CASE REPORT

'Transformation' from amyloid light chain amyloidosis to symptomatic multiple myeloma

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ABSTRACT

Amyloid light chain (AL) amyloidosis and multiple myeloma (MM) are both clonal plasma cell disorders, and may be concurrently present in patients. However, symptomatic MM seldom develops in patients with AL amyloidosis, while the other way around is common. With this case report, we discuss the difficulties in the differential diagnosis between AL amyloidosis and MM, and extend on the possible mechanisms involved in the development of these overlapping disorders. In addition, we provide clinicians with tools that may help improve their management and monitoring of such patients.

KEYWORDS

Amyloidosis, plasma cell dyscrasia, multiple myeloma

What was known about this topic?
AL amyloidosis and MM are both clonal plasma cell disorders. Although both may be concurrently present in a single patient, the development of symptomatic myeloma in AL amyloidosis patients is very rare.

What does this add?
Improved survival of patients with AL amyloidosis may result in the progression of smouldering to symptomatic MM. It is important for clinicians to be aware of this possibility. Especially bone pain should raise awareness and CT or MRI imaging should be used to detect collapsed vertebrae with or not yet with lytic bone lesions.

INTRODUCTION

Amyloid light chain (AL) amyloidosis and multiple myeloma (MM) are both part of the spectrum of plasma cell dyscrasias, in which malignant bone marrow residing plasma cells produce monoclonal proteins, sometimes composed of light chains only. AL amyloidosis is characterised by precipitation of monoclonal immunoglobulin light chain fragments as extracellular amyloid depositions in various tissues, causing organ dysfunction and subsequent disease manifestations.[1] MM is characterised by the CRAB criteria, consisting of hypercalcaemia, nephropathy, anaemia and bone disease.[2] Patients may present with both disorders simultaneously, and the distinction between the two may be very difficult. According to the literature, around 8% of the patients with AL amyloidosis also fulfill the CRAB criteria fitting the diagnosis of MM at the time the diagnosis AL amyloidosis is made, while 1 to 38% of patients diagnosed with MM may have amyloid deposits.[4,5] However, isolated amyloid detected in bone marrow or abdominal fat biopsy but without systemic amyloid deposits with organ dysfunction seldom develops into systemic AL amyloidosis and should therefore not to be considered as AL amyloidosis.[6] In the disease trajectory of patients with MM, approximately 10-15% will eventually develop AL amyloidosis,[7] while patients with AL amyloidosis very rarely develop symptomatic MM.

CASE REPORT

A 56-year-old man who presented with severe weight loss (30 kg in one year), diarrhoea, peripheral sensory neuropathy and orthostatic hypotension was diagnosed with AL amyloidosis. Kappa free light chains (FLC) were elevated to 384 mg/l (normal 3.30-19.40 mg/l) and the FLC ratio was 28.66 (normal 0.26-1.65). M protein was not detected. Amyloid depositions could be confirmed in myocardium, kidney, bone marrow and abdominal fat biopsies. Bone marrow examination showed a kappa positive plasmacytosis of 10%. At diagnosis no lytic bone lesions

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or collapsed vertebrae were seen on low dose CT-whole body scan and also no other CRAB criteria were present. Nevertheless, the presence of 10% monoclonal plasma cells may suggest smouldering MM with associated AL amyloidosis. Treatment of the patient with bortezomib and dexamethasone resulted in a very good partial response.

Two and a half years later, the patient presented with severe back pain and shorter statue. At this time point, low dose CT-whole body scan showed diffuse osteopenia and five collapsed vertebrae, additionally confirmed by total spine MRI scan. Bone marrow examination showed a plasmacytosis of 20% and kappa FLC was increased to 56.80 mg/l. He had no anaemia or hypercalcaemia, but progressive renal insufficiency and non-Bence Jones proteinuria were present. We concluded that the vertebral collapses were most likely due to development of symptomatic MM, although no lytic bone lesions were seen. He received melphalan and dexamethasone, combined with bisphosphonate therapy and again a very good partial response was achieved. Another five and a half years later his renal insufficiency further progressed (creatinine level 368 µmol/l, normal 64-104 µmol/l) and a second biopsy of the kidney confirmed increased amyloid depositions compared with the first biopsy. CT-whole body scan showed, apart from diffuse osteopenia, also a lytic lesion in vertebrae C5. Third-line treatment with endoxan and prednisone was started.

DISCUSSION AND CONCLUSION

In our case, without a confirming biopsy, it remains unclear whether the vertebral collapses were due to symptomatic MM or amyloid deposits in the bone. However, collapsed vertebrae due to AL amyloidosis is very rare, whereas it is a common complication in MM. Moreover, the lytic bone lesion seen some years later strengthens our hypothesis that our patient developed symptomatic MM, while initially having smouldering MM with an associated AL amyloidosis.

In the literature, we found eleven similar case reports of patients with AL amyloidosis who 'transformed' to MM.[8-10] The mean time between the diagnosis of AL amyloidosis and MM in these studies was 35 (range, 9-81) months and survival time after the diagnosis of MM ranged from less than a month to more than 48 months. There are similarities between the progression of monoclonal gammopathy of undetermined significance (MGUS) to MM and the progression of AL amyloidosis to MM.[8] MGUS always precedes MM, but can exist for years without clinical manifestation. Importantly, light chain MGUS is also capable of producing amyloid, and precipitation of these light chain fragments in tissues will result in tissue damage and clinical symptoms of amyloidosis, before abundant clonal proliferation of MM occurs.

In our patient we may conclude the possibility of a smouldering MM (eventually slowly progressing to MM) at the time of diagnosing AL amyloidosis. Difficulties in the differential diagnosis between AL amyloidosis and MM are due to partial overlap in diagnostic criteria. Patients with AL amyloidosis may present with a small number of monoclonal plasma cells in the bone marrow examination, but almost 40% of patients have more than 10% monoclonal plasma cells at the time of diagnosis and thus may be considered as having (smouldering) MM.

With improvement of the survival of patients with AL amyloidosis with the currently available treatment modalities, in the near future more patients may live long enough to develop symptomatic MM. Clinicians should be aware of this possibility and in addition to monitoring AL amyloidosis associated symptoms, also monitor patients for development of MM-induced organ damage such as bone fractures.

DISCLOSURES

The authors declare no conflict of interest.

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REFERENCES

1. Palladini G, Merlini G. What is new in diagnosis and management of light chain amyloidosis? Blood. 2016;128:159-68.
2. Rajkumar SV, Dimopoulos MA, Palumbo A, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. Lancet Oncol. 2014;15:e538-48.
3. Kourelis TV, Kumar SK, Gertz MA, et al. Coexistent multiple myeloma or increased bone marrow plasma cells define equally high-risk populations in patients with immunoglobulin light chain amyloidosis. J Clin Oncol. 2013;31:4319-23.
4. Siragusa S, Morice W, Gertz MA, et al. Asymptomatic immunoglobulin light chain amyloidosis (AL) at the time of diagnostic bone marrow biopsy in newly diagnosed patients with multiple myeloma and smoldering myeloma. A series of 144 cases and a review of the literature. Ann Hematol. 2011;90:101-6.
5. Desikan KR, Dhodapkar MV, Hough A, et al. Incidence and impact of light chain associated (AL) amyloidosis on the prognosis of patients with multiple myeloma treated with autologous transplantation. Leuk Lymphoma. 1997;27:315-9.
6. Chakraborty R, Gertz MA, Disperzieri A. Natural history of amyloidosis isolated to fat and bone marrow aspirate. Br J Haematol. 2017;179:170-2.
7. Kyle RA. Multiple myeloma and other plasma cell disorders. In: Hematology: basic principles and practice. 2[nd] edition. 1995. p. 1354-74.
8. Rajkumar SV, Gertz MA, Kyle RA. Primary systemic amyloidosis with delayed progression to multiple myeloma. Cancer. 1998;82:1501-5.
9. Hoffman J. AL amyloidosis and progression to multiple myeloma with gain (1q). Br J Haematol. 2008;144:963-4.
10. Rodrigues L, Neves M, Sá H, et al. Clinical challenges of an oligosecretory plasma cell dyscrasia. Br Med J Case Rep. 2013;1-4.