Young myeloma patients: a concern to consider

Pacientes jóvenes con mieloma: una preocupación a considerar

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Dear Editor

Multiple myeloma (MM) is usually diagnosed in elderly people with an average age of 70 years at presentation, being exceeding rare before the 30 years of age, and is more often manifested by hypercalcemia, renal insufficiency, anemia and bone lesions.[1-10] MM is commoner in African descendants, and the male to female ratio can be up to 4:11; the pathogenesis involves exposure to dioxins, solvents, radiation, and viruses.[1]

Quetzal and Soler González[9] recently described a 33-year-old male presenting with acute kidney disorder besides accentuated low back pain, and the imaging studies revealed osteolytic lesions in T12, L2, ribs, pelvis, and femur, caused by a MM in the stage III. Laboratory routine showed accentuated anemia and leukopenia, erythrosedimentation rate: 134 mm/h, urea: 103 mg/dl, creatinine: 7.0 mg/dl, and calcium: 14.8 mg/dl. He had sepsis related to a bacterial pneumonia, successfully controlled by antibiotic therapy; his renal function improved, and he was referred to the specialized hematological care. The authors emphasized the role of high suspicion index to consider the hypothesis of MM even in young patients with the manifestations herein reported, because the early diagnosis and prompt adequate treatment have favorable effects on final outcomes.

According to their recommendations about a wider dissemination of such examples, it seems useful to shortly comment on additional literature data about MM in young.[1-8,10] A 24-year-old male had a gradually enhanced dyspnea on exertion and fainting in the last four months, associated with a normocytic normochromic anemia and marked rouleaux phenomenon, in absence of blood loss, hemolysis, bone pain, or renal failure.[1] The bone marrow study revealed hypercellularity with 1% fat, 99% cell ratio, almost totally replaced by pleomorphic plasmacytoid cells of an IgG myeloma in the stage II. The option was induction chemotherapy by standard protocol (velcade, thalidomide and dexamethasone); the authors stressed the challenging MM in a younger age with only anemia and no bone or renal changes, requiring an enhanced cognizance to diagnosis.[1]

A 39-year-old female diagnosed with systemic lupus erythematosus (SLE) in 2018 was admitted because of weight loss and vomiting, chest and abdominal pain for two days.[2] During three years she had used hydroxychloroquine, corticosteroids, and analgesics, without a rheumatologist orientation; and the renal biopsy confirmed lupus nephritis. Admission tests showed proteinuria, hypoalbuminemia, hypogammaglobulinemia, IgG paraproteinemia, high beta-2-microglobulin, and urinary monoclonal IgG light chains. Bone marrow biopsy revealed 70% cellularity, erythroid hypoplasia, low iron reserves, at least 25% of plasma cells and a 17:1 ratio of kappa to lambda cells; as all the skeletal imaging studies resulted normal, the diagnosis of smoldering IgG MM was confirmed; she promptly underwent the treatment schedule with thalidomide and dexamethasone. The authors cited the rarity of concomitant MM and SLE, besides the not uncommon monoclonal gammopathy in SLE, being recommended to investigate a coexistent MM.[2]

A 35-year-old woman had incidental diagnosis of IgG kappa MM in 2016 after a fall causing back pain and imaging study showed pathological vertebral fractures; besides, the levels of monoclonal

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IgG kappa paraprotein and beta-2-microglobulin were high.[3] Bone marrow study revealed 80% plasma cells, and with diagnosis MM in the stage II she underwent vertebroplasties and cycles of velcade, cyclophosphamide, thalidomide, and dexamethasone with good result, before autologous stem cell transplant (ASCT). Four years later she become pregnant and occurred a slow kappa light chain increase; and, worthy of note, the abdominal imaging evaluations showed the fetus with normal development, and the deliver occurred at the 40 weeks of an unremarkable gestation. Because she did not have new osteolytic lesions, with normal bone marrow, calcium levels and renal function, there was no indicative criteria for treatment of myeloma.[3] However, eleven months after deliver, control exams showed anemia, elevated levels of IgG kappa monoclonal protein levels and serum kappa light chain levels; and the bone marrow biopsy revealed an accentuated myeloma infiltrate with CD138 plasma cells.[3] Therefore, the initial treatment included lenalidomide, dexamethasone, and ixazomib with a good response, followed isatuximab, pomalidomide, and dexamethasone; while she waits be referred to the stem cell transplant service to undergo the second ASCT. The authors stressed the rare occurrence of myeloma during pregnancy playing a role in the relapse, phenomenon that requires accurate monitoring including the post-partum.[3]

A 39-year-old African descendant woman presented with epigastric, bilateral lower chest, and low back pains associated with difficulty to ambulate during one month.[4] Admission laboratory exams revealed anemia, elevated levels of creatinine, besides hypercalcemia attributed to the excessive utilization of NSAID as well as antacids. There was no chest or spinal recent changes, the free kappa to lambda light and chain ratio were high; bone marrow biopsy showed over than 50% plasma cells; with MM diagnosis she utilized bortezomib, cyclophosphamide, dexamethasone, and acyclovir. The authors commented on the initial clinical challenges due to the NSAID and antacid chronic intake, delaying the correct diagnosis and the initiation of a needed treatment.[4]

A 34-year-old female was admitted with asthenia, headache, gastric pain, and advanced renal failure; the laboratory tests showed anemia, proteinuria at nephrotic range, high creatinine level, calcium: 2.8 mmol/L, and monoclonal gammopathy type IgG lambda.[5] Her myelogram showed 32% plasmacytosis, and the renal biopsy a MM tubulopathy; as the spinal imaging study was unremarkable, the final diagnosis of the patient was a MM IgG lambda class III of Salmon and Durie, and with the prognostic stage R-ISS II. Therefore, she underwent 6 cycles of bortezomib, thalidomide and dexamethasone; and after conditioning with bortezomib and melphalan she had the successful ASCT. The authors emphasized the challenging course of this case of MM in a young female, and the diagnosis established during the evaluation of her then unexplained renal disorder.[5]

A 33-year-old male had accentuated weight loss and intense low back pain for 3 months obtaining partial improvement utilizing NSAID, and examination revealed tenderness in the sternum and right lower ribs, besides in the lumbar, and right sacroiliac joint areas.[6] Imaging studies showed numerous cranial osteolytic lesions and increased thickness of the bones, multiple vertebral lesions in the thoracolumbar spine and in the pelvis, which were consistent with the hypothesis of MM further reinforced by the serum protein electrophoresis with a peak in beta-1, and the presence of Bence Jones proteinuria. Bone marrow study revealed MM with over than 80% of plasma lineage cells, that was treated by bortezomib, lenalidomide, and dexamethasone before a transplantation; but at the fifth cycle he presented 40°C and pulmonary involvement by COVID-19 infection. He was referred to the infectious isolation and treatment, and the fever rapidly subsided; near three weeks after discharge he claimed of increasing pains in feet and back and there was a MM relapse, which was not successfully managed by different regimens. The authors commented on the need to consider MM as a hypothesis in young patients, and the possibility of maintaining the antineoplastic treatment even during infections.[6]

A 34-year-old man had back pain unrelieved by analgesics and weight loss, abdominal pain, melena, and ascites, with laboratory determinations showing thrombocytopenia, anemia, hypercalcemia, and hyperproteinemia, besides the bone marrow aspirate presenting 30% of plasma cells with CD38, CD56, and kappa light chains positivity.[7] Because of the COVID-19 pandemic, he refused imaging exams in the hospital and, in the same year, had diagnosis of secondary plasma cell leukemia; the chemotherapy was started, but was interrupted due to the myeloid inhibition, and he died 5 months later. The authors highlighted the lack of the initial MM suspicion in this young patient, that favored the evolution to plasma cell leukemia which has a high rate of fatal prognosis.

The clinical characteristics, responses to treatment, and survival rates were analyzed among 103 patients aged 40 years or younger and newly diagnosed MM, comparing with 256 patients aged 41 to 50 years, and with 957 patients aged 51 years or older.[8] There were no differences comparing gender, isotype, International Scoring System, renal involvement, hypercalcemia, anemia, bony lesions, or extramedullary disease. Young patients more often used cyclophosphamide, bortezomib, and dexamethasone; 53% of those 40 years-old or younger received ASCT and 71.1% had maintenance. The overall survival was similar in the patients of the three cohorts, and the ASCT was statistically associated with survival; the authors concluded that the younger people with MM have clinical characteristics, responses, and outcomes similar to the elderly ones.[8]

Review of characteristics at diagnosis, cytogenetics, treatments and outcomes of young myeloma patients described similar clinical

and laboratory data, up to 45% with light chain MM and near 25% predominant ISS [10]. It was not cleared if the young present significant higher familial history of MM or secondary hematological malignancies. Up to 69% of the treatments used proteasome inhibitor and immunomodulatory drugs, the ASCT was utilized heterogeneously and the allogeneic SCT was rarely employed, and the median overall survival of young patients ranged from 61 to 175 months; retrospective large-scale studies should improve their management and outcomes.[10]

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