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**Seyyed Mohammadreza Mortazavizadeh, Yasaman Ayoughi,
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Case Report: A 54-year-old man was admitted with chief complain of bone pain, clinical investigation revealed, lytic bone lesions and infiltration of plasma cells in bone marrow and patient with diagnosis of multiple myeloma received chemotherapy, he was in partial remission, but nine months later a solitary nodule was founded in his thyroid, with high levels of calcitonin and fine needle aspiration (FNA) reported the medullary thyroid carcinoma, after total thyroidectomy which confirmed this cancer the patient recovered and now he is followed- up for these cancers.

Conclusion: Diagnosis of secondary cancer is important because: first to distinguish secondary malignancy from metastatic cancer and then try to investigate the etiology of this association.

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CASE REPORT

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Keywords: Medullary thyroid cancer, Multiple Myeloma, Secondary malignancy, Thyroid carcinoma

How to cite this article

Mortazavizadeh SM, Ayoughi Y, Binesh F, Karbalaieian M. Medullary thyroid carcinoma associated with multiple myeloma: A case report. Int J Case Rep Images 2016;7(7):458–462.

Article ID: Z01201607CR10669SM

doi:10.5348/ijcri-201681-CR-10669

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Received: 20 December 2015

Accepted: 08 March 2016

Published: 01 July 2016

INTRODUCTION

Multiple myeloma (MM) is a hematologic cancer which usually manifested by bone pain, hypercalcemia, anemia, lytic bone lesions and monoclonal gammopathy. The co-existence multiple myeloma and another cancer such as renal cell carcinoma, lung, gastric carcinoma, colon, prostate, breast, bladder, uterus, and liver have been reported severally in literature [1–5], but medullary thyroid carcinoma (MTC) as a second malignancy with multiple myeloma is an extremely rare case which seems has not been reported before, here we are presenting a case with these two types of cancer.

CASE REPORT

A 54-year-old male with diabetes history presented on 17th November 2013 with complaints of severe bone pain on his shoulder and vomiting. The physical examination was unremarkable but a primary photo X-ray in emergency room showed abnormal lytic lesions in the bone and pathologic fracture in clavicle (Figure 1), so he was referred to the oncologist with high suspicious for a malignancy, the primary laboratory investigation revealed ESR:77 mm/h, the skull X-ray showed multiple punched out lesions (Figure 2)

And the whole body scan reported multiple irregular and abnormal uptake in anterior and posterior rib-skull-right shoulder and highly suggestive multiple bone metastasis (Figure 3) in the next laboratory investigation yielded the following findings: β_2 -microglobulin :9.9(1.1-2.4) mg /L, α_2 :17.6 (7.1-11.8) g/L, in his urine electrophoresis, Lambda light chain was 88 (5.9)mg/L, (detailed results laboratory tests are given in Table 1), the aspiration of bone marrow found 25% plasma cells which some were multiple nucleus and others looking plasma blast (detailed reports of bone marrow aspiration is given in Table 2) and biopsy of bone marrow reported that hematopoietic cells have been replaced by proliferation of plasma cells and finally with diagnosis of the multiple myeloma, chemotherapy was initiated for patient with the regiment of VAD (vincristine, adriablastina, , dexamethasone) and zometa.

After four cycles chemotherapy, once more bone marrow aspiration revealed incomplete response to cure with 15 % plasma cells and evaluation of free lambda light chain was 124 (up to 5.9) mg/L so the chemotherapy changed and continued with velzomib, and once more bone marrow aspiration showed mild plasmacytosis 7% and the patient reached a partial remission, about after nine months later, the laboratory tests changed and ESR elevated for second time, during investigation we found a palpable solitary nodule in the thyroid of patient, the thyroid function test showed TSH: 2.6 mIU/L, T4: 8.5 μ g/dL and T3:142 ng/dL and ultrasonography of thyroid reported a well-defined hypoechoic solitary nodule in middle of right lobe of thyroid with numerous and small zones of calcification with no adenopathy in neck and suggested for fine needle aspiration (FNA) because it was suspicious for malignancy, in that time some differential diagnosis were made: metastasis of multiple myeloma to thyroid, or primary thyroid malignancy metastasis to bone and our first diagnosis of multiple myeloma could be rejected by this assumption and the last one diagnosis was thyroid malignancy as a secondary cancer. Therefore, the patient underwent FNA which reported medullary thyroid carcinoma with the laboratory test investigation of calcitonin: 268 ng/L, CEA: 78 μ g/L, ESR: 63 mm/h and with these evidences the probability of metastatic of primary multiple myeloma ruled out. And with diagnosis of MTC, patient was referred to surgeon and after

total thyroidectomy, the histopathology after surgery confirmed medullary thyroid carcinoma (Figure 4).

After surgery the patient was recovered and the laboratory tests return to nearly normal levels. The patient remained in good health and he is followed-up for these malignancies.

DISCUSSION

Second primary cancer is one of the effective prognostic factors among cancer survivors and it is estimated to be the sixth most common form of malignancy in the world [6], although secondary solid neoplasms in patients with multiple myeloma are rare, but some studies have reported the increasing risk of that. In a study by Stegeman et al., multiple myeloma and solid tumor co-existence was found to be 3% [7] and Kyle et al. reported that, in 1027 patients diagnosed with multiple myeloma, the proportion of secondary hematologic malignancy was 0.7% and the proportion secondary solid malignancy was 1.9% [8]. As we mentioned earlier, malignancies synchronized with

Figure 1: Lytic bone lesions and pathologic fracture in shoulder.

Figure 2: Numerous punched lesions in skull.

Figure 3: Bone scan revealed multiple metastasis.

multiple myeloma have been reported before [1–5]. But it was not included medullary thyroid carcinoma which occurs extremely rare, to our knowledge there are no prior reports of this case. The etiology of this correlation in our case is not clear but according to some hypothesis, secondary malignancies associated with MM can be because of behaviors (such as smoking, harmful levels of alcohol consumption and poor diet), inherited susceptibilities and/or the medical treatment

Figure 4: Tumor cells with circle nucleus and granular cytoplasm and there are amount of eosinophilic amorphous between them (H&E stain, x200).

Table 1: Laboratory results of the patients

		Protein fractions (g/L)	
White blood cell	8600 mm ³	Albumin	54.4 9
Hemoglobin	13.9 g/dL	α 1	4.6
Platelet	282000 mm ³	α 2	17.6
ESR	77 mm/h	β 1	4.7
BUN	10 mg/dL	β 2	4.5
Creatinine	1 mg/dL	γ	14.2
LDH	408 U/L		
Alkaline Phosphatase	279 U/L		
SGPT	15 U/L		
SGOT	20 U/L		
Total Bilirubin	1.1 mg/dL		
β 2 microglobulin	9.9 mg/L		
IgG	1577 mg/dL		
IgM	81.6 mg/dL		
IgA	108 mg/dL		

ESR: erythrocyte sedimentation rate, BUN: blood urea nitrogen, LDH: lactate dehydrogenase, SGPT: serum glutamate-pyruvate transaminase, SGOT: serum glutamic oxaloacetic transaminase. Ig: Immunoglobulin

Table 2: Bone marrow biopsy results

Cell count in bone marrow (%)	First time (BMA) Before starting chemotherapy	Second time(BMA) After four cycle chemotherapy	Third time (BMA) After changing chemotherapy to velzomib
Blast	4	4	3
Promyelocyte	7	7	9
Metamyelocyte	8	1	6
Myelocyte	6	3	11
Band cell	12	3	4
Neutrophil	11	17	17
Eosinophil	2	5	3
Plasma cell	25	15	7
Erythroid cells different	14	46	35
	Megakaryocytes sporadically seen	Megakaryocytes sporadically seen	Megakaryocytes seen enough
	Diagnosis: Plasma cell myeloma	Diagnosis: Incomplete response	Diagnosis: Mild plasmacytosis

that cancer survivors have received [9–10]. Further investigations would be done in order to understand of whether this secondary malignancy is only accidental or whether there is any cause and effect relationship, another point of this case is about the differential diagnosis of thyroid nodule which was discovered some months after diagnosis multiple myeloma that could be mistaken by metastasis of multiple myeloma to thyroid gland which has been reported severally [11–13] or the primary cancer was MTC which could metastasis to bone and mimicked the multiple myeloma and it could change the way of treatment. But pathology samples and the elevation of laboratory markers such as calcitonin level excluded it and responding to cure and remission after total thyroidectomy, ruled out the second suspicious diagnosis. And another things which should be kept in mind in these kind of cases, try to investigate and pay attention to the new signs and symptoms which set during disease and may not be related to the primary cancer or complications of it, and another associated disease should be considered even if it is too unusual. In this case, patient reached to remission after chemotherapy but once more elevated ESR caused to investigate more.

CONCLUSION

A rare correlation between multiple myeloma and medullary thyroid carcinoma case is reported, diagnosis of secondary cancer is important because: first: to distinguish secondary malignancy from metastatic cancer then try to investigate the etiology of this association and finally to determine to choose the best treatment because of its good prognosis.

Author Contributions

Seyyed Mohammad Reza Mortazavizadeh – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Yasaman Ayoughi – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Fariba Binesh – Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Moein Karbalaieian – Acquisition of data, or analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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