CASE REPORT

Waldenstrom's macroglobulinaemia: to treat or not to treat?

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SUMMARY

Waldenstrom's macroglobulinaemia (WM) is a rare lymphoproliferative disorder. It is mostly seen in the elderly population with a median age of 65 years at the time of diagnosis. The clinical presentation is variable and the patient may be entirely asymptomatic. The slow progressive nature of the disease allows many patients to survive for more than 5 years. At times it may be difficult for a clinician to determine the timing of therapy. We present an interesting case of WM that highlights the typical course of the disease and timing of its management.

BACKGROUND

Waldenstrom's macroglobulinaemia (WM) is an uncommon B-cell neoplasm characterised by IgM monoclonal gammopathy and infiltration of the bone marrow with malignant lymphoplasmacytic cells (LPCs). The disease has an indolent course and varying clinical presentation, hence it is important to determine the appropriate indications for treatment. We report an interesting case of WM.

CASE PRESENTATION

A 69-year-old man presented to us with painless swelling on the right side of the neck of 3 weeks duration. He denied having any oral ulceration, cough, dysphagia or B symptoms. On examination, he had an enlarged right cervical level II 2 cm×2 cm lymph node. Systemic examination was normal. On further questioning, he revealed that he was diagnosed as a case of lymphoproliferative disorder on routine health check-up in 2009 and was advised follow-up in an oncology centre. However, he declined and so did not have a detailed oncological evaluation. Past reports were reviewed. At that time he had leucocytosis with total leucocyte count (TLC) of 13 590/ μ L. Haemoglobin (Hb) and platelet counts were within normal range. Peripheral smear (PS) was reported as suggestive of mild lymphocytosis with morphology consistent with lymphoproliferative disorder. Serum immunoglobulin M (IgM) was elevated, 2410 mg/dL (normal range: 40–230).

INVESTIGATIONS

We again evaluated the patient in detail. He was found to have raised TLC (24 600/ μ L; 4000–11 000/mL), normal haemoglobin and platelet counts. Peripheral blood film revealed lymphocytosis with some atypical lymphoid cells. Liver function tests and kidney function tests were normal. Serum lactate dehydrogenase was elevated (355 U/L;

105–330 U/L). Aspiration cytology of the cervical lymph node showed features of reactive hyperplasia. Serum protein electrophoresis revealed an M-spike in the γ region (2.03 g/dL). Bone marrow evaluation by aspiration and trephine biopsy showed interstitial and nodular infiltration by atypical lymphoid and plasma-cytoid cells positive for CD79a, CD138 and kappa light chain on immunohistochemistry (figures 1 and 2). Immunoflow cytometry revealed a distinct population of atypical B-lymphoid cells, brightly positive for CD19, CD22, CD79a, CD45 and sIgM+, consistent with B-cell lymphoid disorder. Serum IgM was 1043 mg/dL (normal range: 40–230 mg/dL). Serum IgA and IgE were within normal limits. Serum β 2-microglobulin was 2649 ng/mL (normal range: 600–2360 ng/mL). Funduscopy was normal. Chest X-ray and ultrasonography of the abdomen were normal. The diagnosis of WM was established as per Waldenstrom's Macroglobulinemia International Workshop Criteria.¹ Since the patient was completely asymptomatic, no treatment was offered and he was kept on regular follow-up.

OUTCOME AND FOLLOW-UP

The patient reported to us 4 months later with pain and redness in the neck node. He denied any history of fever. The lymph node was of the same size as on his earlier visit but tender with erythema; no other lymph nodes were palpated. Systemic examination was normal. No sign or symptoms related to WM were appreciated. Blood counts and chemistries were within normal limits. Funduscopy was normal. The patient was advised antibiotics (amoxycylav and levofloxacin) for a period of 7 days. Pain and erythema reduced over a period of a few days and the patient became asymptomatic.

The patient was reviewed 3 months later. This time the neck node had increased in size to 4 cm×4 cm. Abdominal examination showed

Figure 1 Nodular infiltrates of the lymphoplasmacytoid cells in the marrow (H&E 10×10).

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Figure 2 Diffuse infiltration of B lymphoid cells decorated with CD79a immunostaining (40×10).

splenomegaly enlarged 3 cm below the costal margin. The patient's haemoglobin was 12.2 g/dL, TLC was 18 000/μL and platelet count was 300 000/mL (1.500 000–4.500 000/mL). At this point, in view of the progressive enlargement of lymph node and spleen, the patient was advised targeted monotherapy with rituximab. However, he refused and asked for time to decide. He was advised regular monthly follow-up.

DISCUSSION

WM is a rare B-cell disorder characterised by proliferation of small B lymphocytes and LPCs, accompanied by IgM paraproteinaemia and bone marrow infiltration. These two processes lead to its typical manifestations: hyperviscosity syndrome, vascular complication, infiltration of marrow and various organs. Waldenstrom's macroglobulinemia International Workshop Criteria for the diagnosis include an IgM monoclonal gammopathy of any concentration, bone marrow infiltration by small lymphocytes, plasmacytoid cells, plasma cells and a diffuse, interstitial or nodular pattern of bone marrow infiltration.¹ The incidence of WM has been estimated as three per million cases per year.² Though WM remains an incurable disease, the prognosis is highly variable and patients may survive for more than 10 years even without therapy. Patients with smouldering WM (WM without symptoms and signs of end-organ damage) and those who are asymptomatic, thus, do not require any treatment and so avoid the toxicities associated with chemotherapy. These patients usually have an indolent course. A wait and watch policy should be the standard of care and patients should be evaluated every 6 months. The consensus panel from the fourth international workshop on WM recommended that therapy should be initiated under the following circumstances: B symptoms; disease progression (progressive symptomatic lymphadenopathy, splenomegaly, anaemia (haemoglobin of ≤ 10 g/dL) and low platelet count ($<100 \times 10^9/L$); complications of paraprotein (hyperviscosity symptoms (ocular and neurological), neuropathy, amyloidosis, cryoglobulinaemia, renal insufficiency).³ The differential diagnoses for WM include an IGM-multiple myeloma, mantle cell lymphoma, follicular lymphoma and

marginal zone lymphoma. These can be distinguished on the basis of characteristics marrow findings and cytogenetics.

As per the international prognostic scoring system for WM, risk factors associated with poor prognosis are: age >65 years, β_2 -microglobulin >3 mg/L, monoclonal protein >70 g/L, haemoglobin <11.5 g/dL and platelet count <100 000/mL. Low-risk patients (27%) present with none or only one of the adverse characteristics and advanced age, intermediate-risk patients (38%) with two adverse characteristics and only advanced age and high-risk patients (35%) with more than two adverse characteristics.⁴

Our case gives good insight into the course of disease progression of WM and timing of its management. As the patient had raised IgM and an asymptomatic course since 2009, he most probably had smouldering WM. He had declined a detailed evaluation. He presented to us with a lump in the neck and a history of some lymphoproliferative disorder in the past; so we started detailed work up for later. A bone marrow evaluation, immunoflow cytometry and immunoglobulin profile confirmed the condition to be WM. However, the patient did not meet the criteria for treatment, was diagnosed as having smouldering WM and was kept in follow-up. Seven months following initial presentation, the progressively increasing size of lymph node and spleen justified treatment. However, the patient did not consent to it.

Learning points

- ▶ The clinical presentation and progress of Waldenstrom's macroglobulinaemia is highly variable.
- ▶ Asymptomatic patients should be followed regularly.
- ▶ The therapy is required only in patients presenting with symptoms, signs or laboratory findings as described above.

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Competing interests None.

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