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CASE REPORT
ΕΝΔΙΑΦΕΡΟΥΣΑ ΠΕΡΙΠΤΩΣΗ

Fever of unknown origin as the only manifestation of multiple myeloma
A case report

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Πυρετός άγνωστης αιτιολογίας ως η μόνη εκδήλωση του πολλαπλού μυελώματος: Μια ενδιαφέρουσα περίπτωση

Περίληψη στο τέλος του άρθρου

Infection is the most usual cause of fever in multiple myeloma (MM), but only a few reports have described fever of unknown origin (FUO) as the first manifestation of MM. We present the case of a 67-year-old female with FUO as the only manifestation of MM. In contrast to previously published reports, our patient had no other signs of MM, such as hypercalcemia, renal insufficiency, anemia or bone lesions, nor was her fever attributed to an infection. She presented with FUO, and was found to have leukocytosis, thrombocytosis and raised C-reactive protein (CRP), and the diagnosis of MM was established on bone marrow biopsy. After excluding the usual causes of FUO, therefore, MM might also be considered in its differential diagnosis.

Key words

Fever of unknown origin
Multiple myeloma
Plasma cell myeloma

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Multiple myeloma (MM) accounts for approximately 1 to 2% of all neoplasms and more than 17% of hematological malignancies in the United States, whereas its annual incidence is estimated at 4–5 cases per 100,000.[1,2] Patients with MM usually present with anemia and bone pain, while fever is a common manifestation of infections related with immuno-paresis.[3]

Here we describe the case of a female who presented with a fever of unknown origin (FUO) with none of the frequent clinical or laboratory findings indicative of MM.

CASE PRESENTATION

A 67-year-old woman was referred to our tertiary hospital with a 25-day history of fever up to 38.5 °C, with no other symptoms. She had been admitted to another hospital 10 days earlier, where she was treated with broad spectrum antibiotics, but with no fever resolution.

The patient's medical history included arterial hypertension, diabetes mellitus (DM), hyperthyroidism, diverticulosis, cholelithiasis and osteoarthritis of the knee. She reported no symptoms other than fever. On physical examination, no abnormal findings were found except for a known systolic murmur (2/6) at the right upper sternal border.

On admission to our department, complete blood count revealed leukocytosis 14.2×10^9/L (neutrophils 68%, lymphocytes 21.3%, monocytes 9.1%, eosinophils 1.1%, basophils 0.3%), thrombocytosis (platelets 530×10^9/L), hemoglobin (Hb) 12.2 g/dL, and erythrocyte sedimentation rate (ESR) 48 mm/h. The peripheral blood smear revealed rouleaux formation of the red blood cells. Laboratory tests showed marked hypergammaglobulinemia (IgG 4.7 g/dL) and raised C-reactive protein (CRP), 350 mg/L (normal range 0–6 mg/L).

Serial blood and urine cultures were sterile during her hospitalization and no antibiotics were administered. Serological tests for viral and microbial infections were negative. Procalcitonin level was normal, and extensive immunological tests were negative.

Other tests showed: lactate dehydrogenase (LDH) 504 U/L (normal range 115–230 U/L) and β2-microglobulin 3,508 μg/L (normal range 700–3,400 μg/L). Full body computed tomography (CT) was unremarkable and skeletal X-ray survey revealed no lytic lesions. Transesophageal ultrasonography (US) of the heart was negative for endocarditis. Temporal artery biopsy revealed no pathological evidence of arteritis.

Despite the absence of anemia, renal failure and hypercalcemia, MM was suspected because of the presence of rouleaux in the peripheral blood smear and hypergammaglobulinemia. Subsequent tests revealed increased IgA levels (1,140 mg/dL, reference range: 82–453 mg/dL) and κ/λ chains ratio 3.65. Protein electrophoresis revealed a monoclonal band in the gamma region and immunofixation was consistent with the presence of IgA-κ. Bone marrow aspirate showed presence of plasma cells in a percentage of 17%, but the bone marrow biopsy revealed 85% infiltration by immature plasma cells of the IgA-κ type, and the diagnosis of MM was made. Based on the serum albumin of 2.9 g/dL and β2-microglobulin of 3,508 μg/L, the International Staging System (ISS) stage was II. The cytogenetic picture was normal (karyotype 46, XX), fluorescence *in situ* hybridization (FISH) analysis for t(4;14), t(14;16) and delp53 was negative, but the raised LDH was consistent with revised-ISS stage II. Serum free κ chains were 16.5 mg/dL and serum free λ chains were 1,470 mg/dL (ratio involved/uninvolved=89).

Because of the presence of bone marrow plasma cells ≥60%, the patient was treated with bortezomib, cyclophosphamide and dexamethasone, with a plan to proceed to autologous bone marrow transplantation.

DISCUSSION

In contrast to previously published reports,[4,5] we are the first to describe a patient presenting with FUO as the only manifestation of MM.

Our patient presented with fever, thrombocytosis and marked elevation of CRP with no underlying infection. These findings could be attributed to increased levels of interleukin (IL)-6, which is often mentioned as the plasma cell growth factor, plays a major role in the pathophysiology of neoplastic fever, and induces increased thrombopoietin production.[6–8] The neutrophilic leukocytosis noted in our patient could be considered as a plasma cell-related neutrophilic leukemoid reaction attributable to cytokine release by neoplastic plasma cells.[9]

To the best of our knowledge, we are the first to report FUO as the only manifestation of MM. Despite the limitations of a single case report, along with the fact that an infectious disease could not be definitely excluded, our findings could endorse future studies to investigate whether MM should be included in FUO differential diagnosis.

ΠΕΡΙΛΗΨΗ

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Η λοίμωξη είναι η πλέον συνήθης αιτία πυρετού στο πολλαπλό μυέλωμα. Ωστόσο, λίγες μόνο αναφορές έχουν περιγράψει τον πυρετό άγνωστης αιτιολογίας (FUO) ως την πρώτη εκδήλωση του πολλαπλού μυελώματος. Παρουσιάζεται μια 67χρονη γυναίκα με FUO ως τη μόνη εκδήλωση του πολλαπλού μυελώματος. Σε αντίθεση με προηγούμενες δημοσιεύσεις, η ασθενής δεν είχε άλλες εκδηλώσεις πολλαπλού μυελώματος, όπως υπερασβεστιαιμία, νεφρική ανεπάρκεια, αναιμία, οστικές βλάβες, ούτε ο πυρετός της αποδόθηκε σε λοίμωξη. Αντίθετα, εμφάνισε FUO, λευκοκυττάρωση και θρομβοκυττάρωση. Συνεπώς, μετά τον αποκλεισμό των συνηθισμένων αιτιών του FUO, το πολλαπλό μυέλωμα μπορεί επίσης να ληφθεί υπ' όψιν στη διαφορική διάγνωσή του.

Λέξεις ευρετηρίου: Πλασματοκυτταρικό μυέλωμα, Πολλαπλό μυέλωμα, Πυρετός άγνωστης αιτιολογίας

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