Case report

Ameloblastic carcinoma of the mandible

Purmal K1, Alam MK2, Pohchi A3, Rahman SA4

Abstract:
Ameloblastic carcinoma is a highly malignant tumour and requires aggressive treatment. This case report describes an aggressive ameloblastic carcinoma that infiltrated the mandible. Mandibulectomy with right functional radical neck dissection and left supra omohyoid dissection was followed by primary reconstruction with a single free vascularised fibula flap. The post-operative course was uneventful. The 2 year regular follow up revealed no signs of recurrent tumour or metastasis. Future reporting of this rare condition is encouraged in lieu of limited information in its clinical course and prognosis.

Keywords: ameloblastic carcinoma; mandibulectomy; radical neck dissection; malignant tumour; metastasis

Introduction
Ameloblastoma is the most common epithelial odontogenic tumour, representing 1% of all oral neoplasia with incidence of 80% in the mandible and 20% in the maxilla. This benign neoplasm is locally invasive and shows considerable tendency to recur, but rarely behaves aggressively or shows metastatic dissemination. Malignant ameloblastoma on the other hand has a typical benign histological appearance but gives rise to nodal or pulmonary metastasis. Both the primary and metastatic lesions retain their benign histologic appearances. Therefore the ability of ameloblastoma to metastasize cannot be predicted by the histology alone.

Ameloblastic carcinoma which is different entity form malignant ameloblastoma is a rare malignant odontogenic tumour. In fact in 2005, The World Health Organization have reclassified odontogenictumours and defined it as anodontogenic malignancy that combines the histological features of ameloblastoma with cytologicatypia, even in the absence of metastases. It may develop de no vo (primary type) or by malignant transformation of an ameloblastoma (secondary type) with a distinction between intraosseous and periphery ameloblastoma. Ameloblastic carcinoma shows many histologic...
Ameloblastic carcinoma features of malignancy like dysplasia, increased mitosis, and infiltration of surrounding tissues. However, the common features of ameloblastoma like having epithelium in which the basal cells contain columnar or palisaded cells that have a tendency for the nucleus to move from the basement membrane to the opposing end of the cell (reverse polarization) is still present. The epithelium is also known to in the form of islands, strands and medullary arrangements against a background stroma of fibrous connective tissue (follicular pattern) or the epithelium proliferates in a mesh arrangement (plexiform pattern). Clinical presentation of this lesion is the rapid growth, causing pain and may even perforate the cortex. Although rare, these lesions have been known to metastasize mostly to the lung or regional lymph nodes.

Case Report
A 53 year old Malay fisherman came to the School of Dental Sciences University Sains Malaysia with complaints of swelling in the lower jaw. He had first noticed the swelling about 6 months ago. The swelling has been increasing in size with bilateral lower lip parathesia. It was also associated with pain and trismus.

His significant medical history includes pulmonary tuberculosis diagnosed one year ago. He has since completed the regime of anti-tuberculosis drugs and currently on regular follow-up with the respiratory team.

Clinical examination revealed a fit man with no signs and symptoms elsewhere. There was a bony hard swelling from the right ramus to the left ramus. The size of the swelling was 6cm by 5 cm. The overlying skin was normal and not fixed to the lesion (Figure 1). There was reduced mouth opening about 3cm. On the neck the right submandibular lymph nodes (Level I) and right upper cervical lymph nodes (Level II) were palpable. The size of both the lymph nodes was 1cm by 1cm. The lymph nodes were not tender or fixed to the overlying skin. The bony lesion had perforated the oral mucosa of the right side which is highly suggestive of malignancy (Figure 2 and 3).

Intraoral examination showed a partial edentulous arch with mobile (grade 3) teeth. Bony expansion was evident bilaterally.

Orthopantomogram radiograph showed a multilocular osteolytic lesion with distinct margin extending from right to the left angle of mandible (Figure 4). There is resorption of root of lower first left molar in the mandible. No lesion detected in the maxilla. There is multiple retain roots and vertical bone loss around the teeth present.

The posterior anterior chest radiograph shows left upper lobe fibrotic changes (Figure 5).

CT scans of from the base of skull to the abdomen

Figure 2. Right side of the lesion.

Figure 3. Left side of the lesion.

Figure 4. Orthopantomogram radiograph showing extension of the lesion.
Purmal K, Alam MK, Pohchi A, Rahman SA showed the lesion is confined to the mandible. CT guided percutaneous lung biopsy was done. It showed no ameloblastic carcinoma cells on the left upper lobe. Fine needle aspiration cytology of the palpable lymph nodes was done. That showed ameloblastic cells infiltration. TNM staging T4N2bM0

Based on these findings, the diagnosis was ameloblastic carcinoma and the differential diagnosis was intraosseous carcinoma, squamous odontogenic tumour, calcifying epithelial odontogenic tumour, salivary gland neoplasia or other metastatic carcinoma to the jaws from other primary locations.

**Histopathology**

Incisional biopsy revealed the tumour was composed of islands and sheets of odontogenic epithelium exhibiting basal cell palisading and hypercellular stellate reticulum like cells having vacuolated nuclei with prominent nucleoli. The periphery of cells nests exhibited a columnar morphology. These cells contained pleomorphic nuclei with mitotic figures. Squamous metaplasia together with infiltrating well-differented squamous cell carcinoma islands were present in these areas (Figure 6 a-d)

**Treatment**

Surgical excision (2cm clear margin) with primary reconstruction of the defect was the mode of treatment chosen for this patient (Figure 7). Tracheostomy and reconstruction with osteomyocutaneous free fibula flap was planned. The mandible was resected from the right body to the left body preserving both condyles. All the upper teeth which had poor prognosis and retain roots were also extracted. Right functional neck dissection and left supraomohyoid dissection was done.

**Figure 6.** Histopathology: a. Sheets of odontogenic epithelium with palisading basal cell and hypercellular stellate reticulum like cells with vacuolated nuclei. b. Higher magnification showing cells containing pleomorphic nuclei with mitotic figures. c. Squamous cell metaplasia with infiltrating squamous cell carcinoma. d. Higher magnification showing tumour infiltrating the muscle tissues.
A 23 cm length fibula graft with overlying skin was harvested from the right leg. The fibula graft was fixed with the mandible with reconstruction plates and titanium screws. The vessels were anastomosed to the facial artery and veins while the skin from the dorsum of the thigh was used to provide the intraoral cover. Nasogastric tube was inserted to facilitate feeding (Figure 8). The graft and donor site healed without any complications (Figure 9). Post-operative Orthopanthomogram radiograph shows two reconstruction plate with the fibula graft (Figure 10). The resected mandible and lymph nodes were sent for histopathological study. The results confirmed our diagnosis of ameloblastic carcinoma with 2 cm clear margin of the lesion and the remaining lymph nodes free from any lesions. The patient was sent for radiotherapy after 4 weeks to eliminate any residual cancer cells. The dose given was 60 Gy over a 6 weeks period with radiation 5 days a week. Post radiation shows area of fibrosis on the right and left neck area (Figure 11 and 12). Noted wound breakdown on left side of the neck (Figure 12). The breakdown was managed by daily dressing and cleaning with chlorhexidine solution weekly. The wound healed uneventfully. He also complained about the hair growth intraorally which was trimmed regularly. Retrospectively a skin graft from non-hair bearing area might have avoided this problem. After six months, the patient was fitted with upper and lower full dentures. He is able to lead a reasonable normal life after the rehabilitation. After 2 years our patient continues to remain free of local, regional or distant metastasis as he remains on active follow-up with periodic radiographic follow up (Figure 13).

Discussion

Our patient was diagnosed as having pulmonary tuberculosis one year before seeing us. As a consequence, the lesion seen in the chest radiograph (Figure 5) and the palpable lymph node could be also due to the metastasis or pulmonary tuberculosis. Datta et al\(^8\) have mentioned that ameloblastic carcinoma is
an aggressive neoplasm that is locally invasive and
can spread to regional lymph nodes or distant sites
such as lungs and bones. Fine needle aspiration
cytology confirmed the palpable lymph nodes were
infiltrated with ameloblastic cells and biopsy of the
lungs showed no ameloblastic cells in the lungs.
Even though this case demonstrated unusual spread
within short period time (6 months), we had to delay
the treatment because of the patient’s pulmonary
tuberculosis. We waited until his sputum tests were
negative for 3 consecutive weeks before doing the
operation to reduce the chances of cross infection.
The diagnosis criteria of ameloblastic carcinoma
from ameloblastoma or malignant ameloblastoma
are based on cytologic atypia and increased mitotic
activity. Most ameloblastic carcinoma arise de
novo and less than 1% of ameloblastoma undergo
malignant transformation. Some studies have
recorded widespread metastasis to the lung, bones
through lymphatics and bloodstream. These
lesions should be distinguished from metastatic
ameloblastoma which is defined as a histological
benign appearing ameloblastoma with metastasis.
From the differential diagnosis, intraosseous
carcinoma is difficult to differentiate radiographically,
histologically or clinically from ameloblastic
carcinoma. In fact the intraosseous carcinoma may
represent a less differentiated non keratinizing form
of ameloblastic carcinoma both being deprived from
odontogenic epithelial remnants. Nonetheless, typical
features of ameloblastic differentiation which would
justify a diagnosis of ameloblastic carcinoma are
usually lacking in intraosseous carcinoma. Squamous
odontogenic tumour is composed of islands of squamous cells and epithelial odontogenic
tumour contains sheets of epithelial and amylloid like
material with concentric ring calcification which can
differentiate it from ameloblastic carcinoma. Salivary
gland neoplasm or secondary from other sites may
invade the jaws and can be differentiate from the
history and clinical symptoms. Marsuzaki et al have
reported that immunohistochemistry study of
ameloblastic carcinoma will reveal high positive rates
of P53 and Ki67 to aid in the diagnosis of this lesion.
Chromosomal imbalances in ameloblastomatous
losses in chromosom 22 and 10 have been reported.

Figure 10. Post surgery OPG with two reconstruction plate and the fibula graft.

Figure 11. Post radiation right side of the neck.

Figure 12. Left side of the neck post radiation. Wound breakdown noted at angle of the mandible.
In additional to that aneuploidy is more common in ameloblastic carcinoma and may predict its malignant potential.18

In our patient, the histology showed features of malignancy like higher mitotic activity, ell atypia, hyperchromatic nuclear, invasion of bone and muscles. Clinically ameloblastoma have a slow growth with 27 months as the mean duration before any symptoms.19 This case shows growth in only 6 months. Moreover there is perforation of the cortex of mandible intraorally. Ameloblastoma hardly perforates the cortex unless left undetected for a very long time. Pain and parathesia is also not a common finding in ameloblastoma.19 From the demographics, the mean age for ameloblastic carcinoma is 52, male to female ratio is 2: 1 and 66% of the times the lesion is located in the mandible.7 This information is consistent with our patient presented here. Most of the cases of ameloblastic carcinoma in the literature was treated with extensive surgery with margins of 2-3 cm. Radiotherapy was used after the surgery for cases with close resection margin, extracapsular or perineural invasion.6, 20, 21 Chemotherapy did not show any promising results.6 22 Radiotherapy alone is also not recommended given its intraosseous location.23 Recently Perera et al. have reported on the use of gamma knife stereotatic radiosurgery in the management of recurrent ameloblastic carcinoma lesion. The authors showed promising results for recurrent lesions after 2 years of post-resection. Based on the above information, we decided surgical option with concomitant radiotherapy. We managed to preserve the condyle in this patient. Keeping the mandibular condyle allows the patient to preserve the temporo- mandibular joint which gives better mobility to the rest of the jaws and also diminishes post-op pain.

The task of restoring the mandibular defect is a challenging problem for surgeons after ablation of the tumour. Microvascular techniques to transfer vascularized bone to the head and neck region have been successfully applied to solve the problem of various segmental mandibular defects.24, 25 In our case, almost the entire mandible was successfully reconstructed with a vascularised fibula flap.

Local recurrence have been reported between 5 to 151 months.20, 26 Distant metastasis has also been reported as early as 4 months and as late as 47 months after surgery.20, 27 Therefore long term follow-up is mandatory to detect the late recurrence or metastasis. The 5 and 10 year survival rates were 72.9% and 56.8% respectively.21 It is important that people should be fortified to immediately report to a surgeon whenever they see any unusual swelling any discomfort. Management should also include the awareness of the people of their responsibilities regarding their own health, and not wait for the swelling to grow and cause great discomfort and difficulty to themselves in future.28 Nonetheless, it is generally known that there were significant association between histological subtype and recurrence outcome and between treatment and recurrence of ameloblastoma.29

Conclusion

Ameloblastoma shows a spectrum of histology and biologic behaviour ranging from benignity at one end to malignancy at the other end. Cases of ameloblastoma should thus be carefully analysed to detect subtle changes in the histology that may predict its aggressive behaviour. We have reported a rare case of primary ameloblastic carcinoma of the mandible in a 53 year old man. Aggressive wide excision and radiotherapy with primary reconstruction has given a successful outcome. However long term follow up is necessary to detect the late recurrence or metastasis.

Conflict of interest: None declared.
References