A RARE CASE OF MALIGNANT GIANT CELL TUMOR OF THE HYOID BONE TREATED WITH DENOSUMAB

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Abstract

Giant cell tumor of the bone (GCTB) is a benign bone tumor where it typically presents in the long bones, mainly at the knee regions. Rarely, benign GCTB can undergo sarcomatous malignant transformation (MGCTB). We report a case of a 63-year-old lady who presented with a swelling at the right side of the neck associated with dysphagia and voice changes. A contrast-enhanced computed tomography scan revealed a large mass seen arising from the hyoid bone with local mass effect and airway compression. However, no distant metastasis was seen. Multiple biopsies performed on the patient with the histopathology reports concluded as MGCTB. The tumor was unresectable. Therefore, the patient was treated with denosumab. She showed encouraging improvement post-treatment. We are highlighting this case report in view of the rare site of the disease and the use of denosumab in unresectable tumor with good response to therapy.

Keywords: Giant Cell Tumor, Malignant Transformation, Hyoid Bone, Denosumab

Introduction

Giant cell tumor of bone (GCTB) is a locally aggressive benign bone tumor that typically occurs in young adults. Giant cell tumor of bone constitutes approximately 20% of benign bone tumors and accounts for approximately 5% of primary bone tumors (1). Giant cell tumor of bone mainly occurs in the long bones, with most cases involving the knees (50-65%) (2). Atypical locations of GCTB are seen in the spines, hands, feet, patella, talus, skull, and facial bones. Atypical sites of GCTB are commonly associated with multicentric GCTB (3). Giant cell tumor of bone of the hyoid bone is extremely rare, with only three cases of GCTB of the hyoid bone (Table 1) have ever been reported before in our literature review of Google Scholar (4-6). We describe this disease's rare occurrence in the hyoid bone and discuss its imaging features and management strategies, with the highlight of the denosumab treatment in the unresectable cases of GCTB.

Case report

A 63-year-old lady with underlying hypertension and uterine fibroid presented to Hospital Raja Perempuan Zainab II Kota Bharu with a five-month history of right neck swelling. The swelling was increasing in size, leading to progressive dysphagia and voice changes. There was no odynophagia, shortness of breath, noisy breathing, or any episode of aspiration. There were also no accompanying constitutional symptoms. Physical examination revealed a firm mass palpable at the right cheek extending to the right submandibular region measuring approximately 11 x

Table 1: Lists of previous cases of giant cell tumor of the hyoid bone ever reported in literature

Number	Year	Journal	Authors and title
1.	1999	The Journal of Laryngology and Otology	Commins DJ, O'Malley S, Athanasou NA, Jalloh S. Giant cell tumour of the hyoid–first reported case. J Laryngol Otol. 1999;113(6):566-8.
2.	2000	British Journal of Oral and Maxillofacial Surgery	Iype EM, Abraham EK, Kumar K, Pandey M, Prabhakar J, Ahamed MI, et al. Giant cell tumour of hyoid bone: case report. Br J Oral Maxillofac Surg. 2000;38(6):610-1.
3.	2016	Indian J Otolaryngol Head Neck Surgery	Singh HP, Kumar S, Aga P, Kumar M, Usmani SA, Agarwal SP. Huge osteoclastoma of hyoid bone: a case report. Indian J Otolaryngol Head Neck Surg. 2016;68(1):123-5.

10 cm (anteroposterior x width). The mass was not tender on palpation, there were no skin changes and no trismus noted. Sub centimeter cervical lymph nodes were present at right level II and III. A contrast-enhanced computed tomography (CECT) scan showed a large heterogeneously enhancing mass at the anterior aspect of the right neck measuring 5.8 x 8.5 x 8.7 cm (anteroposterior x width x craniocaudal), arising from the hyoid bone. The mass was seen extending to the midline and left side of the neck region (Figure 1). The mass was also seen extending superiorly involving the floor of mouth, displacing the right genioglossus muscle medially. Posteromedially, the mass extended into the laryngeal wall with obliteration of the right side of the vocal cord, with narrowing of the airway from the hypopharynx until the level of subglottic region. Inferiorly, the mass was seen extending until the right supraclavicular region at the C6/C7 level. The lesion eroded the hyoid bone and right thyroid cartilage. No distant metastasis was seen. The patient underwent direct laryngoscopy and transoral biopsy, with the flexible nasopharyngolaryngoscopy revealing a mass occupying the right vallecula and base of tongue, pushing the supraglottis with the epiglottis partially visualized. Both vocal and false cords were not visualized. The lesion was noted to be friable and bled easily during examination. In view of the significant airway narrowing, patient underwent tracheostomy and subsequently transoral biopsy was performed. Intraoperative findings revealed a huge mass involving the base of tongue and hypopharynx, pushing the supraglottis and glottis regions causing airway obstruction. The histopathology result revealed a diagnosis of a malignant giant cell tumor. Considering that there was no previous giant cell tumor at this region, the mass was taken as primary malignant giant cell tumor. Due to the extensive local extension of the mass, its friable nature and the high risk of hemorrhage noted during the biopsy, together with a high possibility of the patient having complicated functional disabilities post-surgery, a comprehensive conference was held involving multidisciplinary doctors, patient, and her relatives. It was concluded that the tumor was unresectable and the patient was started on subcutaneous denosumab injection at 120 mg every 4 weeks for 1 year, starting from 2017 until mid 2019. Upon follow up, the mass has clinically reduced in size, voice hoarseness resolved, no shortness of breath and patient was able to tolerate orally, without significant adverse reaction to denosumab. After denosumab was stopped at the end of 2019, patient complaint that she was unable to tolerate orally associated with odynophagia. She was only able to swallow soft food and complaint of muffled voice. The managing otorhinolaryngology and oncology team decided to continue with denosumab therapy starting from end of 2019 till today. During the patient's recent follow-up, after approximately 3 years on denosumab, follow up CT showed marginal and internal sclerosis with significant mass size reduction of approximately 30%, analyzed manually by the reporting radiologist (Figure 2), with no distant metastasis in keeping with partial treatment response to treatment.

Discussion

Giant cell tumor of bone of the head and neck region are rare, with an occurrence of approximately 2% of all GCTBs. The most common sites are sphenoid, ethmoid, and temporal bones. Purely neck GCTB are extremely rare. The differential diagnosis for the neck GCTB includes giant cell reparative granuloma, brown tumor of hyperparathyroidism, osteoblastoma, chondroblastoma, aneurysmal bone cyst, non-ossifying fibroma, benign fibrous histiocytoma, and osteosarcoma with abundant giant cells. The differentiation based on imaging alone is difficult. The diagnosis can be confirmed from the histopathology result.

Malignant transformation of GCTB (MGCTB) is uncommon and estimated to be approximately 2-9% of the GCTB cases (1). Palmerini *et al.* suggested that MGCTB occurrs when the conventional GCTB undergoes a sarcomatous transformation into a malignant tumor (osteosarcoma, fibrosarcoma, or undifferentiated pleomorphic sarcoma) (7). Malignant transformation of GCTB is further characterized into two subgroups: primary MGCTB and secondary MGCTB. Primary MGCTB is diagnosed when the malignant cells are found at juxtaposition to the benign GCTB or intermixed within it at the initial presentation. Secondary MGCTB is described as the presence of

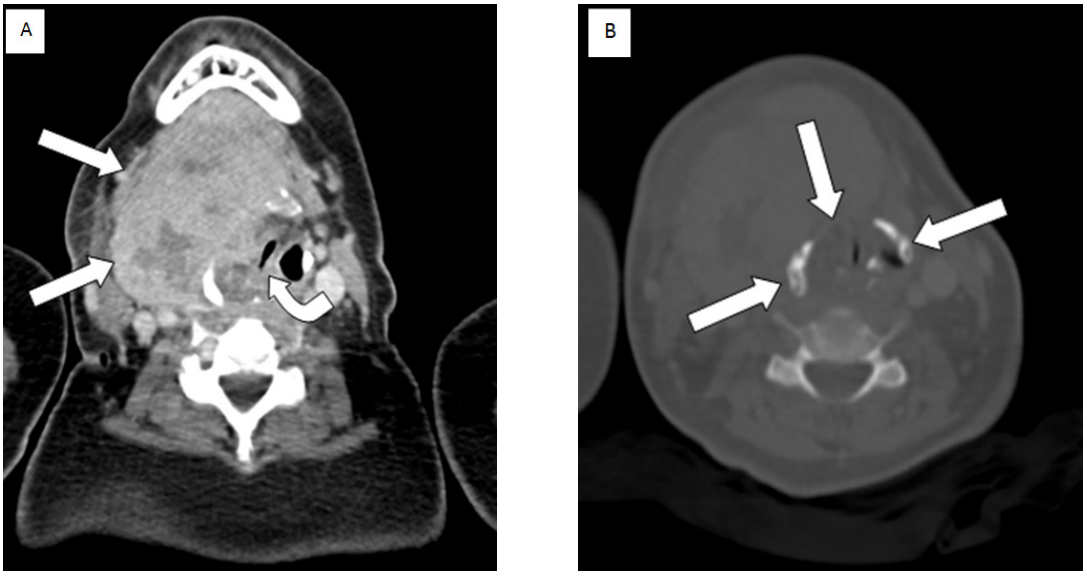

Figure 1: Pre-treatment CECT (axial plane) of the neck in soft tissue window (A) and bone window (B). A: A large heterogeneously enhancing mass (white arrows) seen arising from the right anterior aspect of the neck extending posteromedially crossing the midline to the left side with multiple non-enhancing areas representing necrotic regions. The mass exerted a mass effect onto the hypopharynx, causing airway compression (curved arrow). B: The hyoid bone is eroded and expanded (white arrows)

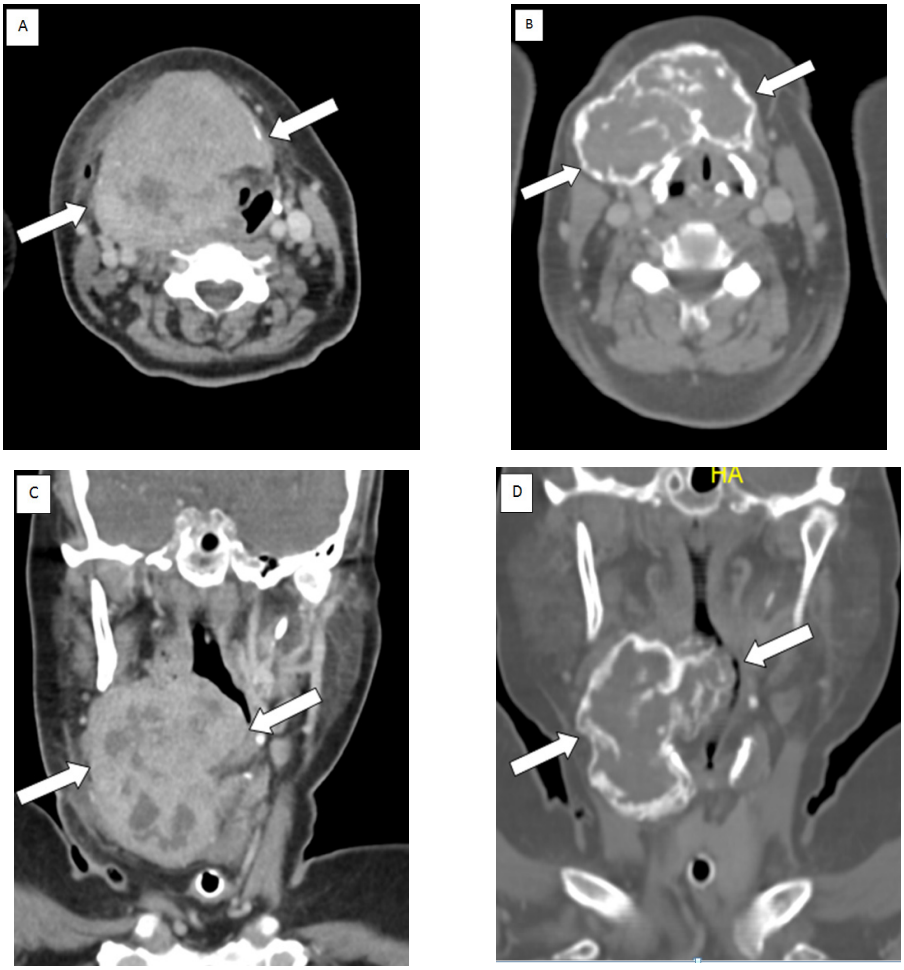

Figure 2: Follow up CECT of the head and neck (in axial and coronal planes) taken in 2016 (A and C) and in 2020 (B and D), 3 years post-treatment with denosumab. Overall features are in keeping with partial treatment response. Noted presence of tracheostomy in the coronal image in 2016 and 2020 in view of airway narrowing. A and C: Large heterogeneously enhancing mass occupying the right lower neck with necrotic components and mass effect to the oropharynx and hypopharynx. B: Marginal and internal sclerosis with significant size reduction and improving mass effect on the airway

malignant cells at previously benign GCTB sites post-surgery, post-radiotherapy, or both (8). In a recent study involving 2315 GCTB patients, the overall incidence of MGCTB constitutes 1.6% of primary MGCTB and 2.4% of secondary MGCTB. Transformation of GCTB into MGCTB is associated with poor prognosis (2). This is due to tumor recurrence post-treatment and the development of distant metastasis. The most common site for distant metastasis is the lung (1). A review has shown that the recurrence rate of benign GCTB and MGCTB is estimated at 9% and 20%, respectively. The 5-year survival of MGCTB patients is 87%, with a 16% total mortality rate (7).

In imaging, MGCTB has no specific characteristic to differentiate it from benign GCTB (3). Palmerini *et al.* in 2019 also highlighted that it is difficult to differentiate GCTB and MGCTB due to lack of specific malignant features, complicated by aggressive features that can also be seen in the benign lesion (7). Plain radiograph and contrast-enhanced magnetic resonance imaging (MRI) are the standard imaging modalities used to diagnose GCTB (2). On a plain radiograph, GCTB is typically seen as a well-defined lytic bone lesion with non-sclerotic margins, located at the eccentric location and usually extends to the subchondral regions. Magnetic resonance imaging characteristics of GCTB usually display low to intermediate signal in T1 weighted images, a high signal in T2 weighted images and enhances post gadolinium. Around 10-14% of the cases show fluid levels within the tumor suggestive of aneurysmal bone cyst component (3). In general, computed tomography imaging (CT) of GCTB typically show purely osteolytic lesion with a geographical bony destruction. Contrast enhanced CT is also used in patients with GCTB / MGCTB to rule out distant metastasis and disease follow-up. According to Van Langevelde in 2020, post denosumab CT demonstrates tumor matrix with marginal sclerosis. Hounsfield Units (HU) is used in CT to quantify tumor density, indicating the tumor response (11). On the other hand, ultrasound is used mainly to assist in the tissue biopsy.

The mainstay treatment for MGCTB is surgery (9). The surgical approach for MGCTB is either en bloc resection or curettage. Curettage has a higher recurrence rate, up to 65%, while en bloc resection has a recurrence rate of 16% (3). In cases of unresectable tumors or when surgery is not feasible due to post-surgical morbidity/functional disability, denosumab has been the ultimate choice of treatment (3). Denosumab is a human monoclonal antibody that prevents RANK/RANKL interactions, which stops the osteoclastic activity in GCTB. Park *et al*. in 2016 mentioned that denosumab was used in a phase-2 trial involving 169 GCTB patients, where 96% of the cases showed improvement of the disease (8). This is further supported by another study by Mavrogenis *et al*. in 2017. In this phase-2 study, 100 GCTB patients where surgery was planned at initial diagnosis were treated with denosumab. Only 26 patients proceeded with the operation, while the other 74 patients showed positive improvement post-denosumab and did not require surgery (3). The other form of treatment for GCTB is radiotherapy (10).

Conclusion

Giant cell tumor of the bone of the hyoid bone with malignant transformation is extremely rare. It should be considered as a differential diagnosis among locally aggressive tumors in the neck, especially when it involves a bone. Malignant transformation of the disease needs to be elicited via imaging and biopsy for prompt treatment initiation. Although the primary treatment of MGCTB is surgery, due to the unresectable nature of the disease, our patient was successfully treated with denosumab.

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Competing interests

The authors declare that there is no conflict of interest.

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Informed consent

Verbal and written informed consent were obtained from the patient's next of kin for inclusion in this case report. Research and ethics committee approval for this case report is not a requirement according to Medical Research and Ethics Committee and Institute of Clinical Research Malaysia.

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