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Multiple Myeloma of the Thyroid Cartilage: A Case Report and Review of Literature

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ABSTRACT

Multiple myeloma is the most common primary malignancy of the bone. Although it has a host of systemic manifestations, it rarely presents as a mass involving the thyroid cartilage. Through this study, we aim to describe one such patient: A 60-year-old man- who came to us with the chief complaint of rapidly expanding neck swelling and dysphagia. During the course of workup, patient sustained a fracture of the humeral shaft. It was subsequently revealed that he had a mass lesion originating from the thyroid cartilage. Needle aspiration cytology from the latter depicted myeloma cells as well as plasma blasts. He also had multiple osteolytic lesions in his skull and mandible. Serum protein electrophoresis showed characteristic M band in the globulin region. Based on the above findings, a diagnosis of multiple myeloma was made and patient advised chemotherapy which he refused. At the last follow up, he was alive and showed no further deterioration of the existing lesions.

Even though rare, multiple myeloma must be kept as one of the differentials in all elderly males presenting with a neck mass. Timely and appropriate treatment with radiation/ chemotherapy can lead to disease remission.

Keywords: Multiple myeloma, Thyroid cartilage, Neck swelling, Osteolytic lesions

INTRODUCTION

Plasma cell neoplasms (PCN) result from excessive proliferation of abnormal plasma cells in the bone marrow. Multiple Myeloma (MM), solitary plasmacytoma of bone (SPB) and extramedullary plasmacytoma (EMP) are all subtypes of PCN [1].

MM is the most common primary bony malignancy, usually seen in elderly males above 50 years of age [2]. The hallmark feature of MM is the presence of myeloma or 'M' protein in the serum along with excessive secretion of Immunoglobulins (Igs), which are responsible for the systemic manifestations of the disease. On the other hand, SPB is a lesion in a single bone without the systemic complications seen in MM i.e. hypercalcemia, renal insufficiency, anaemia and amyloidosis [3]. When a similar pathology occurs outside the bone, it is called an EMP [4].

Classically, MM appears as diffused, osteolytic lesions involving the skeletal system [3]. However, atypical presentations of MM involving the thyroid cartilage have also been reported [5-22].

We hereby present the case of a 60-year-old male who presented to us with a rapidly progressing neck swelling, which turned out to be MM invading the thyroid cartilage.

CASE REPORT

A 60-year-old male presented to the surgical out-patient clinic with chief complaints of left-sided neck swelling for the past seven days, which was insidious in onset but rapidly progressive, causing him to have dysphagia for the past 3 days (more for solids than liquids). He also gave a history of non-specific bony pains associated with low backache for the past one year. Constitutional symptoms like anorexia and weight-loss were present. Severe pallor was noted. Clinical examination of the neck showed a non-tender, 3 x 2 cm ovoid

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swelling which was firm in consistency, had a smooth surface with well-defined margins and was located approximately 1 cm lateral to midline and 3cms above suprasternal notch **(Figure 1A)**. It was mobile with deglutition. Auscultation of the swelling did not reveal any audible bruit. The patient was admitted for further evaluation and management. His hematological parameters revealed severe anemia (Hb-3.6) with thrombocytopenia (Platelet count-80,000) and reduced total white blood cell (WBC) count (pancytopenia). Peripheral smear showed presence of normocytic normochromic along with microcytic hypochromic cells. He was transfused 3 units of packed red blood cells and adequately resuscitated. During the course of admission, the patient had a fall from bed following which he developed swelling and tenderness over the left arm, without any distal neurological or vascular impairment. X rays showed a fracture of the left proximal shaft of humerus (Figure 1b), which was graded according to the Mirel's criteria as we suspected it to be pathological. The score obtained was 6 and hence, fracture was managed conservatively with a U-slab. Our two chief differentials at this point were metastatic carcinoma of the thyroid and multiple myeloma. To differentiate between the two and arrive at a definitive diagnosis, a number of tests were performed.

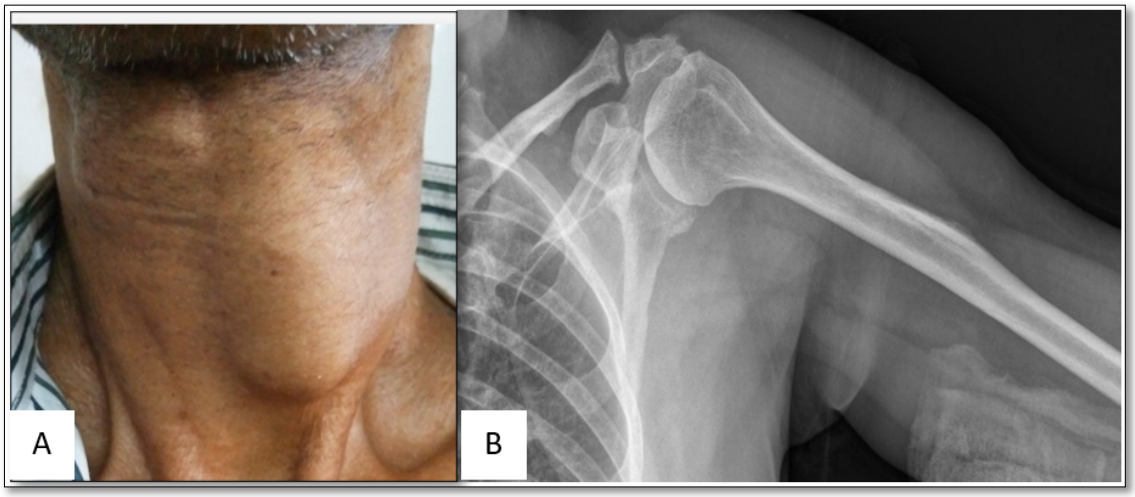

Figure 1. (A) 3×2 cm. firm ovoid swelling, mobile with deglutition anterior to Sternocleidomastoid on the left side of the neck**.** (B) Pathological proximal shaft humerus fracture sustained by the patient.

With the exception of serum uric acid (10.9 mg/dl), serum thyroid stimulating hormone (TSH) (10.75 microIU/ml) and erythrocyte sedimentation rate (ESR) (120 mm/h by Westergen method), remaining blood investigations were all within normal limits, including serum calcium, creatinine and alkaline phosphatase (ALP). Ultrasonography (USG) of the suspicious nodule showed a mass abutting the left thyroid cartilage and guided needle aspiration cytology showed cellular smears with dispersed cell population comprising of plasma blasts, plasma cells and interspersed chondrocytes and normal thyroid follicular epithelial cells in proteinaceous background with a possibility of myeloma. Skeletal survey - X-ray and Computerized Tomography (CT) of the patient revealed diffuse osteolytic lesions in the mandible, skull and the clavicle **(Figure 2B)**. The CECT scan of head and neck region showed a homogenously enhancing mass lesion in the visceral space along the left thyroid cartilage lamina, causing destruction and extending into the larynx **(Figure 2A)**.

Serum protein immune-electrophoresis was carried out which was suggestive of Monoclonal gammopathy ("M" spike seen in gamma globulin region) (Figure 3). Free lambda (light) chain level was also elevated, being 336mg/L (reference range 8.3-27 mg/L), along with a raised free kappa/lambda ratio (0.09). Bone marrow biopsy was inconclusive with plasma cells accounting for 3% of the total cell population.

After co-relating patient's clinical, radiological, laboratory as well as histopathological features, a final diagnosis of MM involving the thyroid cartilage with pathological shaft humerus. Patient was planned for a Bortezomib and Lenalidomide based chemotherapy and concomitant radiotherapy for a better 5-year survival, which he refused. At 3 months follow-up, there was no further deterioration or increase in size of the existing lesions and the fracture had united.

DISCUSSION

The mean age of presentation of MM is about 60 years which is a decade younger than that of SPB and EMP [1]. The condition is frequently preceded by a stage of monoclonal gammopathy of undetermined significance (MGUS) [23].

The defining feature of MM is clonal bone marrow plasma cell count ≥10% or biopsy-proven bony or extramedullary plasmacytoma and any one or more of the following myeloma defining events [3]:

1) Evidence of end organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically:

a) Hypercalcaemia: Serum calcium > 0.25 mmol/L (>1 mg/dL) higher than the upper limit of normal or > 2.75 mmol/L (>11 mg/dL)

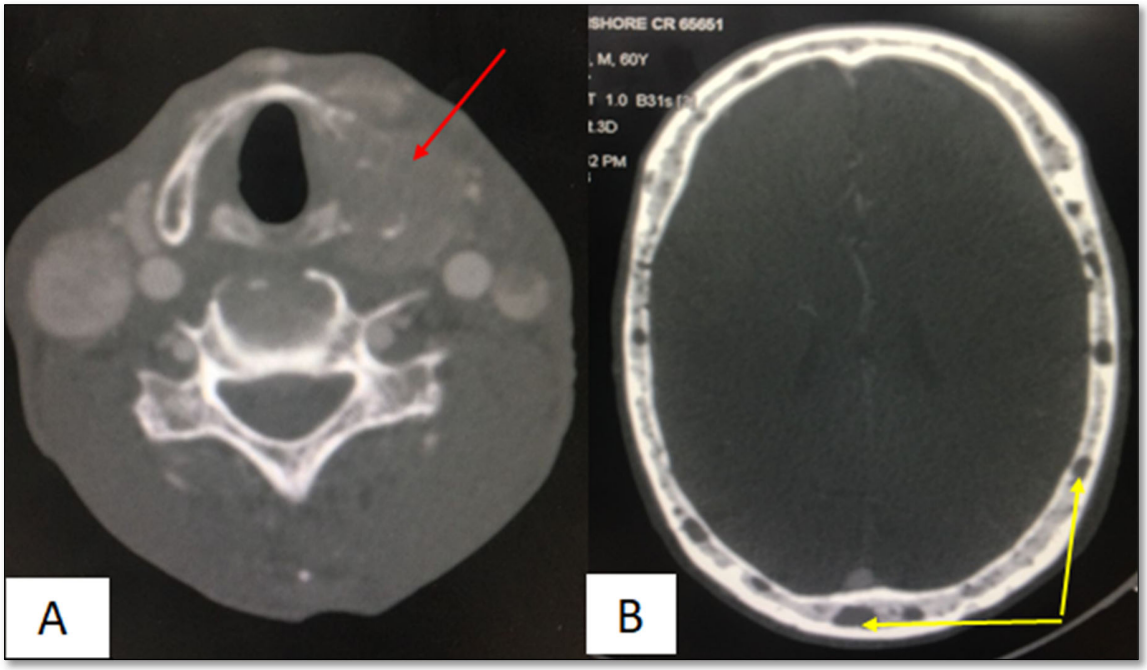

Figure 2. (A) CECT neck showing homogenously enhancing mass invading left thyroid cartilage (RED ARROW). (B) Multiple lytic lesions seen in the skull (YELLOW ARROWS).

b) Renal insufficiency: creatinine clearance <40 mL per min or serum creatinine >177 μmol/L (>2 mg/dL)

c) Anaemia: haemoglobin value of >20 g/L below the lower limit of normal, or a haemoglobin value <100 g/L

d) Bone lesions: one or more osteolytic lesions on skeletal radiography

• Any one or more of the following biomarkers of malignancy:

a) Clonal bone marrow plasma cell percentage ≥60%
b) Involved: uninvolved serum free light chain (of immunoglobulins) ratio ≥100:1
c) >1 focal lesion on Magnetic Resonance Imaging (MRI) studies

Clonality should be established by showing κ/λ-light-chain restriction on flow cytometry, immunohistochemistry, or immunofluorescence. Bone marrow plasma cell percentage should preferably be estimated from a core biopsy specimen. If bone marrow has less than 10% clonal plasma cells, more than one bone lesion is required to distinguish MM from solitary plasmacytoma with minimal marrow involvement [3].

Extramedullary tumours form a very small percentage of PCNs and 80 to 90% occur in the head and neck region. Larynx is involved in 6 to 8% of such cases [21]. MM involving the thyroid cartilage is exceedingly rare [7,9,22].

The presence of cartilaginous involvement in MM is explained by two theories-direct invasions by an adjacent plasmacytoma or by the osseus transformation theory which suggests that the cartilage may undergo osseus transformation with a proper marrow space and this may be the site of origin of the MM [22]. Osseus metaplasia has been proven in cricoid and thyroid cartilages and hence could prove to be the major mechanism for MM arising at such sites but due to the extreme rarity of this condition, it is very difficult to say with certainty. Overall, MM has a very poor prognosis with 5-year survival of 18% and mean survival of 2 years [1].

The differential diagnosis in an elderly male presenting with a neck swelling can be varied. Since, in our case, it was a recent onset swelling which was rapidly progressive in size along with movement on deglutition, a probable diagnosis of solitary thyroid nodule most likely malignant was thought of as the first differential. Further imaging helped us identify thyroid cartilage as the tissue of origin of the swelling. Fine needle aspiration cytology (FNAC), bone marrow aspirate and a serum M band helped us make the final diagnosis. The lack of classical findings on bone marrow aspirate must be borne in mind and other findings such as bony involvement must be thoroughly evaluated. All elderly patients presenting with pathological fractures warrant further assessment with

serum ALP, prostate specific antigen and carcino-embryonic antigen levels to rule out obvious metastasis.

A summary of the findings of similar studies and how they compare with ours is given in **Table 1**.

Table 1. A brief summary of all cases of multiple myeloma involving the thyroid cartilage.

S.no.	Author/Year	AGE/SEX	Clinical Features	PAST H/O of MM	Laboratory & Radiographic Workup	Management	Outcome & Follow-up
1.	van Dyke (1995) [10]	62/M	c/o hoarseness and an anteriorly located neck mass.	H/O MM (diagnosed 4 years ago). Patient taking chemotherapy. Now in relapse.	-CBC/ Serum Ca^{2+}/ KFT: Normal. - Serum/urine protein electrophoresis: M band seen (IgG). -XR/CT: OL lesions seen in ribs initially. Now multiple OL lesions seen on skeletal survey. -BM biopsy: Normocellular initially with monoclonal kappa cell population. BM abnormality increased.	Initially chemotherapy (Doxorubicin, Vincristine and Dexamethasone). Now RT 40 Gy given.	Marked remission and improvement again after 6 months.
2.	Saad (2001) [14]	79/M	c/o pain upon swallowing. Previous h/o back pain.	H/O MM. On remission for 2 years following RT and chemotherapy (Melphalan and Cortisone)	-Serum electrophoresis: Abnormal protein spike. - XR/CT: OL lesions seen in the skull, pelvis, vertebrae as well as long bones.	Patient refused any further treatment at the time of relapse.	Patient expired after 6 months.
3.	Aslan (2002) [6]	70/M	c/o hoarseness of voice with a sense of neck fullness	Nil	-CBC/ S. Ca^{2+}/KFT: Normal. - Serum/ Urine protein electrophoresis: Normal. -Normal serum levels of IgG, IgA, IgM. - XR/CT: No OL lesions. - BM aspirate: Hypercellular with 10% plasma cell infiltration.	Debulking/curettage of the lesion followed by RT (5000cGy).	No further deterioration at 6 months.
4.	Gross (2002) [12]	50/M	c/o hoarseness, feeling of suffocation and enlarging anterior neck mass.	Nil	-Serum electrophoresis: increased IgG (k chain). -Urinalysis: Negative. -XR/CT: Multiple OL lesions noted in the skull and the left femur. -BM biopsy: Normocellular with monoclonal plasma cells seen (5-20%/field).	RT (1500cGy which was increased to 3000 cGy) & chemotherapy (Adriamycin, Vincristine and Dexamethasone. Melphalan added later)	Patient expired several months later.
5.	Patlas (2002) [8]	NR	NR	NR	NR	NR	NR
6.	Sosna (2002) [21]	54/M	c/o increasing hoarseness and difficulty in breathing associated with neck swelling.	Nil	-CBC: Neutropenia and thrombocytopenia. Serum Ca^{2+} normal. - Increased serum IgG (k chain). -Urine test negative for light chain Igs. - XR/CT: OL lesions seen in the skull as well as long bones. - BM aspirate: Monoclonal plasma cell infiltration into bone	RT (1500cGy which was increased to 3600 cGy) & chemotherapy (Adriamycin, Vincristine and Dexamethasone. Melphalan added later)	Patient expired.

					marrow seen (<10%/smear).		
7.	Dispenza (2007) [18]	69/F	c/o hoarseness and progressive dysphagia	K/C/O MGUS	-CBC: Anaemia and leucopenia. -Serum/Urine electrophoresis: increased monoclonal IgA. -BM aspirate: 20% monoclonal plasma cell infiltration.	Chemotherapy (Adriamycin, Vincristine and Dexamethasone).	At 1 year there is no further progression of the disease.
8.	Shimada (2007) [9]	72/M	C/o cervical spine fracture. Neck lesion detected incidentally on CT.	Nil	-CBC/ S. Ca^{2+}/KFT: Normal. - Serum electrophoresis: increased IgG (k chain). - Urine negative for Bence-Jones proteins. - XR/CT: OL lesions limited only to the cervical spine. -BM aspirate: Normocellular with 1.2% plasma cell infiltration.	50 Gy and 30 Gy given to the neck as well as cervical spine. Posterior fixation of the cervical injury was concomitantly performed.	No additional lesions seen after 3 years.
9.	Kumar (2011) [20]	63/M	c/o increasing hoarseness, neck pain, dysphagia and difficulty in breathing.	H/O MM treated with chemotherapy (Adriamycin, Vincristine and Dexamethasone) & ASCT.	-CBC: Pancytopenia - Serum electrophoresis: mildly increased IgG. No M-band. - XR/CT: OL lesions seen in the sternum. Left lobe of thyroid gland involved - BM aspirate: Hypocellular with absence of plasma cells.	Surgical intervention: En-bloc resection of the lesion.	Patient died after 5 weeks due to disease progression.
10.	Kalina (2012) [22]	60/M	c/o hoarseness of voice.	H/O plasmacytoma (later on diagnosed as an indolent MM) of maxillary sinus	- Serum electrophoresis: increased IgG (k chain). - XR/CT: OL lesions seen axial and appendicular skeleton. -BM aspirate: Pan myeloid hyperplasia with aggregates of atypical plasma cells.	-Maxillary sinus plasmacytoma was surgically resected. Recurrence managed with RT. - MM treated with high dose Melphalan and Autologous bone-marrow transplant.	NR
11.	Mitchell (2013) [7]	63/M	c/o hoarseness and expanding midline neck mass.	Previously diagnosed as MM. Now presents as an extramedullary relapse of MM.	-Diagnosis proven by biopsy.	Chemotherapy (Lenalidomide) with EBRT to the larynx.	Patient currently in remission.
12.	Adam (2014) [17]	58/M 58/M 64/M	NR	Nil	-Serum & urine protein electrophoresis: Presence of M band. - Increased IgG (k chain) levels. - XR/CT: Multiple OL lesions in the skeletal system. - BM biopsy: Normocellular initially with monoclonal kappa cell population.	NR	NR

13.	Oral (2015) [5]	43/M	c/o pain and swelling left mid-thigh. Thyroid cartilage lesion detected incidentally.	Nil	PET CT: OL lesions detected in the left scapula as well as the left iliac bone.	Pathological facture fixed with IMN. RT given locally.	NR
14.	Singh (2017) [11]	57/M	c/o hoarseness and mobile right-sided neck swelling.	Nil	-CBC/ S. Ca^{2+}/KFT: Normal. - Serum protein electrophoresis: 2 M bands detected- Ig G and Ig A. Elevated serum levels of kappa and lambda chains. -Urine protein electrophoresis: No M-band. - XR/CT: Multiple OL lesions in the skull and ribs. Right lobe of thyroid gland also involved. - BM aspirate: Normocellular with 10% plasma cell infiltration.	Chemotherapy (Bortezomib, Cyclophosphamide & Dexamethasone)	NR
15.	Gochhait (2018) [15]	57/M	c/o pain and swelling of left arm with rapidly increasing thyroid swelling.	Nil	-Serum Ca^{+2} levels raised. KFT normal. - Serum protein electrophoresis: Presence of M band in IgG region. - Increased IgG (k chain) levels. - XR/CT: Multiple OL lesions detected in the skull, B/L scapular spines, B/L clavicles as well as B/L humeri. Left lobe of thyroid gland involved. -BM Aspirate: Plasma cell count of 9% s/o plasma cell dyscrasia.	Chemotherapy (Bortezomib & Dexamethasone).	Patient lost to follow-up after 5 months.
16.	Kashyap (2018) [16]	54/M	c/o right shoulder swelling. Thyroid lesion detected incidentally.	Nil	-CBC: normocytic hypochromic anaemia with deranged renal parameters and normal serum Ca^{2+}. -Serum electrophoresis: M spike seen i.e. increased IgG (k chain). -PET CT: Multiple lytic areas depicting increased activity in cervical spine, ribs and manubrium sterni as well as right scapula. Right lobe of thyroid gland also involved. -BM aspirate: 60% plasma cell infiltration.	Chemotherapy (Bortezomib, Lenalidomide and Dexamethasone) with RT to the vertebral lesions.	Complete remission after 4 months.

17.	Tandon (2018) [19]	50/M	c/o hoarseness and h/o back pain with associated mobile right-sided neck swelling.	H/O MM diagnosed 2 years ago. Patient was given chemotherapy but has relapsed now.	- Serum electrophoresis: M band detected. - XR/CT: Diffuse OL lesions in the cervical and dorsal vertebrae. OL lesions also seen in the medial end of right clavicle as well as B/L humeral heads. Right lobe of thyroid gland also involved. - BM biopsy: >30% plasma cell infiltration.	Chemotherapy	Patient currently in remission.
18.	Dogan (2019) [13]	55/M	c/o dyspnoea as well as hoarseness	NR	-PET CT: Multiple OL lesions seen. -Diagnosis confirmed on biopsy	Systemic treatment (details NR)	NR
19.	Present Study (2020)	60/M	C/o dysphagia with rapidly increasing left sided neck swelling. Associated with pathological fracture left humerus.	Nil	-CBC: Pancytopenia. Normal serum Ca^{2+} and KFTs. - Serum protein electrophoresis: M- band detected in the IgG region. -Serum light chain (lambda) levels increased. -Urinalysis: Normal -XR/CT: Multiple OL lesions detected in the skull, mandible and clavicle. - BM biopsy: Monoclonal plasma cells accounted for 3% of the total cell population.	Patient advised chemotherapy but he refused. Humerus fracture managed conservatively with U-slab.	At 3 months, no deterioration or increase in size of the lesions.

MM: Multiple Myeloma; CT: Computerized Tomography; PET: Positron Emission Tomography; CBC: Complete Blood Count; KFT: Kidney Function Tests; RT: RT; BM: Bone marrow; IMN: Intra-medullary Nail; ASCT: Autologous Stem-cell transplant; OL: Osteolytic; Ig: Immunoglobulins; MGUS: Monoclonal gammopathy of undetermined significance; EBRT: External beam radiation therapy

CONCLUSION

The differential diagnosis of a midline neck swelling can be varied and a broader perspective must be kept while investigating such cases. MM involving the head and neck cartilages is a rare diagnosis which must be kept in mind while investigating such cases, especially in the elderly age group and a high index of suspicion regarding the same can help avoid misdiagnosis and patient mismanagement.

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None

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