Plasma cell myeloma - a unique case presenting as thyroid plasmacytoma and mimicking of medullary carcinoma: how to avoid pitfall in aspiration cytology

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ABSTRACT

Background: Extramedullary plasmacytoma (EMP) of the thyroid is a rare neoplasm that may present either as a solitary plasma-cell tumor or involvement of plasma cell myeloma (PCM). In this report, we present a unique case of PCM presented as a thyroid mass without previous history, and initially misinterpreted as medullary carcinoma on fine-needle aspiration cytology (FNAC).

Case Presentation: A 77-year-old female presented with shortness of breath and palpitation. Ultrasonography-guided FNAC from the large thyroid mass revealed hypercellular smears composed of monomorphic plasmacytoid cells, focally binucleated, scattered diffusely. Subsequent histopathological examination and immunohistochemistry of thyroidectomy specimen showed infiltration of sheets of plasma cells and diagnosed as EMP. Histology of the bone marrow displayed Lambda positive neoplastic plasma cells. A combination of singly distributed cells and aggregates with plasmacytoid morphology on a proteinous background without clinical suspicion and previous history leads to misinterpretation of FNAC.

Conclusion: Clinical correlation, immunocytochemistry, and complementary cytological approach including various preparation techniques of staining are crucial for avoiding diagnostic pitfalls and the patients' proper treatment.

Keywords: Plasma cell myeloma, case report, thyroid, cytology, medullary carcinoma, FNAC.

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Background

Plasma cell myeloma (PCM) is a bone marrow-based, neoplastic single clonal plasma cell proliferation, and one of the most common lymphoid neoplasms accounting for approximately 20% of deaths from hematological malignancies [1,2]. Extramedullary plasmacytomas (EMP) are rare neoplasms, with localized atypical plasma cell proliferation, comprising approximately 1% of all plasma cell neoplasms [2]. The most common location for EMP is the upper air passage, with occurrence in the thyroid being one of the rarest sites [2,3]. Diagnosing EMP using fine-needle aspiration cytology (FNAC) is challenging for many reasons; it is a rare condition, it has cytological similarities with medullary thyroid carcinoma (MTC), lymphomas, poorly differentiated carcinomas, etc., and plasmacytoid features and the possibility of amyloid in the background [3,4]. EMP associated with PCM at diagnosis has been reported in several studies [5]. Herein, we report a PCM case, presented as a thyroid mass in a patient without a previous history. The condition was initially misinterpreted as medullary carcinoma using FNAC.

Case Presentation

A 77-year-old female with no significant previous medical history attended the outpatient clinic with shortness of breath and palpitations. Thyroid ultrasonography detected an ill-defined heterogeneous solid mass in the right lobe, measuring 6 cm in the greatest dimension. FNAC of the thyroid mass revealed hypercellular smears, composed of plasmacytoid cells arranged in sheets, scattered diffusely. The cells were round to ovoid, with enlarged and irregular contoured eccentric nuclei (Figure 1). Binucleation was observed in some areas. In focal areas, proteinaceous material was seen in the background. The FNAC diagnosis was malignant cytology. In the cytology report, the notes stated that a diagnosis of medullary carcinoma was primarily considered, but it also reported that the possibility of lymphoma or metastasis of a poorly differentiated carcinoma could not be completely excluded. Total excision and serum measurements of Calcitonin and Carcinoembryonic antigen were recommended.

The patient underwent a total thyroidectomy. At the gross examination of the right lobe, a white-grey colored solid mass of 6 × 4.5 × 4.3 cm in dimensions was detected. Other areas were colloidal and fleshy. Histopathological examinations of multiple sections showed infiltration of monomorphic plasma cells, arranged in nodules (Figure 2). These cells exhibited diffuse cluster of

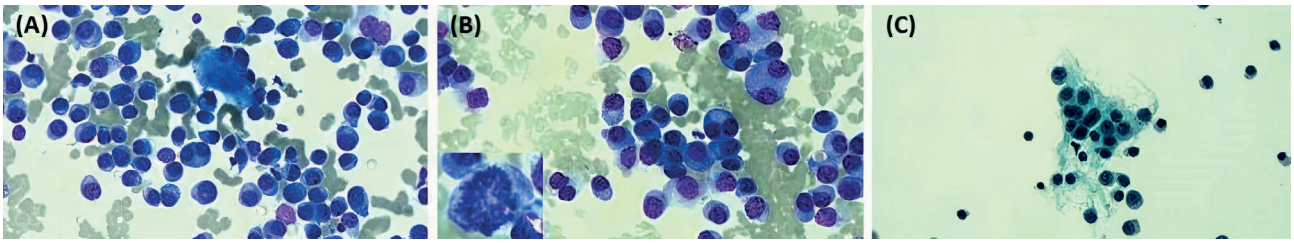

Figure 1. *Hypercellular smears composed of diffusely scattered cells with plasmacytoid morphology (A) MGG* (×40). Cells with multiple nuclei were occasionally seen (B) MGG* (×40) a typical mitotic figure is in the insert photo. Loose clusters of cells with eccentric nucleus with prominent nucleoli (C) liquid-based preparation (×40).*

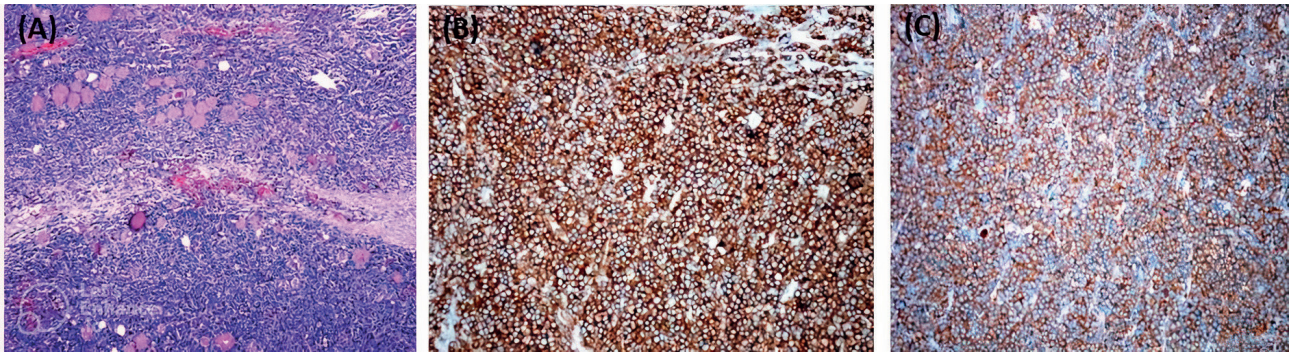

Figure 2. *Diffuse infiltration of monomorphic plasma cells in the thyroid gland (A) H&E** (×40). Neoplastic cells in thyroidectomy shows immunreactivity with CD38 (B, × 10), and lambda stain (C, × 10).*

differentiation (CD)38, CD138, and Lambda positivity. Calcitonin, Thyroid transcription factor 1 (TTF-1), and Kappa immunoreactivity were not detected (Figure 2). Histopathological diagnosis was made as 'Lambda positive monoclonal plasma cell proliferation and the pathology report also suggested systemic investigation of the patient, and if there was no bone marrow and bone involvement, the case could be accepted as EMP. Routine laboratory tests showed mild anemia. While serum IgM and IgA levels are low, IgG levels were found elevated. Bone marrow biopsy and laboratory tests were performed. The bone marrow was hyper-cellular, with approximately 70% consisting of neoplastic plasmacytoid cells. Immunohistochemistry revealed plasmacytoid cells, with diffuse positivity for CD38, CD138, and Lambda markers (Figure 3). Based on these findings, plasma cell myeloma, with extramedullary involvement was finally diagnosed.

Discussion

PCM is a neoplastic clonal proliferation of plasma cells derived from immunoglobulin-producing B cells. The disease has a spectrum pathology, from localized lesions to disseminated forms, with the involvement of various organs [6,7]. PCMs are relatively common tumors comprising 10%-15% of hematopoietic neoplasms. Most are observed in the elderly. The condition is more common in men, with a male-to-female ratio of 1.1:1 [1]. It is not uncommon for the involvement of multiple organs by neoplastic plasma cells to produce various symptoms [8]. EMPs are rare neoplasms composed of monoclonal plasma cells, located in single tissues other than bone, but without bone marrow involvement. Most neoplasms occur in males in the 4th to 7th decades [2,9]. The most common location for EMP is in upper air passage mucous membranes, but they may be observed at other sites, such as the gastrointestinal tract, lymph nodes, bladder, breast, thyroid gland, testes, parotid glands, skin, and the central nervous system [2,3,10]. The thyroid is a rare site for EMP, but several cases have been reported in the literature [9-12].

The diagnosis of EMP is challenging with FNAC, especially at rare locations such as the thyroid gland. Highly cellular smears composed of plasmacytoid cells with eccentric nuclei, with proteinaceous material in the background, could be easily misinterpreted as medullary carcinoma. Similar cases have been previously reported in the literature by Bhat et al. and Bourtsos et al [3,4]. It is possible to make generalizations about the histological and cytological appearance of MTC, but many tumor variants exist, and this morphological diversity causes serious diagnostic difficulties. Aspirate smears of MTC are moderate to markedly cellular and consist of cells in single and syncytial clusters. The cells are plasmacytoid, polygonal, round, or spindle-shaped. In up to 35% of cases, an almost pure plasmacytoid appearance is observed [3]. In some cases, long cell extensions may also be present. Binucleation and multinucleation are also common morphologies. Amyloid can be seen as colloid-like dens, amorphous material in the background [3]. Most of these morphological features were present in smears from our case, suggesting MTC. Additionally, a lack of cell blocks/

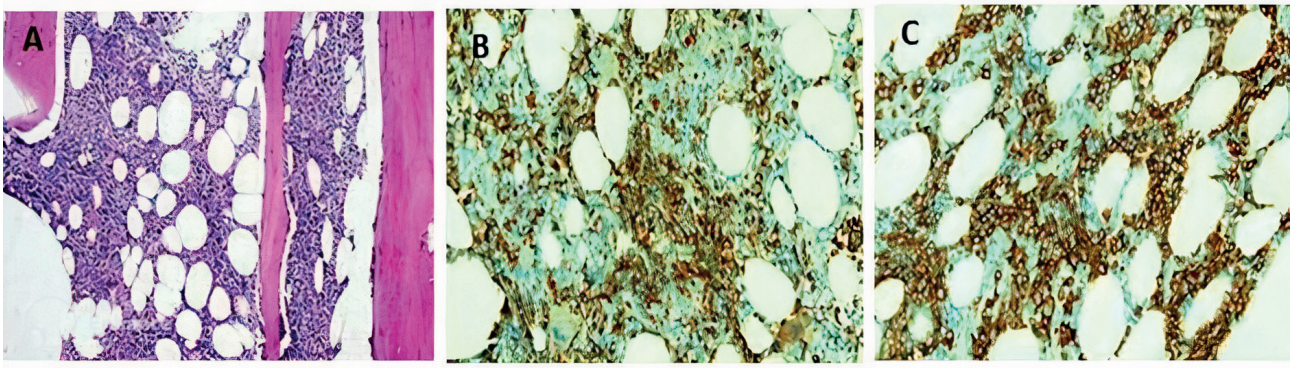

Figure 3. *Neoplastic cells infiltrating bone marrow (A, × 10), showed positivity with lambda (B, × 20) and CD138 (C, × 20).*

* May-Grünwald Giemsa
** Hematoxylin and Eosin

cytospins and immunohistochemistry of smear preparations also led to misinterpretations in this case.

Cytomorphologically, cells of plasmacytoma and multiple myeloma may look different from normal plasma cells and equally, may be difficult to recognize using FNAC. A spectrum of cytological changes can be observed, such as larger blast-like cells, cytoplasmic shedding, and fraying cell borders [3]. Although binucleation/multinucleation is a common finding of MTCs, it has also been reported in plasmacytomas [3,4,11]. It appears that medullary carcinomas tend to be overdiagnosed using FNAC [3]. In differential diagnoses, cytoplasmic changes such as fraying cell borders, the presence of hyaline inclusions or vacuoles, intracytoplasmic Russel bodies, and intranuclear Dutcher bodies favor an EMP diagnosis. However, the neuroendocrine appearance in alcohol-fixed preparations, triangular cytoplasmic tails, and red cytoplasmic granules, favor a medullary carcinoma diagnosis. Notwithstanding these issues, many overlapping features still exist between medullary carcinoma and EMP, to complicate a definitive diagnosis [3].

In a meta-analysis comprising fifteen studies, involving 641 FNAC cases, Trimboli et al. [13] reported that immunohistochemical staining for Calcitonin was inconsistent for MTC diagnosis and that the detection rate in demonstrating MTC was 56.4% for cytology. Bourtsos et al. [3] also found equivocal Calcitonin positivity from immunohistochemical staining, performed in a smear from a plasmacytoma case, mimicking MTC. On the other hand, MTC cases with undetectable serum Calcitonin levels had previously been reported [14,15].

The extramedullary spread of PCM is not a rare entity at diagnosis, or during disease progression [5]. Previous studies and case reports have shown extramedullary involvement in up to 17% of patients with PCM at diagnosis [5,6,10,12]. An EMP diagnosis should always be considered, after a full patient systematic evaluation.

Our case had no previous history or clinical indications for EMP or PCM. The patient presented with shortness of breath and palpitations, therefore detailed laboratory tests were unaccomplished, except complete blood counts and thyroid function tests before FNAC. After detecting monoclonal plasma cell proliferation from a histopathological examination of the thyroid gland, a systemic evaluation and bone marrow biopsy was performed. Further tests showed that the patient had PCM, presenting with extramedullary involvement of the thyroid gland. At this point, we regard this case as relatively unique.

Conclusion

EMP or extramedullary involvement of PCM should be considered at differential diagnosis in FNAC smears of the thyroid gland, especially with predominant monotonous plasmacytoid morphology, potentially mimicking MTC. Different FNAC techniques and proper cytological management are essential approaches for these cases. We recommend evaluating the patient as a whole, together with pathological, clinical, and laboratory findings should minimize possible diagnostic errors.

What is new?

The authors report a plasma cell myeloma case, presented as a thyroid mass in a patient without a previous history. Plasma cell myelomas may be initially misinterpreted as medullary carcinoma using FNAC without clinical information. It is important to keep in mind plasma cell myeloma or extramedullary plasmacytoma for differential diagnosis in smears with plasmacytoid morphology and know the cytopathological clues.

List of Abbreviations

EMP	Extramedullary plasmacytoma
FNAC	Fine-needle aspiration cytology
MTC	Medullary thyroid carcinoma
PCM	Plasma cell myeloma

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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Consent for publication
Written and informed consent was taken from the patient to publish this case report.

Ethical approval
Ethical approval is not required at our institution to publish an anonymous case report.

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References
1. Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood. 2016;127(20):2375–90. https://doi.org/10.1182/blood-2016-01-643569
2. Fletcher CDM, Bridge JA, Hogendoorn P, Mertens F. WHO classification of tumours of soft tissue and bone. Lyon: IARC; 2013. 312 p.
3. Bourtsos EP, Bedrossian CW, De Frias DV, Nayar R. Thyroid plasmacytoma mimicking medullary carcinoma: a potential pitfall in aspiration cytology. Diagn Cytopathol. 2000;23(5):354–8. https://doi.org/10.1002/1097-0339(200011)23:5<354::AID-DC15>3.0.CO;2-7
4. Bhat V, Shariff S, Reddy RAN. Extramedullary plasmacytoma of thyroid - a mimicker of medullary carcinoma at fine needle aspiration cytology: a case report. J Cytol. 2014;31(1):53–6. https://doi.org/10.4103/0970-9371.130710
5. Varettoni M, Corso A, Pica G, Mangiacavalli S, Pascutto C, Lazzarino M. Incidence, presenting features and outcome of extramedullary disease in multiple myeloma: a longitudinal study on 1003 consecutive patients. Ann Oncol. 2010;21(2):325–30. https://doi.org/10.1093/annonc/mdp329
6. Singh K, Kumar P, Pruthy R, Goyal G. Multiple myeloma presenting as thyroid plasmacytoma. Indian J Med Paediatr Oncol. 2017;38(4):552–4. https://doi.org/10.4103/ijmpo.ijmpo_43_16
7. Cambruzzi E, Molinari AS, Uchôa M, Yépez V. Primary plasmacytoma of the thyroid gland: a case report of a rare neoplasia. J Bras Patol Med Lab. 2012;48(4):281–5. https://doi.org/10.1590/S1676-24442012000400009
8. Kyle RA, Gertz MA, Witzig TE, Lust JA, Lacy MQ, Dispenzieri A, et al. Review of 1027 patients with newly diagnosed multiple myeloma. Mayo Clin Proc. 2003;78(1):21–33. https://doi.org/10.4065/78.1.21
9. Ridal M, Ouattassi N, Harmouch T, Amarti A, Alami MN. Solitary extramedullary plasmacytoma of the thyroid gland. Case Rep Otolaryngol. 2012;2012:282784. https://doi.org/10.1155/2012/282784
10. Chen HF, Wu TQ, Li ZY, Shen HS, Tang JQ, Fu WJ, et al. Extramedullary plasmacytoma in the presence of multiple myeloma: clinical correlates and prognostic relevance. Onco Targets Ther. 2012;5:329–34. https://doi.org/10.2147/OTT.S35348
11. Gilani JA, Iqbal S, Nasreen S, Shahid S. Plasmacytoma of the thyroid gland. J Ayub Med Coll Abbottabad. 2011;23(4):131–2.
12. Nangia JR, Lakhani AA, Loew JM, Gregory SA. Multiple myeloma with multiple extramedullary plasmacytomas. Clin Adv Hematol Oncol. 2011;9(8):630–2.
13. Trimboli P, Treglia G, Guidobaldi L, Romanelli F, Nigri G, Valabrega S, et al. Detection rate of FNA cytology in medullary thyroid carcinoma: a meta-analysis. Clin Endocrinol (Oxf). 2015;82(2):280–5. https://doi.org/10.1111/cen.12563
14. Sand M, Gelos M, Sand D, Bechara FG, Bonhag G, Welsing E, Mann B. Serum calcitonin negative medullary thyroid carcinoma. World J Surg Oncol. 2006;4:97. https://doi.org/10.1186/1477-7819-4-97
15. Brutsaert EF, Gersten AJ, Tassler AB, Surks MI. Medullary thyroid cancer with undetectable serum calcitonin. J Clin Endocrinol Metab. 2015;100(2):337–41. https://doi.org/10.1210/jc.2014-3095

Summary of the case

1	**Patient (gender, age)**	77 year old female
2	**Final diagnosis**	Plasma cell myeloma with extramedullary disease
3	**Symptoms**	shortness of breath and palpitations
4	**Medications**	
5	**Clinical procedure**	FNAC, Total thyroidectomy and bone marrow biopsy
6	**Specialty**	Extramedullary extension of plasma cell myeloma may mimic cytopathological features of medullary thyroid carcinoma. At presentation, without clinical history of plasma cell myeloma, when evaluating FNAC from a thyroid mass, the differential diagnosis must be done carefully.