting a 35-year-old female. The lesion was located in the right buccal space. The occurrence and pathogenesis of peripheral ameloblastomas in general, are reviewed. The tumour was excised and no recurrence has been observed after twenty four months of surgery.

Keywords Granular cell ameloblastoma · Peripheral ameloblastoma

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Introduction

Ameloblastomas of all types comprise 1–2% of all cysts and tumors occurring in the jaws. It is prevalent in the 4th decade of life, but is seen in the age range from 6 months to 76 years.

Granular cell ameloblastoma is a rare variant of ameloblastoma that histopathologically has numerous large granular cells. These cells usually form the central mass of the epithelial islands and cords [1]. This type of ameloblastoma account for only 5% of the lesions. Recent electron microscopic studies of the granular cells have shown the presence of abundant lysosomes. This gives the cells their granular appearance and the function of these lysosomes has not yet been established.

Ameloblastoma is a tumor that frequently reoccurs after treatment. The rate of recurrence ranges from 4.5% for en bloc resection to 54.1% for conservative therapy. The recurrence rate of the granular cell variant was 73% in the Armed Forces Institute of Pathology (AFIP) series for all modes of therapy combined [2].

Many studies have shown that ameloblastoma may on rare occasions metastasize. The most common site for tumor dissemination is the lungs. Most

patients with pulmonary metastasis have undergone multiple surgical procedures because of incomplete surgical excision at the initial operation [2].

The peripheral ameloblastoma is histologically indistinguishable from the typical central or intraosseous ameloblastoma but is different in that it occurs in the soft tissue overlying alveolar bone but separate from it. An origin from either surface epithelium or remnants of the dental lamina is favored [1].

Granular cell ameloblastoma is a variant of ameloblastoma that histopathologically has numerous large eosinophilic granular cells. These cells usually form the central mass of the epithelial tumor islands and cords. The periphery of the islands consists of non-granular tall columnar cells. The granular cell ameloblastoma is rich in lysosomal granules. In granular cell ameloblastoma there is marked transformation of the cytoplasm, usually of stellate reticulum like cells, so that it takes a very coarse, granular, eosinophilic appearance. Granular cell variety of ameloblastoma appears to be an aggressive lesion with a marked proclivity for recurrence. In addition several cases of this type has been reported, as metastasizing [2].

A case of an peripheral granular cell ameloblastoma is reported.

Case report

A 35-year-old female reported to our hospital with a history of swelling over right side of face for past 5–6 months. History of slowly progressing intraoral swelling of right buccal space with no apparent distress. She had moderate right facial swelling but no facial paralysis, paresthesia, or anesthesia and no palpable regional lymphadenopathy. Patient gave a history of undergoing an operative procedure (Hemimandiblectomy) for ameloblastoma of right mandible 4 years back.

Extra oral examination revealed: Facial asymmetry with well defined swelling on the right side of face. The swelling extended from corner of mouth to the angle of mandible. Colour of skin over the swelling was normal. Shape - ovoid. Size - 2x4 cm. Surface - smooth. No pulsation or impulse on coughing.

On extraoral palpation, a firm, freely movable mass could be felt, measuring approximately 3.0 cm in diameter. It appeared medial to the buccinator muscle.

On local examination: Size, shape, extent was confirmed. Surface was smooth and firm. Edges merging into the surrounding tissues. Non tender, non pulsatile, no fixity to overlying skin or

Fig. 1 Preoperative View

Fig. 2 Granular cell ameloblastoma growing in the typical island-like pattern. There are large, pink staining cells in the center of the tumor islands (hematoxylin-eosin, original magnification 5).

underlying structures and it was non-compressible.

Intra oral examination revealed: Moderate orodental hygiene and right lower edentulous area. Right buccal mucosal swelling of size 4 x 3 x 4 cm was seen. Swelling was firm, non tender and extending upto retromolar area (Fig. 1).

Investigations: Routine biochemical and hematological investigations were within normal limits. Panoramic view skiagram revealed absence of right side of mandible from bicuspid onwards. No

bony infiltration observed. CT scan showed well defined soft tissue density mass lesion of 5 x 3 x 4.5 x 3.5 cm over right buccal space. Areas of punctate calcification and smooth indentation over lateral wall of right maxillary sinus. Superiorly - involvement of right infratemporal fossa was observed. X-ray chest was normal and showed no signs of metastasis.

Differential diagnosis included recurrence of:

1. Ameloblastoma
2. Fibroma
3. Lipoma
4. Ossifying fibroma
5. Granular cell ameloblastoma

Histopathological report of incisional biopsy taken from right buccal space reported densely fibrous connective tissue stroma with patchy cellularity. Few single endothelially lined dilated blood vessels are seen. At one end odontogenic foci are seen which are either in the form of follicles or in plexiform pattern. Many stellate reticulum like cells appear as large oval / round shaped cells with granular cytoplasm. These cells at places are seen forming the clumps. Features were suggestive of peripheral ameloblastoma of granular cell variety (Fig. 2).

Management: The case was managed by intraoral surgical removal of the tumour mass under general anaesthesia. The mass was dissected free with relative ease from the buccinator muscle (Fig. 3). A fibrous capsule separated the mass from the surrounding tissues.

The patient tolerated the procedure well. Twenty four months after surgery there was minimal trismus, normal function of the right parotid gland, and no sign of clinical recurrence of the lesion. The follow-up protocol included periodic chest skiagrams to rule out any metastasis.

Discussion

Peripheral Ameloblastoma (PA) is a rare odontogenic soft tissue tumor that accounts for 1–5% for all ameloblastomas [3]. Kuru first reported PA in 1911 [5]. Peripheral ameloblastoma is typically a slow, benign, single, sessile, symptomatic lesion. Histologically, this lesion is identical to the classic intraosseous ameloblastoma but appears exclusively in the oral mucosa.

A review of the English literature disclosed 66 well documented cases of PA. Nauta et al. [6] had reviewed 52 cases that had been previously published. Since then Redman et al. [7] reviewed and reported four additional cases. Seven cases were reported by Guraol and Burkes [8], one case by Califano et al. [9] two cases by Orsini et al. [10] and one case by El-Hakim and El-Khashab [11] Kishore Shetty [12] have presented three additional cases in his paper for a total of 70 cases. Zhu et al. have published and reviewed a total of 43 cases of PA in the Japanese literature between 1967 and 1995.

The peripheral ameloblastoma is a lesion of adulthood with approximately 52% of patients ranging from 40 to 60 years of age. Radiographic findings were usually negative, although in some cases, saucerization of the underlying bone was evident. Certain cases showed continuity of the neoplasm with the overlying epithelium. Of the eighteen cases that had follow-up information, four cases had recurrences within 2 months, 9 months, 18 months, and 8 years. One case involved a recurrent lesion noted 5 years after initial treatment. The recurrences were all in the group treated by excision of the lesion. Other modalities of treatment included enbloc resections, curettage, and cryosurgery plus radiation [5]. Despite the apparent non-aggressive course and low recurrence rate of peripheral

Fig. 3(A) Intra-OP View showing tumour bed

Fig. 3(B) Specimen

Fig. 3(C) Postoperative View

ameloblastoma, long-term follow-up is absolutely necessary, as evidenced by the case presented here. Although rare in frequency, the possibility of recurrence and association with, or the progression of these tumours into dysplasias and malignancies cannot be overlooked. Recurrences have been reported in the literature to occur as many as 8 years after initial presentation and, therefore, it would be prudent to follow involved patients indefinitely.

The oral mucosa can be thought of as an extension of the skin. Just as there are skin appendages, so there are teeth. Lever and Schaumburg-Lever [3] believe that the basal cell carcinoma, the least differentiated of the skin appendage neoplasms, arises from the pluripotent cells that form continuously during life and have the potential to form hair and sebaceous and apocrine structures. The ameloblastoma, the least differentiated of the epithelial odontogenic neoplasms, can conceptually arise from similar pluripotent cells of the basal layer of oral epithelium or their derivatives, namely, dental lamina rests (glands of Serres). These epithelial vestiges of odontogenesis can usually be found within the maxilla and mandible near teeth, are associated with developmental cysts, and can be found also in soft tissue overlying the tooth-bearing areas of the jaws. In this location, they are the suggested origin for a host of developmental odontogenic cysts and neoplasms. Therefore, it is not surprising that peripheral ameloblastomas and/or basal cell carcinomas of the oral cavity arise on mucosa overlying the alveolar processes.

However, it is difficult to explain the origin of a peripheral ameloblastoma that arises in the buccal mucosa on the basis of dental lamina rest proliferation, since such rests must occur rarely in such a location. This may explain the extremely rare incidence of peripheral ameloblastoma in the buccal mucosa. Another possibility lies in the rests being not so much of dental lamina origin as remnants of the vestibular lamina, which is involved in the formation of the buccal sulcus and mucosa. Although the presence of ectopic glands of Serres cannot be ruled out, a more likely explanation is origin from pluripotent cells in the basal cell layer of the mucosal epithelium.

Immunohistochemistry

The granular cell ameloblastoma are S-100 protein and α -1-anti-trypsin positive. They

are negative for Vimentin, NSE[Neuro-specific enolase], EMA[Epithelial membrane antigen], CMA[Common muscle actin/ muscle specific actin] and Prekeratin [13].

Ultrastructural features

No true desmosomes or other epithelial ultrastructural features were seen in the study conducted by Mirchandani R et al. but the granular cells have shown to be of epithelial derivation [13]. They reported that in the cases of granular cell ameloblastoma there was pseudo epitheliomatous hyperplasia of the overlying mucosa. The theory of ectomesenchyme of neural crest origin having a persisting influence on the odontogenic apparatus and basal layer of surface epithelium in adult life may account for a change on the surface and centrally within the mandible [13].

Immunoperoxidase studies revealed a heterogeneous expression along mesenchymal and neural lines in all cases except for the congenital epulis of the newborn. In the latter there was only mesenchymal expression, consistent with most previous reports. Although they used a larger panel of markers than in previous immunohistochemical studies, their results were in concurrence with previously and recently reported studies. In spite of using two epithelial markers, the ultrastructurally proven granular cells with epithelial features did not show prekeratin or EMA reactivity. Most investigators believe that the granular cell is either of Schwann cell origin or a derivative of an undifferentiated mesenchymal cell. 1,3,4–14–16P previous ultrastructural studies on granular cell ameloblastoma have shown the granular cells to be of epithelial origin.

Because both the odontogenic epithelium and Schwann cell are neural crest derivatives, it could be postulated that all granular cells are derived from a common precursor cell of neural crest origin. If so, one must account for the different phenotypic expressions. This may possibly be explained by a common precursor cell differentiating to a certain level epithelial/mesenchymal/neurogenic). This phenomenon may alter the phenotypic expression [13].

The differential diagnosis of this lesion includes the odontogenic gingival epithelial hamartoma, the peripheral odontogenic fibroma, and a salivary gland neoplasm. Pindborg, Kramer, Shafer and co-workers

believe the first two are related lesions. They are predominantly mesenchymal processes with abundant fibrous elements and various amounts of calcified material and odontogenic epithelium [14]. In our patient it could be a case of seeding of the original central mandibular ameloblastoma. We unfortunately do not have the biopsy report of the original tumor.

Conclusion

Early diagnosis and prompt surgical treatment in peripheral granular cell ameloblastoma is of prime importance. Malignant transformation and metastasis to lungs should be ruled out in cases of peripheral granular cell ameloblastoma. Whether these lesions should be separated from the peripheral ameloblastomas of the attached soft tissues and be called basal cell carcinomas is a matter of semantics. The origin of both lesions in the oral cavity is either from the pluripotent cells of the basal cell layer or from native or ectopic epithelial rests. Because dental lamina rests must occur infrequently in the buccal mucosa, if at all, it is likely that a peripheral ameloblastoma arising in this location would most probably originate from pluripotent cells in the overlying basal layer.

Complete local excision is the treatment of choice. Although the innocuous nature of this lesion has been stressed, on reviewing nineteen cases with follow-up information, the recurrence rate is 26%. Patients should be kept under periodic observation because of reports of recurrences even up to 8 years after initial treatment.

References

1. Yamamoto G, Yoshitake K, Tada K, Yoshida K, Yokota H, Fukuda Y, Ishida T (1989) Granular cell ameloblastoma: a rare variant. *Int J Oral Maxillofac Surg* 18(3): 140–141
2. Cranin AN, Bennett J, Solomon M, Quarcoo S (1987) Massive Granular cell ameloblastoma with metastasis: Report of a case. *J Oral Maxillofac Surg* 45(9): 800–804
3. Shafer WG, Hine MK, Levy BM (1983) A textbook of oral pathology, ed. 4, Philadelphia, W. B. Saunders Co. 276–285
4. Neville BW, Damm DD, Allen CM, Bouquot JE (1995) *Oral &*

- maxillofacial pathology. Pennsylvania: W.B. Saunders Company p 519
5. Wettan HL, Patella PA, Freedman PD (2001) Peripheral ameloblastoma: Review of the literature and report of recurrence as severe dysplasia. *J Oral Maxfac Surg* 59(7): 811–815
 6. Nauta JM, Panders AK, Schoots CJ, Vermey A, Roodenburg JL (1992) Peripheral ameloblastoma. A case report and review of literature. *Int J Oral Maxillofac Surg* 21(4): 40–44
 7. Redman RS, Keegan BP, Spector CJ, Patterson RH (1994) Peripheral ameloblastoma with unusual mitotic activity and conflicting evidence regarding histogenesis. *J Oral Maxillofac Surg* 52(2): 192–197
 8. Gurol M, Burkes EJ Jr (1995) Peripheral ameloblastoma. *J Periodontol* 66(12): 1065–1068
 - [9] Califano L, Maremonti P, Boscaino A, De Rosa G, Giardino C (1996) Peripheral ameloblastoma: report of a case with malignant aspect. *Br J Oral Maxillofac Surg* 34(3): 240–242
 10. Orsini G, Fioroni M, Rubini C, Piattelli A (2000) Peripheral ameloblastoma: a report of 2 cases. *J Periodontol* 71(7): 1174–1176
 11. El-Hakim IE, El-Khashab MM (2000) Peripheral and mural ameloblastoma in the mandibular canine region of a 13 year old boy. *J Oral Maxillofac Surg* 58(10): 1150–1154
 12. Kishore Shetty (2005) Aetiology from surface epithelium? Case report and review of literature. *Oral Oncology Extra* 41: 211–215
 13. Mirchandani R, Sciubba JJ, Mir R (1989) Granular cell lesions of the jaws and oral cavity: A clinicopathologic, immunohistochemical and ultrastructural study. *J Oral Maxillofac Surg* 47(12): 1248–1255
 14. Kessler HP (2004) Intraosseous ameloblastoma, *Oral Maxillofac Surg Clin North Am* 16(3): 309–322

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