Laroussi *et al.*
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CASE REPORT Open Access

Thymic plasmacytoma presenting as polyneuropathy and revealing multiple myeloma: a case report

Syrine Laroussi[1*], Khadija Sonda Moalla[1], Faten Kallel[2], Saadia Makni[3], Nozha Kallel[4], Nouha Farhat[1], Mariem Damak[1], Moez Elloumi[2], Tahya Sellami[3], Khaireddine Ben Mahfoudh[4] and Chokri Mhiri[1]

Abstract

Background: Multiple myeloma (MM) is the most frequent malignant plasma cell disorder with proliferation of neoplastic plasma cells in the bone marrow or other tissue, most commonly in the upper aerodigestive tract. The invasion of the thymus is exceptional. Neurological complications are usual, but represent exceptionally the revealing symptom.

Case presentation: We report a case of polyneuropathy revealing a thymic plasmacytoma as a mediastinal invasion of MM in a 48-year-old woman. She was admitted after developing progressive ascending distal paresthesias and weakness in lower limbs. Examination showed symmetrical distal sensorimotor impairment with axillary and inguinal adenopathies. Electroneuromyography revealed a sensorimotor length-dependent neuropathy. Serum protein electrophoresis showed monoclonal protein peak in β-γ globulin region. Immunoelectrophoresis showed IgA lambda monoclonal gammapathy. Myelogram and bone marrow biopsy revealed plasmocytosis of 5%. Chest computed tomography showed a histologically confirmed thymic plasmacytoma associated with a lytic lesion of the 5th rib leading to the diagnosis of MM.

Conclusions: The association between a thymic plasmacytoma and peripheral neuropathy is rare and a workup for MM is necessary to guide therapeutic management.

Keywords: Polyneuropathy, Extramedullary plasmacytoma, Multiple myeloma, Thymus, Case report

Background

Monoclonal gammopathies are a heterogeneous group of disorders, caused by proliferation of monoclonal plasma cells or B-lymphocytes, ranging from the subclinical monoclonal gammopathy of undetermined significance, to malignant systemic disorders such as multiple myeloma (MM). Multiple myeloma is the most frequent malignant plasma cell disorder with proliferation of neoplastic plasma cells in the bone marrow (BM) or other tissues, most commonly in the upper aerodigestive tract and rarely in the anterior mediastinum [1]. Neurological complications are usual, but represent exceptionally the revealing symptom, particularly when it comes to polyneuropathy (PN) [2]. We report the case of PN revealing a thymic plasmacytoma as a mediastinal invasion of MM.

Case presentation

A 48-year-old woman, with no medical history, was admitted to our neurology department after developing gradually ascending distal paresthesia in the lower limbs over 2 months followed by lower limb weakness and gait disorders one month later with deterioration of the general condition. Family history was negative for inherited

*Correspondence: laroussi.syrine@gmail.com

[1] Neurology Department, Habib Bourguiba University Hospital, 3029 Sfax, Tunisia
Full list of author information is available at the end of the article

polyneuropathy. No history of infection was reported. She denied high-risk sexual behavior, any toxin exposure, bone pain or any sphincter impairment. Neurological examination showed sensory ataxia with a positive Romberg test and symmetrical distal motor impairment. Areflexia was noted in lower limbs with flexor plantar responses and hypoesthesia of gloves–socks type with no cranial nerve involvement. General exam revealed an axillary and inguinal adenopathies measuring 1 cm each. Electroneuromyography showed a severe sensorimotor length-dependent neuropathy with axonal mechanism in lower limbs. Cerebrospinal fluid (CSF) examination showed normal cellularity with an increased protein level (0.81 g/L). Brain magnetic resonance imaging (MRI) was normal. Spinal MRI showed osteolytic vertebral lesions. Complete blood count, urinalysis and other laboratory tests including calcium levels, thyroid hormones and cryoglobulin level were within normal limits. Viral serologic testing including human immunodeficiency virus, varicella-zoster virus and syphilis serology, tumor markers, antinuclear and antineuronal antibodies were negative. Monoclonal protein peak in β-γ globulin region measuring 5 g/l and elevated beta2 microglobulin (7 g/l) were noted on serum protein electrophoresis and IgA monoclonal gammapathy with lambda light chain restriction following immunoelectrophoresis. Myelogram and BM biopsy revealed plasmocytosis of 5%. VEGF serum level was normal. No amyloid deposits were found in the labial gland biopsy. Computed tomography scan showed a $35 \times 30 \times 50$ mm mass in the right anterior and superior mediastinal region arising from the thymus (Fig. 1) with pleural effusion as well as a lytic lesion measuring 1.5 cm

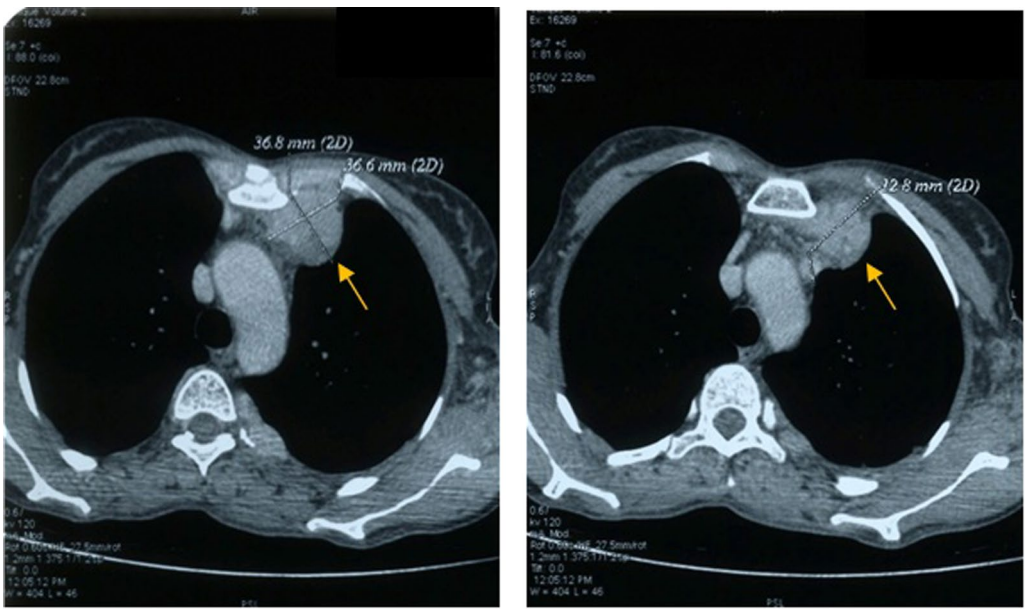

Fig. 1 Chest computed tomography scan: mediastinal window. 36 × 36 × 50 mm mass in the right anterior and superior mediastinal region arising from the thymus (yellow arrows)

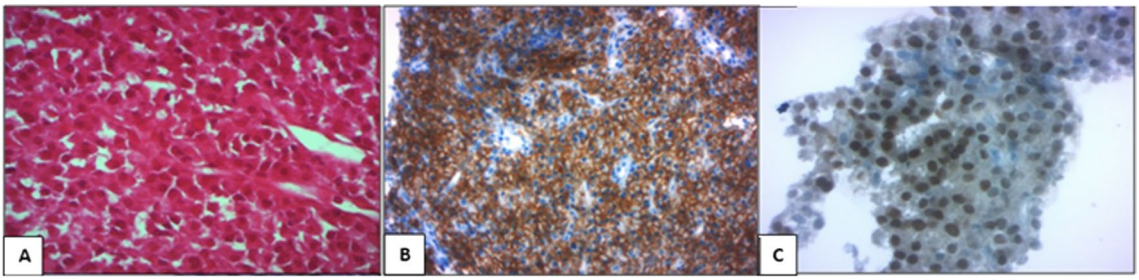

Fig. 2 Microscopic examination of the thymus biopsy showed diffuse infiltrates of plasma cells with large and eccentric nuclei and abundant cytoplasm (H&E × 400) (**A**). Immunohistochemistry showed tumor cells with diffuse reactivity to CD138 (× 200) (**B**) and nuclear positivity to MUM1 (× 200) (**C**)

Table 1 Clinical, radiological and biological data of patients with thymic plasmacytoma revealing a multiple myeloma

Patient N°	Age/sex	Medical history	Symptoms leading to consultation	MRI /CT	Initial diagnosis	Mediastinal mass biopsy	BMB: marrow involvement (%)	CRAB criteria	Beta microglobulin	Serum protein electrophoresis + immunofixation	Diagnostic criteria for MM
1 [7]	53/F	NM	Protruding mass on the right chest wall + local pain Fatigue	48.7 × 60 × 52 mm mass in the thymus	Malignant thymoma	Plasmacytoma	57%	Anemia (95 g/l)	Elevated (24.30 mg/L)	Monoclonal protein negative in the serum	Clonal bone marrow plasma cell ≥ 10% + Biopsy-proven EMP + Anemia
2 [14]	66/F	GERD Osteoporosis Hypercholesterolemia Smoking	Low back pain Nausea Retching Dyspnea	– 3.9 × 4.2 cm mass in the thymus – 8th right rib fracture – abnormal BM signal in multiple areas	Lung cancer with mediastinal involvement and skeletal metastasis		10%	Anemia (107 g/l)	Elevated (5.2 mg/L)		
Our patient	48/F	None	Gradually ascending distal paresthesias in the lower limbs Gait disorders	– 36 × 36 × 50 mm mass in the thymus – Pleural effusion – 5th rib lytic lesion with cortical bone rupture and soft tissue extension	Thymic plasmacytoma		5%	≥ 1 osteolytic lesion	Elevated (7 g/L)	IgA lambda monoclonal gammopathy	Biopsy-proven EMP + ≥ 1 osteolytic lesion

BM: Bone marrow; *BMB*: bone marrow biopsy; *CT*: computed tomography; *EMP*: extramedullary plasmacytoma; *F*: female; *GERD*: gastroesophageal reflux disease; *MM*: multiple myeloma; *MRI*: magnetic resonance imaging; *NM*: not mentioned; *NP*: not performed

of the 5th rib with cortical bone rupture and soft tissue extension. The patient underwent percutaneous thymus biopsy and the lesion was histologically diagnosed as plasmacytoma. Tumor cells were positive for CD138 and multiple myeloma oncogene-1 (MUM-1) (Fig. 2). The diagnosis of multiple myeloma was made with the presence of a histologically confirmed plasmacytoma and one CRAB criteria (≥ 1 osteolytic lesion) [3]. The patient was referred to hematology department for further therapeutic management.

Plasmacytoma is a plasma cell neoplastic proliferation of the soft tissue, which frequently occurs in the BM, but can occasionally be located at extramedullary sites with the most common site being the upper aerodigestive tract [1]. The anterior mediastinum, particularly the thymus, is rarely involved and the literature consists mainly of reports of single cases [1]. Neurological complications represent exceptionally the revealing symptom, particularly when it comes to polyneuropathy. Our case presented initially a diagnostic dilemma; we initially thought of the diagnosis of extramedullary plasmacytoma (EMP) with tissue biopsy showing monoclonal plasma cell histology and bone marrow plasma cell infiltration not exceeding 5%. However, with the clinical presentation at onset, it is exceptional for a neuropathy [4] to be the revealing symptom of an EMP, especially when it comes to PN. Moreover, it is recommended with IgA monoclonal gammopathy to search for MM or POEMS (polyneuropathy, organomegaly, endocrinopathy, myeloma protein, and skin changes syndrome) and with an axonal neuropathy to search for amyloidosis or cryoglobulinemia [5]. Amyloid deposits were not found on labial biopsy and cryoglobulin level was normal. Our patient did not meet the criteria for POEMS syndrome with two mandatory major criteria, polyneuropathy and monoclonal gammopathy, and two minor criteria, pleural effusion and adenopathy. Even with the cytoalbuminologic dissociation in CSF examination, electroneuromyography did not fulfill the criteria for chronic inflammatory demyelinating polyneuropathy, which is the typical presentation during POEMS syndrome [6]. The diagnosis of thymic plasmacytoma with MM was reached after completing investigations with the presence of skeletal metastasis fulfilling the CRAB criteria [3], which has rarely been reported. Only 5% of patients with EMP have coexistent MM [7]. Another particularity is that IgA neuropathies are less common than IgM and IgG neuropathies (10 to 15%) [8, 9]. They are unlikely to be causally related to peripheral neuropathy [8] and could have a high tendency to evolution and malignancy [10]. Although some studies have shown deposition in the myelin sheath of crystalline inclusions in the peripheral nerve of a patient with IgA lambda monoclonal gammopathy of undetermined significance suggesting a possible causal link to the neuropathy [11], it was not observed or reported with MM yet. MM may cause neurological complications in the central or peripheral nervous system, dominated by spinal cord compression [6]. However, MM-related PN is rare [9], especially at onset. A recent study reported only 4 cases of MM out of 193 patients after investigating a clinic-biological presentation of polyneuropathy associated with monoclonal gammopathy and additional 4 patients who developed MM at a 3-year follow-up [2].

Its physiopathology is still not well understood. The main cause of MM-related PN is drug-related neurotoxicity [12], which is not the case of our patient. In general, the young age at onset pleads for the true causal association even though there is no specific test to confirm it [8]. It usually manifests as a length-dependent axonal sensorimotor neuropathy with involvement of all sensory modalities and mild distal weakness as in our patient [8, 13]. The presentation can be diverse and most often develop after the diagnosis of myeloma [9]. With our patient, PN was the revealing symptom. Our patient represents the third and youngest reported case to our knowledge to have an EMP in the thymus leading to the diagnosis of MM (Table 1). It is unique as an EMP was revealed by a polyneuropathy, which is extremely rare, but also the unusual site of the EMP in the thymus. Another interesting aspect is that the plasmacytoma raised the question of whether to consider it as a metastatic site of myeloma or the primary site of tumor growth resulting eventually in a MM.

Conclusion

Thymic plasmacytoma is rarely associated with PN and a workup for MM invasion is mandatory even in the absence of BM plasmocytosis. The diagnosis rests largely on biological and biopsy results.

Abbreviations

MM: Multiple myeloma; BM: Bone marrow; PN: Polyneuropathy; CSF: Cerebrospinal fluid; MRI: Magnetic resonance imaging; MUM-1: Multiple myeloma oncogene-1; EMP: Extramedullary plasmacytoma.

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Machines used in the study

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Author contributions

SL, KSM and FK wrote the paper. SM and TS provided pathology data. NK and KBM contributed to the analysis of radiology data. NF, MD, ME and CM provided clinical revision of the paper. All authors approve of this final manuscript and accept responsibility for their respective roles. All authors have read and approved the final manuscript.

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Availability of data and materials
The corresponding author takes full responsibility for the data, has full access to all of the data, and has the right to publish any and all data separate and apart from any sponsor.

Declarations

Ethics approval and consent to participate
All procedures performed in the study were in accordance with the ethical standards of the Faculty of Medicine of Sfax.

Consent for publication
Written informed consent was obtained from the participant for publication of this case and accompanying images.

Competing interests
The authors declare that they do not have any competing interests.

Author details
[1]Neurology Department, Habib Bourguiba University Hospital, 3029 Sfax, Tunisia. [2]Hematology Department, Hedi Chaker University Hospital, 3029 Sfax, Tunisia. [3]Pathology Department, Habib Bourguiba University Hospital, 3029 Sfax, Tunisia. [4]Radiology Department, Habib Bourguiba University Hospital, 3029 Sfax, Tunisia.

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