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Case study

Transient monoclonal gammopathy induced by *Candida* fungemia

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Summary A 41-year-old woman was admitted for *Candida* fungemia. On hospital day 4, a routine complete blood count and peripheral smear showed circulating plasma cells. Initial workup showed an M-component on serum protein electrophoresis with 6% λ-predominate plasma cells by flow cytometry. The patient was treated with intravenous antifungal therapy. Her 6-month follow-up laboratory evaluation revealed resolution of the M-component and only rare polyclonal plasma cells in peripheral blood by flow cytometry. This case illustrates that transient monoclonal gammopathy can be induced by fungal infection. It is important to exclude a plasma cell neoplasm or a B-cell lymphoma and to follow the patient until resolution of abnormal findings.

1. Introduction

The presence of a monoclonal immunoglobulin (M-protein) typically suggests a plasma cell neoplasm or a B-cell malignancy. If the M-protein is less than 3 g/dL, bone marrow clonal plasma cells are <10%, no end-organ damage is present, and there is no evidence of a B-cell lymphoma, a diagnosis of monoclonal gammopathy of undetermined significance (MGUS) is made [1]. There have been documented cases of MGUS associated with infections caused by bacteria such as *Staphylococcus aureus* [2] and *Bartonella quintana* [3] and viruses including cytomegalovirus [4] and human immunodeficiency virus [5]. To our knowledge, there have not been reported cases of transient MGUS associated with fungal infections. Here, we report a case of transient MGUS found incidentally in a patient during hospitalization for *Candida albicans* fungemia.

2. Materials and methods

2.1. Case presentation

A 41-year-old woman presented to the emergency department with fever, myalgias, dyspnea, cough, and a skin rash. Her medical history is significant for a Roux-en-Y gastric bypass surgery that was followed by chronic abdominal pain and multiple abdominal surgical procedures. She subsequently developed short gut syndrome and was put on long-term total parenteral nutrition. She was admitted to the hospital for sepsis. A chest computed tomography showed evidence of pneumonia, and she was treated with antibiotics. Blood cultures grew *C albicans*. *Candida* fungemia was presumed to be from her total parenteral nutrition port, which was removed.

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On day 4 of her hospital stay, she was found to have 16.5% circulating plasma cells (white blood cell 20 800/mm^3, absolute plasma cell count 34 000/mm^3) and normocytic anemia (hemoglobin 11.4 m/dL, hematocrit 34%, mean corpuscular volume 95 fL) on a routine complete blood count and subsequent smear review (Fig. 1). Retrospectively, a peripheral smear was reviewed at time of admission, and there were no circulating plasma cells at that time. Serum protein electrophoresis (SPEP) was then performed and showed an M-component, and follow-up serum immunofixation electrophoresis (IFE) demonstrated 2 M-components, both IgG λ, measuring 0.73 g/dL and trace. β-2 microglobulin was elevated at 3.9 mg/L. By flow cytometric analysis, 6% of total cells were plasma cells with expansion of those expressing cytoplasmic λ with a κ/λ ratio of 1:3. This finding raised the possibility of a plasma cell neoplasm or a B-cell lymphoma. There was no monoclonal B-cell population detected by flow cytometric analysis, and the patient did not have lymphadenopathy or organomegaly to suggest a B-cell lymphoma. Multiple myeloma fluorescence in situ hybridization (FISH) panel was performed and showed a normal hybridization pattern.

The patient did not have bone pain, pathologic features, kidney failure, or hypercalcemia. Hematology/oncology service was consulted, and a diagnosis of MGUS, likely secondary to infection, was rendered. They recommended follow-up during hospital stay and periodic long-term follow-up every 6-12 months. They did not feel that a bone marrow biopsy was warranted during this hospitalization. Serial peripheral blood smears performed on subsequent days while the patient was in the hospital demonstrated a gradually decreasing leukocyte trend with decrease in circulating plasma cells.

The patient was placed on intravenous fluconazole, stabilized, and discharged home with a peripherally inserted central catheter in place. She received fluconazole for 2 months. Six months after the diagnosis of MGUS, a follow-up peripheral smear and flow cytometric analysis showed rare polyclonal plasma cells, and SPEP showed no M-component.

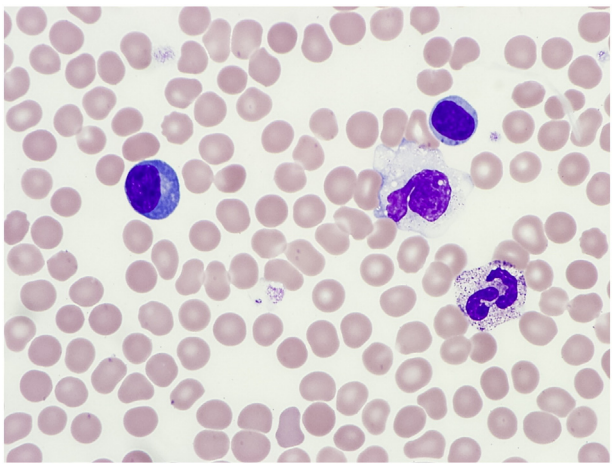

Fig. 1 Circulating plasma cells (original magnification ×400).

2.2. Flow cytometry

Flow cytometric analysis was performed on peripheral blood. The following antibodies were analyzed: CD5, CD10, CD19, CD20, CD34, CD38, CD49d, CD45, CD56, CD138, CD200, κ, λ, cytoplasmic κ, and cytoplasmic λ (BD Biosciences).

2.3. Serum protein electrophoresis and immunofixation electrophoresis

SPEP was performed by capillary electrophoresis with fractionation into 5 protein zones: albumin, α1, α2, β, and γ, with quantitative evaluation of M-proteins (Sebia). IFE was performed on agarose gel electrophoresis with antisera for IgG, IgA, IgM, κ, and λ (Sebia).

2.4. Fluorescence in situ hybridization

Multiple myeloma FISH panel was performed on direct cell preparation obtained from peripheral blood. This panel was designed to detect 2 common translocations, t(4;14) and t(14;16); gain or loss of 1p32.3 and 1q21.3; chromosome 17 aneuploidy; and deletion of 17p/TP53. The probes used were *CDKN2C, CKS1B; FGFR3, IGH; IGH, MAF;* and *D17Z1, TP53* (Abbott Molecular, Inc).

3. Results

3.1. Flow cytometry

Flow cytometric analysis performed during hospitalization showed a population of plasma cells that comprise 6% of total events; expressed bright CD38, CD138, and dim CD19; and were negative for CD56 (Fig. 2B). These plasma cells showed a cytoplasmic κ/λ ratio of 1:3, consistent with expansion of λ plasma cells. It also raised the possibility of biclonal plasma cell populations. Morphologic examination of the cytospin demonstrated a population of atypical plasma cells that were enlarged in size and had prominent nucleoli. Follow-up flow cytometric analysis 6 months later showed rare polyclonal plasma cells (Fig. 3B).

3.2. Serum protein electrophoresis and immunofixation

SPEP performed during hospitalization showed 2 M-components: 0.73 g/dL (M Comp 1) and trace (M Comp 2) (Fig. 2A). Both M-components were IgG λ by IFE (Fig. 2A, inset). SPEP performed 6 months later showed no M-component (Fig. 3A).

3.3. Fluorescence in situ hybridization

Multiple myeloma FISH panel showed a normal hybridization pattern (negative for t[4;14][p16.3;q32] *FGFR3/IGH* fusion; negative for deletion/aneuploidy of the *TP53* gene,