

Extramedullary myeloma in ectopic parathyroid adenoma: A case report

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Abstract

Extramedullary myeloma, a subgroup of multiple myeloma, is a rare condition characterised by extra-skeletal infiltration of clonal plasma cells. Although parathyroid adenoma's co-morbidity with multiple myeloma is common, extramedullary myeloma, an ectopic parathyroid adenoma has not been reported in the literature. This is the first study in literature that presents extramedullary myeloma that infiltrated ectopic parathyroid adenoma in the mediastinum after multiple myeloma treatment. In its course of relapse, the extramedullary myeloma created mass effect and no laboratory findings were present due to its non-secretory nature.

Keywords: Myeloma, Metastasis, Adenoma, Parathyroid.

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Introduction

Extramedullary myeloma (EMM) is a subgroup of MM that is characterised by the presence of extraskelatal clonal plasma cell infiltration. This rare tumour can be seen during the initial diagnosis of myeloma as well as during relapse.^{1,2}

Among all parathyroid adenomas 5-10% are located in the ectopic glands.

Approximately 95% of ectopic adenomas are located in the thymus, and 5% are located in the mediastinum.³ Patients with parathyroid adenoma and MM have been reported in the literature, but only one case of parathyroid adenoma has coexisted with MM at the time of diagnosis.¹ Herein is reported the first EMM in the literature, which created mass effect on the ectopic parathyroid adenoma located in the mediastinum in the course of relapse after MM treatment.

Case Report

A 49-year-old Caucasian woman was admitted to the

University of Health Sciences Kartal Dr Lutfi Kirdar Training and Research Hospital on January 5, 2018 with complaints of constipation, abdominal and hip pain and weakness of the legs. Calcium level was 14.25 mg/dl (8.4-10.6). Due to the possibility of hyperparathyroidism, the patient's parathormone (PTH) level was examined and was found to be 309.7 pg/ml (n=12-88). Parathyroid Positron Emission Scintigraphy (PET/CT) was performed with the preliminary diagnosis of parathyroid adenoma. In the scintigraphic examination, a nodular lesion measuring 23 mm in diameter with no activity in the late period was observed in the mediastinum. Radiological correlation was suggested because the lesion did not show any activity compatible with parathyroid adenoma. The thorax and pulmonary Computed Tomography (CT) Angiography were interpreted in favour of a 25x19 mm soft tissue lesion compatible with an asymptomatic lymphadenopathy (LAP) or ectopic thymus. An abdominal CT scan revealed multiple lytic lesions in the skeletal system. On the PET/CT, pathological FDG uptake was not observed in the lytic lesions. Accordingly, histopathological examination was recommended.

In the patient's serum immune electrophoresis, a kappa light chain of 69.41 mg/dl (170-370) and a lambda light chain of 15.59 mg/dl (90-210) were detected. The kappa and lambda light chains were negative in the patient's urine. Measurements for total protein 5.9 g/dl (6.6-8.5),

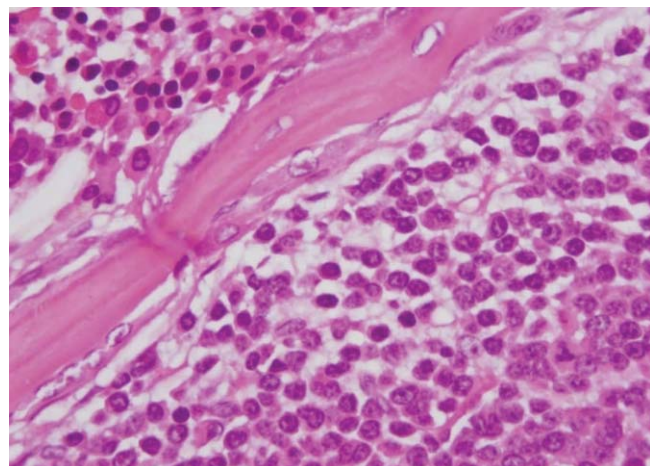


Figure-1a: Haematoxylin & Eosin (H&E)x100. Diffuse plasma cell infiltration in bone marrow.

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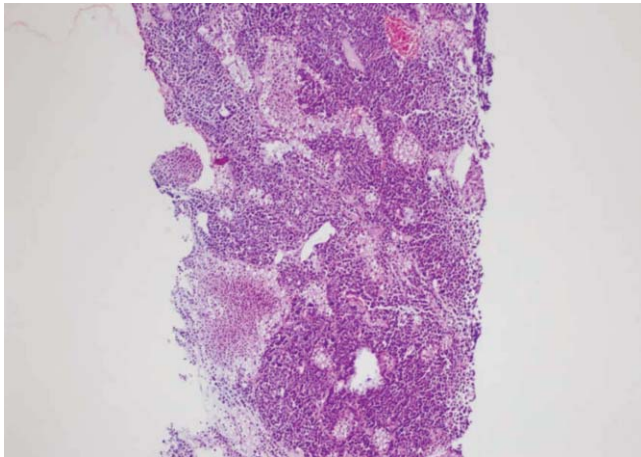


Figure-1b: Haematoxylin & Eosin x10 Intertwining of blastic plasma cells and epithelial cells with clear cytoplasm morphology.

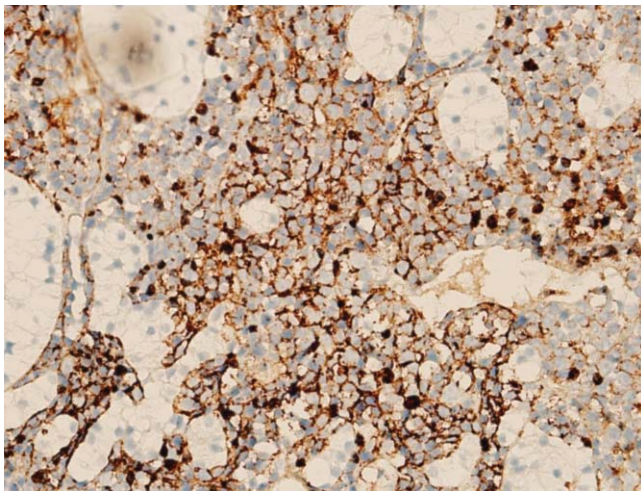


Figure-1c: CD138x40 CD138 positive blastic plasma cells.

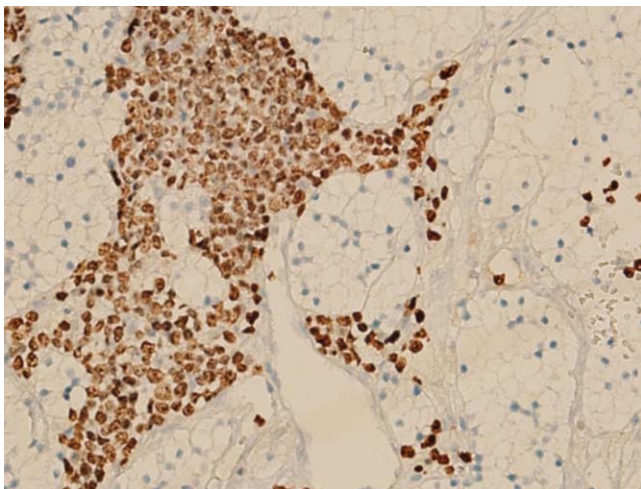


Figure-1d: Ki67x40 High proliferation index in blastic plasma cells.

IgG 476 mg/dl (700-1600), IgM <20 mg/dl (40-230), IgA 26 mg/dl (70-400), and beta 2 microglobulin 2882 ng/ml (609-2366). Bone marrow biopsy was performed and microscopic examination of the 2x0.2x0.2 cm biopsy material showed uniform plasmacytoid cell infiltration which constituted 60-65% of the total population infiltrating the bone marrow area in the diffuse and interstitial patterns (Figure-1a).

Immunohistochemical (IHC) examination showed positivity with CD138 and CD38, whereas no staining was observed with kappa, lambda, CD3, CD20, CD23, CD5, CD79alpha, cyclin D1, IgG, IgA, Ig D, IgM, Pax5, or SOX11. Kappa and lambda light chain analysis, performed with the SISH method, revealed kappa positivity. The case was

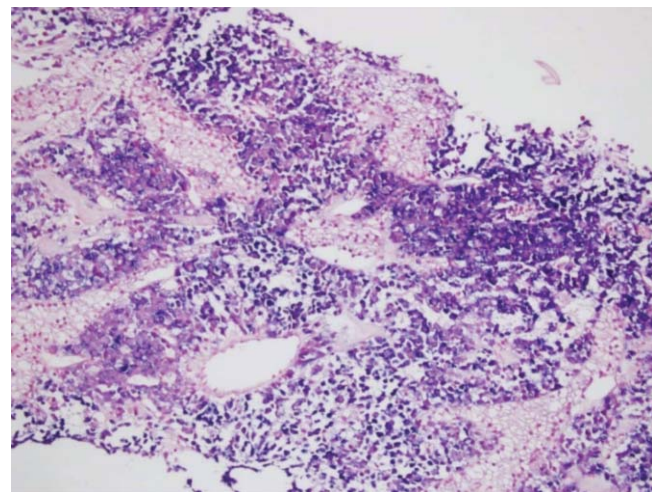


Figure-2a: Kappa chromogenic in situ hybridisation (CISH)x20 Kappa positive blastic plasma cells.

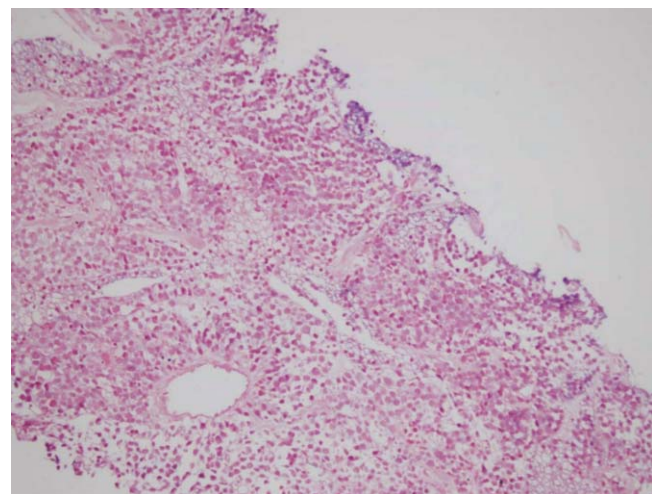


Figure-2b: Expression of Epstein Barr virus-encoded small RNA (EBER) x 20. EBER negative blastic plasma cells.

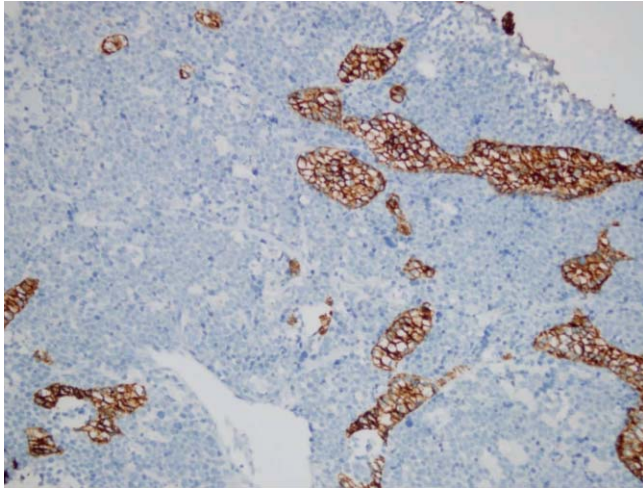


Figure-2c: Cytokeratin(CK) x20. CK positive epithelial cells.

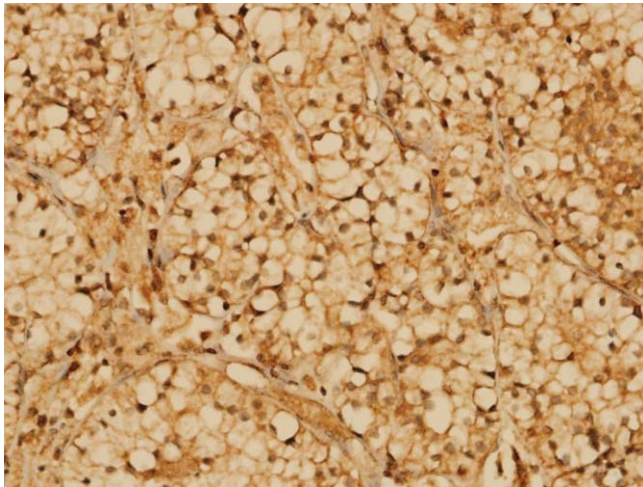


Figure-2d: Parathormone (PTH) x40. Parathormone positive epithelial cells.

reported as plasma cell myeloma, kappa monotypic. No pathology was observed in the chromosomal karyotype examination.

The patient received four cycles of Bortezomib + Cyclophosphamide + Dexamethasone. After treatment, the calcium level was 12.50 mg/dl (8.4-10.6). Six months later, a PET/CT was performed. Mediastinal mass volume and F18-FDG maximum uptake value (SUV max: 42.2) had increased as compared to the previous picture. Histopathological evaluation was recommended.

A Tru-cut biopsy specimen measuring 0.8x0.2x0.2 cm, which was taken from the mass in the mediastinum showed a diffuse infiltration with large round nuclei, conspicuous nucleoli, and granular cytoplasm suggesting blastic morphology. Accompanying and intertwining the

tumoural cells, a different group of cells were observed with epithelial morphology consisting of glandular and trabecular structures with uniform, small round nuclei and clear cytoplasm in the hyalinised stroma (Figure-1b). In the IHC, blastic morphology showed strong positive staining with CD138, CD38, CD56, EMA, and focal weak positive staining with CD30 and kappa. In this component, Ki67 proliferation index was more than 95% (Figure-1c, 1d). In CISH, positive staining with kappa was obtained in these cells and no staining was observed with lambda and EBER (Figure-2a, 2b). Negative EBER staining in tumour cells and clinical MM history suggested plasmablastic myeloma.

While epithelial neoplasm showed positive staining with CK, CAM5.2 and chromogranin, no staining was detected with synaptophysin (Figure-2c). The other markers of IHC used for the differential diagnosis were CD117, CD34, CD99, CEA monoclonal, MPO, OCT3 / 4, PLAP, S-100, SALL4, TFE3, TLE1, WT-1, all of which showed no staining in both the tumours. The epithelial component was evaluated regarding the pattern, morphological and IHC characteristics, besides the patient's laboratory findings and was reported as an ectopic parathyroid adenoma. Surgical resection was done and 7x7x1.5cm, brownish tissue fragments were obtained. In addition to IHC markers performed in Tru-cut biopsy for epithelial component, parathormone and GATA3 staining were positive (Figure-2d).

Discussion

Primary hyperparathyroidism (PHPT) and MM co-occurrence were first described by Drezner and Lebowitz in 1979 and later 29 more cases were reported. While initial diagnosis was PHPT in 11 cases, 10 cases were MM and 7 cases were both. The initial diagnosis of one case is unknown. Only one case was a non-secretory type.⁴ In our case, initially, parathyroid adenoma was considered because of the elevated serum calcium and parathyroid hormone levels but since scintigraphy, CT and CT angiography showed no uptake in the mass in the mediastinal area, this diagnosis was excluded. A PET/CT examination of skeletal system, lytic lesions suggested haematologic malignancy and the diagnosis of MM was made after bone marrow biopsy. There was no light chain increase in serum and urine before the biopsy which proves the non-secretory nature of the disease. The mechanism of the co-occurrence of PHPT and MM are unknown.^{5,6}

The recorded cases of co-existing MM and PHPT are all between the age range of 45-92 years and most patients are females.⁴

During the course of MM, myeloma cells most commonly

infiltrate the skin, liver, kidney, breast, lymph nodes and central nervous system.²

In literature, there is only one case with the involvement of parathyroid adenoma. Vincent et al described an incidentally discovered EMM presenting with infiltration in a parathyroid adenoma.¹ The infiltration was determined during initial diagnosis and did not create any mass effect.¹ EMM seen in our case was discovered after MM treatment in an ectopically located parathyroid adenoma and caused a mass effect.

Plasma cells in EMM patients are reported to have a more immature and anaplastic morphology than malignant plasma cells in the primary bone marrow area.⁶ In our case, primary bone marrow biopsy showed uniform plasma cell proliferation, while biopsy from extramedullary diffuse para mediastinal mass included large, atypical anaplastic cells containing blasts, and highly mitotic, necrotic areas.

Primary treatment for parathyroid adenomas is surgical removal. In EMM, the primary treatment is surgery or radiotherapy (RT). In our case, surgical resection was applied to the mediastinal mass after Tru-cut needle biopsy.^{1,7} RT was planned for EMM treatment but the patient died due to pulmonary infection in the post-operative period.

Conclusion

EMM cases may present with soft tissue mass at different locations primarily or in the course of recurrence. Although there is a marked anaplasia and loss of differentiation, the clinical history of MM should bring to mind EMM. However, as seen in our case, when the

tumour spreads into an ectopic tumour, the first diagnosis is not usually EMM. Since, there are no reports in the literature where EMM presented with ectopic parathyroid tissue or adenoma, ours is the first case described with its current features.

Informed Consent: Informed consent was taken from the patient for publishing the case report.

Disclaimer: None to declare.

Conflict of Interest: None to declare.

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