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CASE REPORT

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Concomitant lymphoplasmacytic lymphoma, multiple myeloma, and amyloidosis: A diagnostic and therapeutic challenge

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Abstract

We report a case based on simultaneous occurrence of Waldenström macroglobulinemia, myeloma and amyloidosis as a collision neoplasm. The strangeness and severity of the case presented a diagnostic and therapeutic challenge, which required individualised treatment and close follow-up to achieved stringent complete response.

KEYWORDS

amyloidosis, autologous stem cell transplant, myeloma, Waldenström macroglobulinemia

1 | INTRODUCTION

The differential diagnosis of small B-cell lymphomas with plasmacytic differentiation is frequently challenging because numerous types of B-cell lymphoproliferative disorders may show plasmacytic differentiation, with or without an associated serum M protein.[1] Most cases are readily classifiable based on overall morphologic features, immunophenotype, and molecular genetics. However, borderline cases are challenging. When a B-cell neoplasm display a significant plasma cell component, the possibility of a coexisting plasma cell neoplasm also needs to be ruled out.[1,2]

The association of multiple myeloma (MM) with another B-cell lymphoproliferative disease has been frequently reported, specially, the simultaneous occurrence of MM and chronic lymphocytic leukemia.[3] The coexistence of MM with other diseases such as follicular lymphoma, MALT lymphoma, and mantle cell lymphoma is rarer,[4] and even more uncommon, the simultaneous presentation of Waldenström macroglobulinemia (WM)/lymphoplasmacytic lymphoma and MM with only eight cases so far reported.[5,6]

Although MM is the most common cause of secondary amyloid light-chain (AL) amyloidosis, this has also been reported in rare cases of WM or extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue.[7] Careful consideration is required to distinguish from plasma cell neoplasm with CCND1 translocation, especially for the cases with minimal or no B-cell component.

2 | CASE REPORT

Here, we describe a patient who presented with simultaneous occurrence of MM, WM, and AL amyloidosis as collision neoplasm. A 66-year-old man was diagnosed in 2014 with asymptomatic WM (L265P mutation in the MYD88 gene) with a serum M component of 0.5 g/dl. In 2018 the patient started with symptoms of sensory neuropathy. The electrophysiological findings showed a demyelinating neuropathy with a distal accentuation of conduction slowing, and signs of posterior cord syndrome. The anti-myelin-associated glycoprotein (MAG) antibodies, previously determined in 2014 with a value of 8.74, were even more elevated (14.27) with a serum M component of only 0.6 g/dl; leading-together with the diagnosis of anti-MAG neuropathy.

Later, on March 2019, patient suffered from back pain, and a magnetic resonance imaging (MRI) was performed to better assess the complications on the skeletal system, and it detected diffuse infiltration patterns, pathological fractures in 11th and 12th thoracic vertebrae and 1st lumbar vertebrae with an epidural mass compressing the posterior spinal cord in T8. The 18-F-fluoro-deoxy-2-glucose positron-emission tomography/computed tomography (18-FDG PET/CT) confirmed the diffuse infiltration in the bone marrow, with a mass in T8.

The serum monoclonal IgM lambda paraprotein remained stable (0.7 g/dl) with serum-free light chains lambda of 672 mg/dl. The blood count revealed normal hemoglobin, and biochemical analysis showed moderate hypercalcemia and moderate renal insufficiency with an elevated creatinine of 1.36 mg/dL. Albumin level was 4.5 g/dl, and the beta-2-microglobulin level was 5585 mcg/L.

A bone marrow aspirate showed lymphoplasmacytic infiltration (33.6%) together with 14%

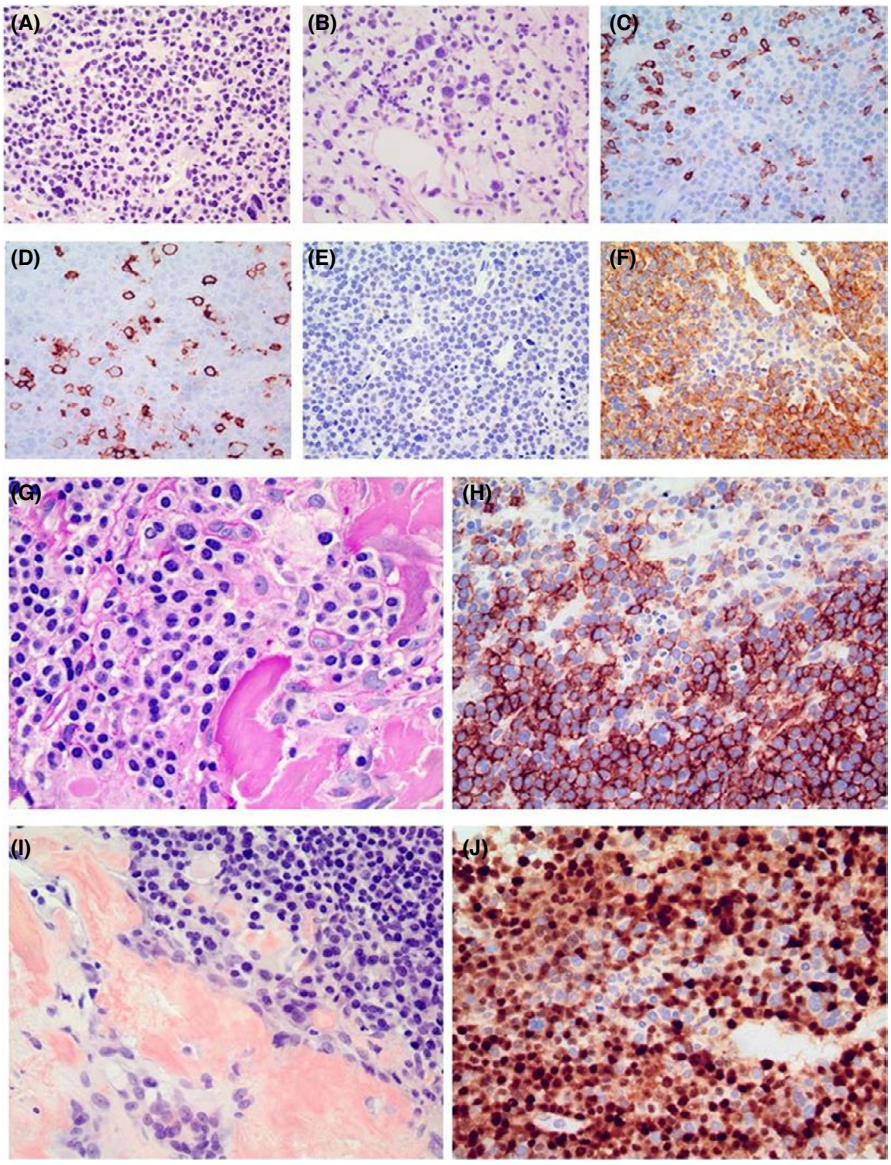

FIGURE 1 (A) Tumor is densely cellular and shows diffuse growth; with three cell types are seen in the tumor: small lymphocytes, plasma cells, and plasmacytoid cells (Hematoxylin and eosin [H&E], ×200). (B) Large plasmacytoid cells of large size and anaplasia with frequent binucleation, large nucleoli, and intranuclear pseudoinclusions (H&E, ×400). (C) Small lymphocytes were positive for CD45. (D) Small lymphocytes and some plasmacytoid cells were positive for CD20. (E and F) In situ hybridization shows clonal restriction of Lambda light-chains. (G) Interstitial deposit between tumor cells of a homogeneous, hyaline acellular material, slightly Periodic acid–Schiff (PAS) positive (PAS, ×400). (H) Plasma cells and plasmacytoid cells of large size and anaplasia were diffusely positive for CD138. (I) The interstitial deposit was Congo red positive (congo red, ×400). (J) Plasma cells showed diffuse and intense nuclear positivity for cyclin D1

TABLE 1 Clinical and biological characteristics at diagnosis, and its evolution through the treatment; before autologous stem cell transplant (ASCT) and at day 100 after ASCT

	At diagnosis	Before ASCT	After ASCT
ECOG	2	1	0–1
Blood count			
Hemoglobin (12–17 g/dl)	Hb 11.6 g/dl	Hb 14 g/dl	Hb 13.8 g/dl
Leucocytes (4–11 × 10^9/L)	L 7 × 10^9/L	L 7.5 × 10^9/L	L 4.7 × 10^9/L
Neutrophils (1.8–4 × 10^9/L)	N 5.8 × 10^9/L	N 6.1 × 10^9/L	N 2.6 × 10^9/L
Lymphocytes (1–4 × 10^9/L)	L 1 × 10^9/L	L 0.5 × 10^9/L	L 1.3 × 10^9/L
Creatinine (0.72–1.25 mg/dl)	1.36 mg/dl	0.92 mg/dl	0.78 mg/dl
Calcium (8.4–10.2 mg/dl)	11.2 mg/dl	9.5 mg/dl	9.4 mg/dl
B2 microglobulin (0–2400 μg/L)	5585 μg/L	2552 μg/L	
Albumin (35–52 g/L)	38 g/L	43 g/L	46 g/L
Serum quantitative IgM (0.22–2.4 g/L)	1168 mg/dl	<0.25 g/L	<0.25 g/L
Lambda free light (5.7–26.3 mg/L)	672 mg/L	29.7 mg/L	1.7 mg/L
N-terminal pro-brain natriuretic peptide (NT-proBNP) (0–125 pg/ml)	1420.9 pg/ml	148.2 pg/ml	88.2 pg/ml
Monoclonal protein level	Positive 0.6 g/dl	Positive 0.03 g/dl	Positive 0.03 g/dl
Flow cytometry in bone marrow aspirate	14.8% monoclonal B cells (lambda+) 7.92% abnormal plasma cells (CD38+, CD19−, CD45−)	There are no monoclonal B cells (lambda+) suggestive 1.08% abnormal plasma cells (CD38+, CD19−, CD45−)	B cells normal Absence of plasma cells
Bone marrow aspirate	33.6% lymphoplasmacytic lymphocytes	Absence of lymphoplasmacytic lymphocytes	Cytomorphology normal
Bone marrow histomorphology	14% plasma cells	3.6% of plasma cells	

pathologic plasma cells confirmed by flow cytometry. Immunohistochemical studies revealed two different populations of plasma cells in the bone marrow biopsy; a population of plasma cells with different grades of cell maturation were positive for CD20, CD138, CD43, and cyclin D1; being negative for CD56, CD117, SOX11, c-Myc, and p53; and other population of bigger plasma cells positive for CD138, CD20, CD43, and negative for cyclin D1. The plasma cells exhibited cytoplasmic light restriction by fluorescence hybridization in situ (FISH). CCND1 translocation was detected by FISH in 70% of the nuclei studied.

A sort of CD19 and CD 138 was performed to study their genetics separately. As a result, 70% of plasmatic cell population had del(17p) and 30% had IgH translocation, different from t(4;14) and t(14;16). However, clonal B lymphocyte had none of these abnormalities, and MYD 88 study was positive in B lymphocytes but negative for plasma cells.

Biopsy of the vertebral body showed markedly increased cellularity with a diffuse infiltrate of two morphologically distinct cell populations: small mature lymphocytes and large plasma cells. An interstitial deposit of a homogeneous, hyaline acellular material is observed, slightly PAS positive and Congo red positive with green birefringence, which originates a foreign body-type multinucleated giant cell reaction (Figure 1). The histomorphology was described as collision of three hematolymphoid proliferative disorders histologically distinct; constituted by WM, MM, and amyloidosis.

Treatment including therapy anti-MM and WM therapy with carfilzomib, dexamethasone, cyclophosphamide, and rituximab was started. Bearing in mind the precedent of neuropathy, carfilzomib was chosen over bortezomib due to its lower risk of neurotoxicity.[8–10] Before initiating the treatment, we ruled out the involvement by AL amyloidosis in the heart by means of an echocardiogram and normal cardiac troponins levels. Local radiotherapy was performed over spinal cord mass at T8, as analgesic effect and to prevent worsening symptoms of the compression.

After 6 cycles of chemotherapy, the bone marrow study showed the absence of monoclonal B lymphocytes with still presence of 1.08% plasma cells immunophenotypically aberrant.

Due to the pandemic situation for SARS-CoV2, autologous stem cell transplant (ASCT) date was delayed. As bridge therapy, 4 cycles of carfilzomib and dexamethasone were administered to the patient. The re-evaluation PET showed complete metabolic response.

On August 21, 2020, ASCT was performed with high-dose melphalan (200 mg/m^2) transplant conditioning regimen.[11] After 4 cycles of chemotherapy, apheresis of peripheral stem cells had been performed; being collected 2.7×10^6 CD34+ cell/kg.

Day-100 response post-ASCT showed the persistence of a minor IgM lambda (λ) component (<0.02 g/dl) with monoclonal serum-free light chain (Table 1). Due to the efficacy of induction therapy, complexity of treatments and p53 mutation, post-ASCT maintenance with carfilzomib-dexamethasone was scheduled. After 5 cycles, the monoclonal component has disappeared, and the patient is in stringent complete response.

To conclude, the synchronous coexistence of WM, MM, and amyloidosis is rare and infrequent; being necessary the integration of the clinical, morphological, histological, immunophenotypic, and cytogenetic studies to arrive at the correct diagnosis. Complications and clinical signs set the pace for the treatment; hence, it was necessary to adapt it to the needs of the patient and to plan a completely individualized therapy.

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CONFLICT OF INTEREST

The authors have no potential conflicts of interest to disclose.

AUTHOR CONTRIBUTIONS

CC and CA collected the data and wrote the paper. CC, CA, MCR, AP, IQ, AZ, and YB interpreted and analyzed the data. All authors revised the paper critically and approved the final manuscript.

CONSENT

Written informed consent was obtained from the patient to publish this report. In addition, no identifying personal details are included in this manuscript.

DATA AVAILABILITY STATEMENT

The data that support the finding of this study are available from the corresponding author [CA] upon reasonable request.

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