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Association of Multiple Myeloma and Giant Cell Arteritis – A Case Report

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ABSTRACT

Autoimmune diseases (AID) have been associated with a variety of lymphoproliferative disorders. Multiple myeloma (MM), one of the most common haematologic malignancies characterized by clonal proliferation of bone marrow plasma cells, has been associated with a range of autoimmune disorders. In this report, we described a case study of a patient admitted to our Internal Medicine Department for a bone marrow biopsy and myelogram due to a monoclonal peak observed by his general practitioner. However, at admission he presented typical giant cell arteritis (GCA) complaints, suggesting the coexistence of both diseases. The possible pathogenesis, as found in the literature, explaining the association will be discussed.

LEARNING POINTS

- A relationship between AID and lymphoproliferative diseases, although rare, may occur and some studies suggest that the diagnosis of autoimmune disease has a negative impact on survival in MM patients.
- Bone marrow plasmacytosis can present a diagnostic dilemma, since it may be due to neoplastic or non-neoplastic conditions (that is, reactive plasmacytosis associated with AID, chronic infection, metastatic carcinoma, liver diseases and acquired immunodeficiency).
- Immunophenotyping in a myelogram or immunohistochemistry in bone marrow studies are useful in confirming a monoclonal plasma cell proliferation.

KEYWORDS

Giant cell arteritis, multiple myeloma, autoimmunity

INTRODUCTION

Multiple myeloma (MM) is a plasma cell disorder characterized by clonal proliferation of bone marrow plasma cells[1]. The aetiology is poorly understood but there is some evidence that immune dysregulation or sustained immune stimulation plays an important role in the pathogenesis of this disease. Therefore, the incidence of MM or monoclonal gammopathy of undetermined significance (MGUS) is higher in patients with a history of autoimmune diseases (AID)[2,3]. Giant cell arteritis (GCA) is a chronic vasculitis of medium- and large-sized vessels that involves particularly extracranial branches of the aortic arch arteries. There is a higher incidence in patients over 50 years of age and it is usually characterized by headaches, fatigue, low-grade fever, jaw claudication during mastication, loss of vision, scalp tenderness, polymyalgia and acute loss of vision[4]. The relationship between AID and lymphoproliferative diseases is described in the literature.

CASE DESCRIPTION

A 78-year-old man was admitted to our Internal Medicine Department for bone marrow biopsy and aspiration due to monoclonal protein observed by his general practitioner. At admission, the patient presented complaints of strong frontal headache, pain in the ear–jaw articulation that was worse during mastication and visual changes. He also reported loss of weight, arthralgias and night sweats. He had

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a medical history of high blood pressure, diabetes mellitus type 2 and dyslipidaemia. Physical examination revealed scalp tenderness on palpation, jaw claudication on mastication and diplopia. His vital signs were normal. The blood work revealed moderate normochromic normocytic anaemia, slightly elevated calcium and an elevated erythrocyte sedimentation rate (ESR). An IgG/kappa peak was observed on serum protein electrophoresis and bone marrow aspirate was assessed, revealing 26% clonal bone marrow plasma cells (*Table 1*). This result was compatible with smouldering MM, since there were no CRAB criteria present.

Parameter	*Results at admission*	*Results after discharge*
Haemoglobin (g/dl)	*11.3*	*13.1*
Leucocytes (10^9/l)	*6.5*	*10.1*
Platelets (10^9/l)	*274*	*278*
ESR (mm/h)	*129*	*45*
Calcium (corrected – mg/dl)	*10.9 mg/dL*	*10.5 mg/dL*
Creatinine (mg/dl)	*1.1*	*1.2*
C-reactive protein (mg/dl)	*9*	*15*
IgG (g/l)	*29.8*	
IgA (g/l)	*1.75*	
IgM (g/l)	*0.5*	
Light chain κ (g/l)	*846*	
Light chain λ (g/l)	*99*	
Free light chain (FLC) ratio	*8.55*	
β2-microglobulin (mg/l)	*4.37*	
ANA	*negative*	
ANCA	*negative*	
HIV	*negative*	
Bone marrow aspirate	*26.2% clonal bone marrow plasma cells*	
Temporal artery biopsy	*Revealed fibrinoid necrosis tissue*	

Table 1. Laboratory results

Due to visual impairment, ophthalmology consultation was requested and the patient immediately started intravenous corticoid treatment. After several days of treatment, there was clinical improvement with resolution of the headache and diplopia and the patient was able to eat with no pain; analytically, the ESR decreased. Temporal artery biopsy was carried out which revealed unspecific histological changes; bone marrow biopsy produced insufficient material for analysis. The patient was later discharged with no symptoms and referred to rheumatologist and haematologist consultations, for monitoring progression of MM and GCA. Since the patient refused to repeat the bone marrow biopsy, was asymptomatic and had no criteria to start treatment due to smouldering MM, bone marrow biopsy was not repeated, and therefore, it was not possible to realize immunohistochemical studies. Immunophenotyping using a myelogram is not possible to conduct in our hospital.

DISCUSSION

Although temporal artery biopsy gave unspecific findings, the diagnosis of GCA cannot be excluded since, according to some authors, 70% of patients with temporal arteritis may have normal findings on a temporal artery biopsy[2]. In this case, the ESR may have been elevated due to GCA or MM. However, since the patient was over 50 years of age, had new-onset localized headache, temporal artery tenderness and had other key symptoms of active large vessel vasculitis such as sudden onset of visual disturbances, jaw claudication and a good clinical and analytical response to therapy, a diagnosis of GCA was assumed according to the 1990 ACR criteria (*Table 2*) and the 2018 Update of the EULAR recommendations[4, 5].

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Criteria	Definition
Age at disease onset ≥50 years	Development of symptoms or findings beginning at age 50 or older
New headache	New onset or new type of localized pain in the head
Temporal artery abnormality	Temporal artery tenderness to palpation or decreased pulsation, unrelated to arteriosclerosis of cervical arteries
Elevated erythrocyte sedimentation rate	Erythrocyte sedimentation rate ≥50 mm/hour
Abnormal artery biopsy	Abnormal artery biopsy showing vasculitis with mononuclear cell or granulomatous inflammation, usually with giant cell infiltrates

Table 2. 1990 ACR criteria for the classification of giant cell (temporal) arteritis

For purposes of classification, a patient shall be said to have giant cell (temporal) arteritis if at least 3 of these 5 criteria are present. The presence of any 3 or more criteria yields a sensitivity of 93.5% and a specificity of 91.2%.

Our patient manifested a monoclonal IgG/kappa peak on serum protein electrophoresis, a bone marrow aspirate revealing 26% clonal bone marrow plasma cells and no CRAB criteria. Unfortunately, the bone marrow biopsy was inconclusive (due to insufficient material) raising the suspicion of smouldering MM, according to the 2014 International Myeloma Working Group updated criteria for the diagnosis of MM[1]. It should be noted that other pathologies such as AID, chronic infections, metastatic carcinoma, liver diseases or acquired immunodeficiency syndrome may be associated with reactive plasmacytosis. Reactive plasmacytosis is a rare condion which is usually associated with a polyclonal gammopathy. Immunohistochemical staining or immunophenotyping studies may help to distinguish the monoclonal gammopathies from reactive plasmacytosis[6,7]. In this case, a preliminary diagnosis of MM was made; however, it was not possible to perform immunohistochemical or immunophenotyping studies.

Although the pathogenesis associating MM and autoimmunity is still not clear, some hypotheses were raised. On the first hand, there could be a spontaneous transformation of clonal B cells, which later on undergo physiological maturation and produce autoantibodies, thereby explaining the autoimmune manifestations. On the other hand, it appears that autoimmunity favours the escape of abnormal clones of B cells from regulatory mechanisms, leading to the emergence of neoplastic B cell clones[8]. Other authors have reported a relationship between MM and GCA and hypothesized that they may have a common inflammatory process. Particularly, GCA may be related to an immune response secondary to the production of cytokines in MM or due to amyloid deposits secondary to MM[9].

A study conducted by Lindqvist et al. (2017) suggested that a history of AID has a negative impact on the survival of patients with MM. These authors hypothesized that this may be due to the sharing of underlying genetic factors, or that patients with AID may develop more severe forms of MM or it may simply be due to the cumulative comorbidity of the diseases[4].

The unusual association between these 2 entities, their negative impact with respect to outcome for the patient, and the difficulty in distinguishing the plasmacytosis associated with the diseases, compel the authors to share this case.

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