



CASE REPORT



## Lung consolidation as a rare presentation of lymphoplasmacytic lymphoma with extramedullary Waldenström's macroglobulinemia

Omar Abdulfattah <sup>a</sup>, Ebad Ur Rahman<sup>b</sup>, Bikash Bhattarai<sup>a</sup>, Sumit Dahal <sup>b</sup>, Zainab Alnafoosi<sup>b</sup>, David Trauber<sup>c</sup>, Danilo Enriquez<sup>a</sup> and Frances Schmidt<sup>a</sup>

<sup>a</sup>Medicine Department, Pulmonary and Critical Care Division, Interfaith Medical Center, Brooklyn, NY, USA.; <sup>b</sup>Medicine Department, Interfaith Medical Center, Brooklyn, NY, USA; <sup>c</sup>Medicine Department, Hematology/Oncology Division, Interfaith Medical Center, Brooklyn, NY, USA

### ABSTRACT

**Objectives:** Lymphoplasmacytic lymphoma (LPL) is a mature B cell lymphoma that usually involves the bone marrow, spleen and lymph nodes. Extramedullary involvement, including the lung, is rarely reported.

**Case description:** A 73-year-old female initially presented to our hospital complaining of productive cough of white-colour sputum for three weeks duration. She reported unintentional weight loss of ten pounds over the last five months. There was no history of haemoptysis, fever, night sweats, chills, recent infections or hospitalization. Chest imaging showed right lower lobe consolidation, small right pleural effusion. She was treated with oral antibiotic for pneumonia. After two months, a follow up chest imaging revealed persistent right lower lobe consolidation. Therefore, she was worked up for the possibility of malignancy. Bronchoscopy showed polypoid nodularities surrounded by black discoloured mucosa in the sub-segmental bronchi of the right lower lobe, and biopsy specimen revealed atypical B cell lymphocytic infiltrate. Polymerase chain reaction confirmed a clonal B-cell gene rearrangement supportive for a low-grade B-cell Lymphoma. Subsequently; serum immunofixation showed IgM of 1491 mg/dL (normal range 26–217 mg/dl) with normal levels of IgG and IgA. Urine contained free kappa light chains. Cytology with immunophenotyping of pleural fluid revealed lymphoplasmacytic lymphocytes. This combination of lab and bronchoscopy findings established the diagnosis of extramedullary Waldenström's macroglobulinemia.

**Conclusion:** Waldenström's macroglobulinemia, a manifestation of LPL, is associated with an IgM monoclonal gammopathy in the blood. Extramedullary involvement including the lung is rarely seen in LPL. Physicians need to be aware of this rare presentation.

### ARTICLE HISTORY

Received 21 December 2017  
Accepted 9 February 2018

### KEYWORDS

Lymphoplasmacytic lymphoma; Waldenström's macroglobulinemia; extramedullary Waldenström's macroglobulinemia; lung consolidation; pleural effusion

## 1. Introduction



Lymphoplasmacytic lymphoma/Waldenström Macroglobulinemia (LPL/WM) is a small B cell neoplasm which is composed of lymphocytes, plasmacytoid lymphocytes, and plasma cells in variable proportion. It is an indolent LPL B cell neoplasm that secretes a monoclonal IgM paraprotein. It typically involves the bone marrow, lymph nodes, and spleen. In rare instances, diffuse Lymphoplasmacytic infiltration of the lung, stomach, or bowel may occur [1,2].

Herein, we describe a case of LPL/WM with extramedullary involvement that initially presented as right lower lobe consolidation and lymphocytic pleural effusion.

## 2. Case description

A 73-year-old female presented initially to our emergency department complaining of cough for three weeks

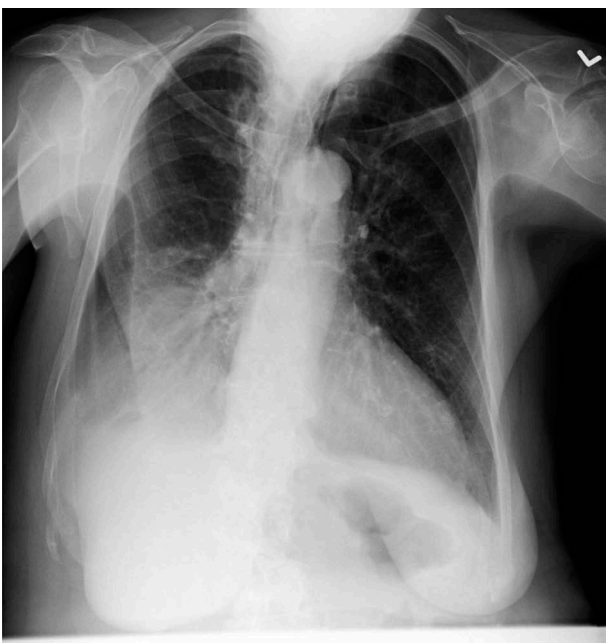
duration. She reported productive cough of white-colour sputum, right-sided pleuritic chest pain, exertional shortness of breath and acute limitation of functional capacity to less than two blocks. There was no history of haemoptysis, fever, night sweats, chills, recent infections or hospitalization. She had loss of appetite and unintentional weight loss of ten pounds over a period of 5 months. Past medical history was non-contributory. She was a lifetime nonsmoker with no history of alcohol or illicit drug abuse. She was afebrile, normotensive and maintaining optimal oxygen saturation on room air. The rest of the physical examination was unremarkable. Laboratory testing showed white blood cell count of  $5.1 \times 10^3/\mu\text{L}$ , haemoglobin 10.8 g/dl, haematocrit 32.4% and platelet count  $276 \times 10^3/\mu\text{L}$ . Comprehensive metabolic panel revealed serum sodium 141 mmol/L, potassium 4.4 mmol/L, chloride 103 mmol/L, bicarbonate 31 mmol/L, BUN 12 mg/dl, creatinine 0.6 mg/dl, calcium 9.3 mg/dl, bilirubin total 0.5 mg/dl, AST 15 mg/dl, ALT 6 mg/dl, ALP 78 mg/dl, total protein 7 g/dl of which albumin was 3.5 g/dl. Serum B<sub>2</sub>-microglobulin was 3.3 mg/L.

**CONTACT** Omar Abdulfattah  [oabdufattah@interfaithmedical.com](mailto:oabdufattah@interfaithmedical.com); [omaralhafidh@yahoo.com](mailto:omaralhafidh@yahoo.com)  Medicine Department, Pulmonary and Critical Care Division, Interfaith Medical Center, 1545 Atlantic Avenue, Brooklyn, NY 11213, USA;

© 2018 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

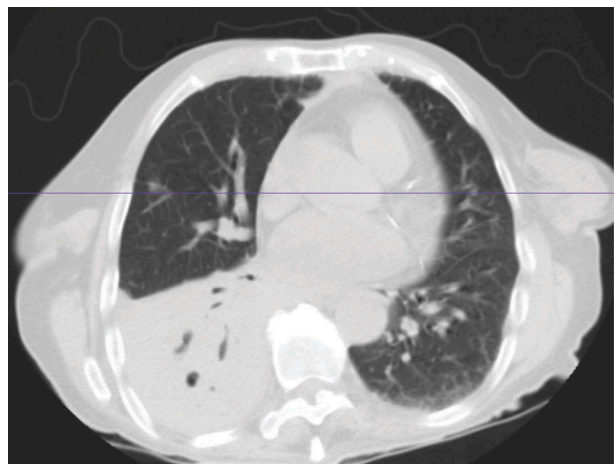
Thyroid function tests and iron studies were within normal limits. Chest x-ray (Figure 1) revealed right lower lobe consolidation and pleural effusion. In comparison, an old chest x-ray performed 3 years ago showed no active lung disease (Figure 2). Computerized tomography of the chest without IV contrast (Figure 3) on second day of hospital stay revealed moderate right-sided pleural effusion and right lower lobe consolidation. Treatment with levofloxacin was started. She was clinically stable and was discharged with a plan to continue antibiotic for total duration of 7 days. She was scheduled for follow up with chest clinic in 2 weeks. The patient came back after 2 months for follow up at chest clinic. She reported unchanged cough and worsening shortness of breath. Since her symptoms were worsening, she was admitted to the hospital for further evaluation. On the second hospital admission vital signs were stable, chest CT scan (Figure 4) revealed no significant change in complete consolidation of right lower lobe as compared to previous chest CT scan there was a moderate right-sided pleural effusion and new right upper lobe infiltrate. Abdomen and pelvis CT scan revealed homogeneous attenuation of the liver. Size and contour were maintained with no focal lesions, the pancreas was intact without ductal dilatation, the spleen was normal in size, the adrenal glands were intact, no enlarged lymph nodes were found, no ascites was present and no worrisome osseous lesions were demonstrated. PET/CT scan revealed 2.5 cm infiltrate in right upper lobe and another larger lesion in right lower lobe, both with significant uptake. Moderate right pleural effusion. Bronchoscopy showed polypoid nodularities surrounded by black discoloured mucosa in the sub-segmental bronchi of the right lower lobe, transbronchial biopsy specimen revealed minute fragments of



**Figure 1.** Chest x-ray: Right lower lobe consolidation with right-side pleural effusion.



**Figure 2.** Chest x-ray: No evidence of active lung disease.



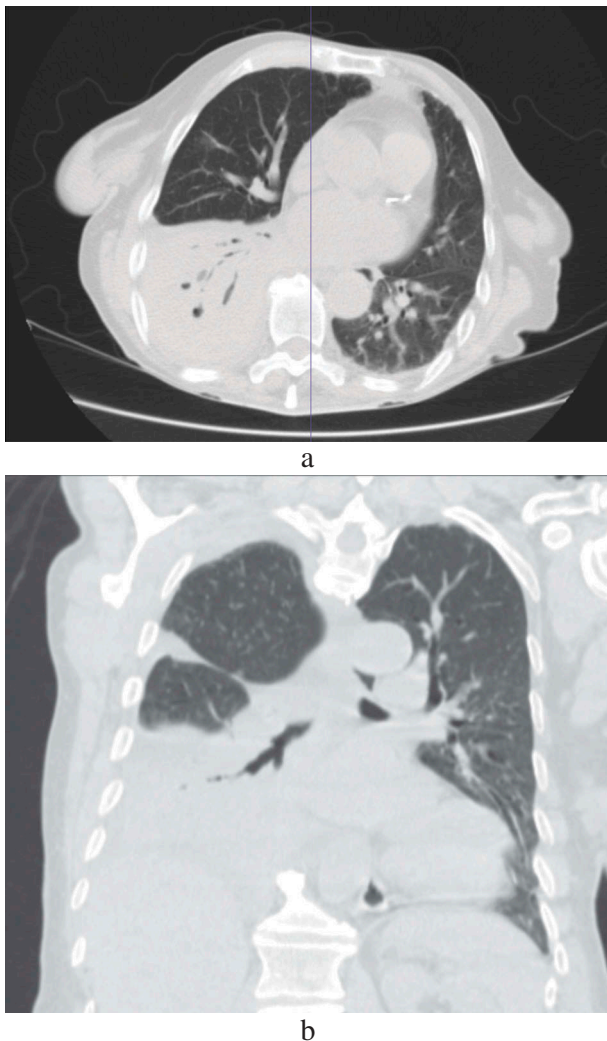
a



b

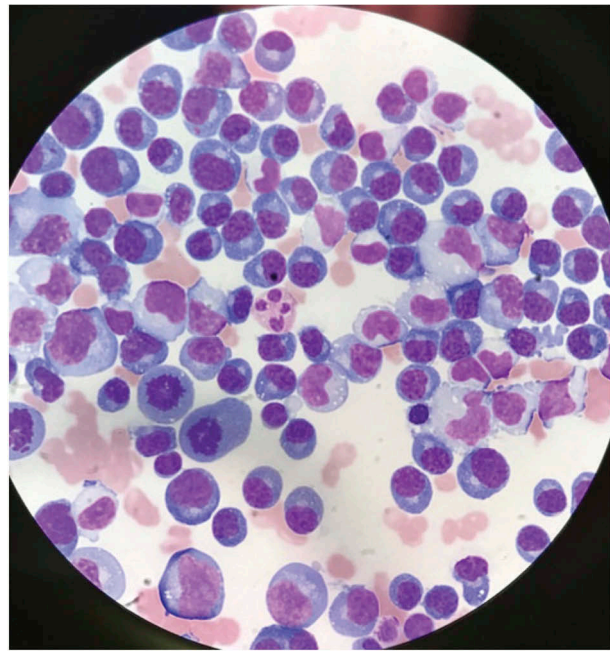
**Figure 3.** (a) Chest CT scan-axial view. (b) Chest CT scan-coronal view. (a&b). Chest CT scan: Moderate right pleural effusion and right lower lung Consolidation.





**Figure 4.** (a) Chest CT scan-axial view. (b) Chest CT scan-coronal view. (a&b) Chest CT scan: No significant change in complete consolidation of the right lower lobe as compared to previous Chest CT scan and moderate right-side pleural effusion.

respiratory epithelium with atypical B cell-rich lymphocytes with no evidence of amyloid deposition. Polymerase chain reaction confirmed a clonal B cell gene rearrangement, findings suggestive of low-grade B cell lymphoma. Pleural fluid was sampled and analysis revealed straw-coloured fluid, pH 7.3, white blood cell count of 6400 cells, red cell count of 3750, fluid albumin of 2.2 g/dl (serum albumin 3.0 g/dl), fluid lactate dehydrogenase 52 IU/L (serum lactate dehydrogenase 199 IU/l). Pleural fluid cytology (Figure 5) with immunophenotypic flow cytometry revealed plasmacytoid lymphocytes. Serum immunofixation and free light-chain analysis unveiled large quantity of monoclonal paraproteins which was classified as IgM Kappa immunoglobulin. Concentration of IgM was 1491 mg/dl (range 26–217 mg/dl) while IgG and IgA levels were normal. Urine contained free kappa light chains. The clinical picture, serum IgM paraprotein, bronchoscopy specimen findings and pleural fluid analysis led to the diagnosis of Extramedullary Waldenström's Macroglobulinemia. Patient was started on cyclophosphamide, prednisone



**Figure 5.** Pleural fluid cytology: Plasmacytoid lymphocytes.

and rituximab. Plan was to follow up with IgM level monthly and Chest CT scan after four months.

### 3. Discussion

Lymphoplasmacytic lymphoma/Waldenström Macroglobulinemia (LPL/WM) is an uncommon lymphoid neoplasm. The overall annual age-adjusted incidence of WM is 3.8 cases per million persons per year. It is nearly twice as common in males and whites as compared with females and non-whites, respectively [3].

It is predominantly a disease of elderly whites, with the median age range of 63–73 years at diagnosis. The incidence rate of WM is age dependent [4].

The median disease-specific survival of WM is estimated at 11 years [5].

The clinical manifestations of LPL/WM can be attributed to two main factors: the effects of the monoclonal IgM paraprotein and tissue infiltration by neoplastic cells.

Symptomatic hyperviscosity is seen in 10–30% of WM patients, and serum viscosity increases sharply at IgM concentrations of greater than 3 g/dL, with most patients manifesting symptoms at levels greater than 5 g/dL [6,7]. In our case; serum IgM concentration was less than 3 g/dL; therefore, the patient did not have symptoms of hyperviscosity.

Cryoprecipitation of the monoclonal IgM (type I cryoglobulinemia) may be seen in up to 20% of patients, with a minority of such patients exhibiting symptoms of Raynaud's phenomenon, acrocyanosis, or less frequently, renal manifestations [8,9]. In other patients, the monoclonal IgM may behave as a type II cryoglobulin and demonstrate IgG autoantibody activity,

leading to symptoms of purpura, arthralgias, renal insufficiency, and peripheral neuropathy [8,10].

Symptoms related to direct tissue infiltration by neoplastic cells is most commonly due to bone marrow involvement, which leads to peripheral cytopenias. Nodal and splenic involvement may be present. Extramedullary and extranodal sites of disease involvement by LPL that have been reported include lung, soft tissue, skin, gastrointestinal and hepatobiliary tracts, kidney and central nervous system (CNS) [11–14].

In a retrospective analysis of one single institution, 985 patients with WM were evaluated for extramedullary disease; and the result revealed only 4.4% (43 patients) had extramedullary disease, 21% of them (9 patients) had it at the time of diagnosis and 79% of them (34 patients) developed the extramedullary disease after therapy. Most frequent extramedullary sites involved were pulmonary (30%), cerebrospinal fluid (23%), soft tissue (21%), bone (9%), and renal (8%) [12].

Pulmonary involvement; seen in less than 5% of patients, may be in the form of nodules, masses, diffuse infiltrates or pleural effusions, and results in symptoms of cough (most commonly), dyspnea, and chest pain [12]. Lymphocytic pleural effusion is very rare [15]. Our patient had both lung and pleural involvement.

Gastrointestinal system involvement may present as bleeding, malabsorption, intestinal obstruction, diarrhoea, or bleeding. Central nervous system involvement is very rare and known as Bing–Neel syndrome, which classically presents with headache, diplopia, impaired hearing, vertigo, ataxia, and eventually coma. Periorbital and retro-orbital infiltration also have been reported [11].

Like most other low-grade B cell lymphomas, the clinical course in LPL/WM is generally indolent, with most patients experiencing slowly progressive disease and treatment refractoriness [8].

Treatment decisions of WM should not be based solely on serum monoclonal IgM levels, as it is more essential to treat symptomatic patients with bone marrow involvement and cytopenia, bulky adenopathy, organomegaly, soft-tissue mass, hyperviscosity, amyloidosis, severe neuropathy, cold agglutinin anaemia, or evidence of disease transformation. Treatment options are usually based on multiple factors; these factors include the need for rapid disease control, age, candidacy for autologous transplantation, comorbidities, presence of cytopenias, hyperviscosity, lymphadenopathy, IgM-related end-organ damage, and patients' preferences [16].

Patient with cytopenias, most commonly anaemia, and/or organomegaly; are usually treated with rituximab, cyclophosphamide and steroids [17]. Patient with symptomatic hyperviscosity, cold agglutininemia, or cryoglobulinemia can be treated initially with plasmapheresis then induction with bortezomib followed

by rituximab [18]. Patients with paraprotein-related nephropathy can be treated with plasmapheresis initially then with rituximab [19].

International Prognostic Scoring System for Waldenström macroglobulinemia (ISSWM) is based on the following risk factors: Age more than 65 years, Haemoglobin  $\leq 11.5$  g/dL, Platelet count  $\leq 100 \times 10^9/L$ , Serum B<sub>2</sub>-microglobulin  $> 3$  mg/L and Serum monoclonal protein  $> 70$  g/L. Low risk is defined by the presence of  $\leq 1$  adverse variable except age, intermediate risk by the presence of 2 adverse characteristics or age  $> 65$  years or high risk by the presence of  $> 2$  adverse characteristics. Based on these parameters, patient will be categorized into low, intermediate or high risk with 5-year survival rates of 87, 68, and 36%, respectively [20]. ISSWM score for our patient placed her at high risk since her age is more than 65 years, haemoglobin  $< 11.5$  g/dL and serum B<sub>2</sub>-microglobulin is  $> 3.0$  mg/L with a 5-year survival rate of 36%.

The median overall survival in large series ranges from 5 to 10 years, with variability in outcome reported based on a number of clinical and laboratory prognostic factors [20,21].

## Disclosure statement

No potential conflict of interest was reported by the authors.

## ORCID

Omar Abdulfattah  <http://orcid.org/0000-0002-7092-3631>

Sumit Dahal  <http://orcid.org/0000-0001-8199-709X>

## References

- [1] Sabattini E, Bacci F, Sagrmoso C, et al. WHO classification of tumours of haematopoietic and lymphoid tissues in 2008: an overview. *Pathologica*. 2010;102(3):83–87.
- [2] Gertz MA. Waldenstrom macroglobulinemia: 2015 update on diagnosis, risk stratification, and management. *Am J Hematol*. 2015;90(4):346–354.
- [3] Wang H, Chen Y, Li F, et al. Temporal and geographic variations of Waldenstrom macroglobulinemia incidence: a large population-based study. *Cancer*. 2012;118(15):3793–3800.
- [4] Boise LH, Kaufman JL, Heffner LT, et al. Changing epidemiology and improved survival in patients with Waldenstrom macroglobulinemia: review of surveillance, epidemiology, and end results (SEER) data. *Blood*. 2013;122(21):3135.
- [5] Ghobrial IM, Fonseca R, Gertz MA, et al. Prognostic model for disease-specific and overall mortality in newly diagnosed symptomatic patients with Waldenstrom macroglobulinaemia. *Br J Haematol*. 2006;133(2):158–164.
- [6] Kwaan HC. Hyperviscosity in plasma cell dyscrasias. *Clin Hemorheol Microcirc*. 2013;55(1):75–83.
- [7] Gertz MA, Kyle RA. Hyperviscosity syndrome. *J Intensive Care Med*. 1995;10(3):128–141.

- [8] Treon SP, Soumerai JD, Hunter ZR, et al. Long-term follow-up of symptomatic patients with lymphoplasmacytic lymphoma/Waldenstrom macroglobulinemia treated with the anti-CD52 monoclonal antibody alemtuzumab. *Blood*. 2011;118(2):276–281.
- [9] Harel S, Mohr M, Jahn I, et al. Clinico-biological characteristics and treatment of type I monoclonal cryoglobulinaemia: a study of 64 cases. *Br J Haematol*. 2015;168(5):671–678.
- [10] Cesana C, Barbarano L, Miqueleiz S, et al. Clinical characteristics and outcome of immunoglobulin M-related disorders. *Clin Lymphoma*. 2005;5(4):261–264.
- [11] Lin P, Bueso-Ramos C, Wilson CS, et al. Waldenstrom macroglobulinemia involving extramedullary sites: morphologic and immunophenotypic findings in 44 patients. *Am J Surg Pathol*. 2003;27(8):1104–1113.
- [12] Banwait R, Aljawai Y, Cappuccio J, et al. Extramedullary Waldenstrom macroglobulinemia. *Am J Hematol*. 2015;90(2):100–104.
- [13] Grewal JS, Brar PK, Sahijdak WM, et al. Bing-Neel syndrome: a case report and systematic review of clinical manifestations, diagnosis, and treatment options. *Clin Lymphoma Myeloma*. 2009;9(6):462–466.
- [14] Malkani RG, Tallman M, Gottardi-Littell N, et al. Bing-Neel syndrome: an illustrative case and a comprehensive review of the published literature. *J Neurooncol*. 2010;96(3):301–312.
- [15] Mansoor A, Wagner RP, DePalma L. Waldenstrom macroglobulinemia presenting as a pleural effusion. *Arch Pathol Lab Med*. 2000;124(6):891–893.
- [16] Dimopoulos MA, Kastritis E, Owen RG, et al. Treatment recommendations for patients with Waldenstrom macroglobulinemia (WM) and related disorders: IWWM-7 consensus. *Blood*. 2014;124(9):1404–1411.
- [17] Dimopoulos MA, Anagnostopoulos A, Kyrtsolis MC, et al. Primary treatment of Waldenstrom macroglobulinemia with dexamethasone, rituximab, and cyclophosphamide. *J Clin Oncol*. 2007;25(22):3344–3349.
- [18] Dimopoulos MA, Garcia-Sanz R, Gavriatopoulou M, et al. Primary therapy of Waldenstrom macroglobulinemia (WM) with weekly bortezomib, low-dose dexamethasone, and rituximab (BDR): long-term results of a phase 2 study of the European myeloma network (EMN). *Blood*. 2013;122(19):3276–3282.
- [19] Leger JM, Viala K, Nicolas G, et al. Placebo-controlled trial of rituximab in IgM anti-myelin-associated glycoprotein neuropathy. *Neurology*. 2013;80(24):2217–2225.
- [20] Morel P, Monconduit M, Jacomy D, et al. patients with the description of a new scoring system and its validation on 253 other patients. *Blood*. 2000;96(3):852–858.
- [21] Morel P, Duhamel A, Gobbi P, et al. International prognostic scoring system for Waldenstrom macroglobulinemia. *Blood*. 2009;113(18):4163–4170.