

Concurrent Multiple Myeloma, Sickle-Cell Disease and Diabetes Mellitus: A case report

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RESUMEN

Hay muy pocos informes acerca de la asociación de anemia drepanocítica y diabetes mellitus. Se ha discutido la posibilidad de que la concurrencia de diabetes con drepanocitosis homocigota tenga relación con la mayor esperanza de vida de los pacientes falcémicos. Hasta donde hemos podido investigar, no encontramos casos de ocurrencia sincrónica de drepanocitosis, mieloma múltiple y diabetes mellitus. Se reporta un caso en el que esto ocurrió y se discuten sus posibles explicaciones.

Palabras clave: mieloma múltiple, anemia drepanocítica, diabetes mellitus.

ABSTRACT

There are a few reports of the association of sickle cell disease and diabetes mellitus but there are no satisfactory explanations for the uncommon association of these two diseases. One explanation is that the majority of patients with sickle cell anemia died early, therefore, a relatively small number of patients survived for the clinical manifestation of diabetes. The association of sickle cell disease, diabetes mellitus and multiple myeloma, to the best of our knowledge has not been reported before; we describe here the association of these three conditions.

Key words: Multiple myeloma, sickle-cell disease, anemia, diabetes mellitus.

Hematological malignancies in adults with SS and SC disease were thought to be extremely rare until thirty years ago. One explanation for the paucity of reported malignancy was that these patients succumbed to complications of their disease before they had a chance to develop neoplastic disorders (Nicoleau et al, 1999). Concurrent sickle-cell disease (SCD) and diabetes mellitus (DM) is also rare (Mohapatra, 2005). Here we report the case of a patient with hemoglobin SC disease, multiple myeloma (MM) and DM.

CASE PRESENTATION

On January 2011 a 58-year-old man with a medical history of type 2 DM treated with glibenclamide, presented to the emergency department with fatigue, fever, pallor, jaundice, respiratory symptoms, mild mental status changes and pain and edema of the right leg. Admission laboratory values included a Hb level of 6.0 g/dL, reticulocyte count of 5.6 percent, white cell (WBC) count of $6.9 \times 10^9/L$, a platelet (PLT) count of $256 \times 10^9/L$, erythrocyte sedimentation rate (ESR) level of 145 mm/h, glucose level of 12.5 mmol/L, creatinine level of 1.2 mg/dL, albumin level of 28 g/L, total protein level of 95 g/L and serum viscosity level of 4.5. The patient was immediately treated with antibiotic therapy and fluids. Further evaluation led to a diagnosis of multiple myeloma based on the presence of an abnormal monoclonal band by serum immunofixation electrophoresis corresponding to monoclonal immunoglobulin A (IgA kappa). At that time, serum IgA values were 4.6 g/dl, and serum beta-2-microglobulin was 4.2 ng/ml. Hemoglobin electrophoresis showed HbSC. Anisopoikilocytosis, target cells, rouleaux formation,

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Este artículo debe citarse como: Ramón Rodríguez L, Espinosa Estrada E, Ávila Cabrera O, Izquierdo Cano L, Gutiérrez Díaz A, Hernández Padrón C. Concurrent Multiple Myeloma, Sickle-Cell Disease and Diabetes Mellitus: A case report. Rev Hematol Mex 2012;13(1):36-38.

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polychromasia, and basophilic stippling was found in the peripheral blood smear. An increase in normoblast and sixty percent plasma cell infiltration was found in the bone marrow aspiration. A marrow biopsy revealed sheets of CD138+ and kappa__ plasma cells. Chest x-rays showed bilateral bronchopneumonia with pleural effusion, skeleton CT-scan revealed disseminated osteolytic lesions without encephalic damage, and the echo-doppler of the right leg showed a popliteal deep vein thrombosis (DVT). At that time several diagnoses were made including uncompensated DM, SCD (hemoglobin SC disease), acute chest syndrome, MM stage IIIA, hyperviscosity syndrome, and DVT. Neurological symptoms disappeared after a blood exchange transfusion and serum viscosity returned near to normal. The patient began therapy for multiple myeloma consisting of melphalan, prednisolone and zoledronic acid. The supportive treatment consisted of antibiotics, insulin, intravenous Immunoglobulin, erythropoietin, ferrous fumarate, vitamin D, calcium carbonate, low molecular weight heparin, and warfarin. After 6 months of melphalan and prednisolone, warfarin was stopped and serum IgA levels were reduced to 2.1 g/dl. Other laboratory studies showed an Hb level of 9.2 g/dL, ESR level of 49 mm/h, albumin level of 37 g/L, total protein level of 83 g/L and the bone marrow aspirate showed 30 % of plasma cells. Then, a partial response was achieved. After twelve months the patient has already completed chemotherapy and he is on reevaluation. His quality of life is good and no symptoms of MM or SCD have been manifested. DM is under control with a daily dose of insulin.

DISCUSSION

Malignancy in patients with SCD has been previously reported, but the types of cancer and their incidence remain undefined. The International Association of Sickle Cell Nurses and Physician Assistants identified 52 cases of cancer (49 patients) among 16,613 patients with SCD, followed at 52 institutions (Schultz & Ware, 2003). The association of MM and SCD has been reported in thirteen cases (Talerman et al, 1971; Anderson et al, 1975; Sarma et al, 1986; Stricker et al, 1986; Nicoleau et al, 1999; Kaloterakis et al, 2001; Schultz & Ware, 2003; Tormey et al, 2008). There is probably no link between these two diseases since their association is rare.

There are a few reports of the association of SCD and DM (Miodovnik et al, 1987; Reid et al, 1990; Adekile et al, 1991; Koduri et al, 1994; Mohapatra, 2005) but there are no satisfactory explanations for the uncommon association of these two diseases. One explanation is that the majority of patients with sickle cell anemia died early, therefore, a relatively small number of patients survived for the clinical manifestation of diabetes (Adekile et al, 1991). Another explanation is genetic. In support of this hypothesis is the fact that both the α -globin and the insulin genes are present in short arm of chromosome 11 (Morrison et al, 1979). It is not known whether the genetic loci of insulin and α -globin have any inhibitory effect on the inheritance pattern or penetrance of the other. Therefore, the relationship between diabetes mellitus and sickle cell anemia needs further evaluation.

Blood viscosity may be increased in MM, SCD and DM (Wells, 1970) and the risk of thrombosis is high (De Franceschi et al, 2011). Thalidomide and lenalidomide containing regimens must be used with precaution and anticoagulant prophylaxis is considered standard therapy. (Zamagni et al, 2011). Up to now we have not used thalidomide in our patient as he presented with DVT, but we will use it with caution at the appropriate time. The use of blood exchange instead of plasma exchange at the beginning was a procedure that played an important role in the control of both MM and SCD. On the other hand, the use of granulocyte-colony stimulating factor (G-CSF) for mobilization, collection, and transplantation of autologous hematopoietic progenitor cells (HPCs) in patients with hemoglobinopathies can be complicated by severe vasoocclusive crises. Erythrocytapheresis before G-CSF administration may help prevent these complications in patients with MM and SCD eligible for transplantation (Christopher et al, 2008). Finally we agree with Nicolaou et al who recommended a comprehensive evaluation including bone marrow studies in patients with SCD in whom a fall in hemoglobin cannot be attributed to increased hemolysis, sequestration or concurrent infection.

To the best of our knowledge, the association of MM, SCD and DM has not been reported before. On the other hand, our patient is the second where both diagnosis of hemoglobin SC disease and MM were made at the same time.

Conflict of interest and funding disclosure

The authors declare no conflict of interest; this report received no financial support.

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