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Multiple myeloma in a 17-year-old adolescent, report of the youngest case with multiple myeloma known in Mexico. A report from the National Cancer Institute of Mexico.

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Abstract

We present the case of a 17-year-old male patient who presented with a month of evolution after physical exertion with incapacitating pain in the dorsal region that left him in a wheelchair. Imaging studies are taken with lytic lesions in vertebral bodies. Extension studies are performed by visualizing a monoclonal peak (PM) in the gamma region corresponding to an immunoglobulin of type G (IgG) with kappa light chains (FLC) by immunofixation (If). Bone marrow aspirate (BMA) with abundant plasma cells (PC) with pathological characteristics in 90%. with phenotype by flow cytometry (CMF) of pathological PC in 6.42%. In addition, the following was documented: hypercalcemia, acute kidney injury, anemia, increased total globulins, and other markers such as beta 2 microglobulin (B2MG) and uric acid. Also, we confirmed the histopathological evidence of a malignant neoplasm of plasma cells in the biopsy of dorsal vertebra 5 (T5). Finally, imaging studies such as magnetic resonance imaging (MRI) and positron emission tomography (PET CT) showed clear images of lytic lesions throughout the axial and appendicular skeleton with characteristics of myeloma tumor activity. Based on all of the above, we conclude that the patient has Multiple IgG Kappa myeloma with an ISS III. Therefore, it was decided to start the CyBorD scheme, zoledronic acid, radiotherapy, kyphoplasty, radiofrequency ablation and, due to family history, he was sent to the hereditary cancer clinic. After three months of treatment, he achieved Very Good Partial Response (MBRP), and he was sent for evaluation by the bone marrow transplant unit (UTMO). His subsequent evolution has been favorable with strict complete response sustained from month 6 and up to 3 years of follow-up. It is an exceptional case since it debuted with the CRAB criteria (Hypercalcemia, Renal failure, Anemia, Bone lesions) and other events that define myeloma (MDE). In addition, the hereditary component is very important, which makes the case more interesting to follow. his evolution and report the clinical evidence in this regard and document his behavior since he is possibly one of the youngest cases to receive proteasome inhibitors for induction and maintenance thalidomide and the youngest documented in Mexico to date.

Keywords: *symptomatic multiple myeloma, M protein, beta 2 microglobulin CD138, Kappa chains, age.*

Introduction

Multiple myeloma accounts for about 1% of malignancies in the United States. It is described as a malignancy predominantly in those 70 years of age or older and only 2% in those younger than 40 years;1,2 it is even rarer in younger people. of 30 years, with an incidence of less than 1%, this was reported by the Mayo Clinic, in a group of patients under 30 years diagnosed with multiple myeloma, which represents an incidence of 0.3%,3,4. In Mexico the hematological group of Morelia Michoacán reported in 2015 the case of an 18-year-old patient with a previous diagnosis of primary hyperthyroidism and chronic evolution of anemic syndrome with monoclonal IgG kappa gammopathy, without lytic lesions, hypercalcemia or renal failure, with plasma cells in the bone marrow, without evidence of extramedullary plasmacytomas.5. The cases described in the literature for children and adolescents are very rare and appear to be the clinical presentation of myeloma. seemed to be less aggressive than adults 6,7. There are reports of approximately 30 cases of MM in patients under 15 years of age.6,8,9 It is believed that many of the cases described as myeloma patients under 20 years of age may correspond to other diseases related to B lymphocytes because many Most of these reports document laboratory techniques with poor specificity and sensitivity used at later dates when it was more limited compared to those used today. Perhaps the youngest case reported in the literature corresponds to an 8-year-old boy (mulatto) diagnosed with immunoglobulin (Ig) G k, Durie and salmon (DS) stage IIIB and International Staging System (ISS) stage 3.10

We present what seems to be the youngest patient with multiple myeloma in the country reported in the literature. An exceptional case has already debuted with the CRAB criteria and other MDE according to the IMWG diagnostic criteria. In addition, the hereditary component is very important, which makes the case more interesting to follow its evolution and report the clinical evidence in this regard. Also perhaps the first young man in the country was treated with the combination based on the CyBorD scheme plus thalidomide and interventional pain management plus radiotherapy. Most of the world literature consulted showed cases of patients over 18 years of age and only one of 8 years of age 6, None of whom had direct relatives with myeloma, and most of the published cases did not meet the full CRAB or MDE criteria. Presentation of the case: A 17-year-old male with an important family history, paternal grandfather has treated at our institution in 2011 with a diagnosis of IgA kappa ISS stage 1 multiple myeloma with a plasmacytoma in the lumbar spine 3. (Figure 1)

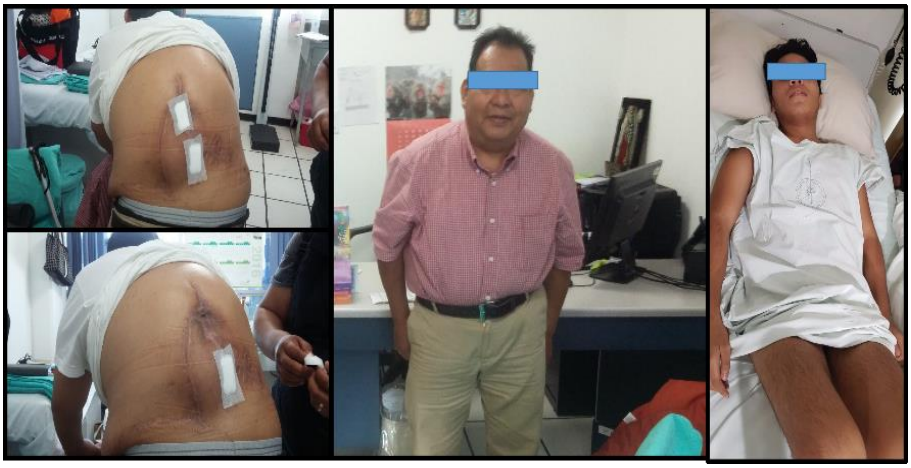

Figure 1. Adolescent patient with MM and his grandfather with MM and spinal cord injury treated in this institution, spinal instrumentation outside this institute, in another hospital.

The adolescent began his condition a month ago, after carrying weights in a gym; She noted progressive, disabling, sudden low back pain with decreased pelvic limb strength. which forced him to use a wheelchair. It was protocolized with imaging studies documenting lytic lesions in vertebra T5; He was assessed by Pediatric Hematology who performs AMO with 61% of CP reason for sending to this institution. Upon admission to the MM clinic of this institute, preclinical studies were performed (Table 1) that documented hypercalcemia, renal failure, anemia, and biochemical changes associated with high activity of the disease. (globulins, total serum immunoglobulins, uric acid, B2MG).

Tabla 1 Estudios preclinicos iniciales			
Calcio	↑	12.9	mg/dL
Creatinina	↑	5	mg/dL
Hemoglobina	↓	9.3	g/dL
Albumina	↓	3.1	g/L
Globulina	↑	8.6	g/L
inmunoglubulinas G	↑	23.7	g/L
Acido ürico	↑	15.8	mg/dL
B2MG	↑	8.2	mg/L

From the most specialized preclinical studies, an M or PM component was documented in serum and urinary protein electrophoresis (PFE). With positive IgG Kappa immunofixation in peripheral blood (SP) and with free light chains kappa in urine. The AMO with 90% of pathological CP and CMF with detectable pathological CP. In the imaging studies, the MRI showed: the collapse of the vertebral bodies in pathological terrain at T3, T5, T6, T8, T12, L1, L3, L4, and L5. The posterior wall of these vertebral bodies is observed with normal characteristics, except for the vertebral body of T5, where its displacement towards the spinal canal is observed, molding the adjacent dural sac (2G). There are also multiple lytic lesions in the different bone structures of the axial and appendicular skeleton with heterogeneous metabolism and focal areas, the site of greatest metabolism being in the left iliac with SUVmax of 3.0 and right iliac with SUVmax of 3.8 visualized (2H) by PET CT . (figure 2). Also, we confirmed the histopathological evidence of a malignant neoplasm of plasma cells in the biopsy of dorsal vertebra 5.

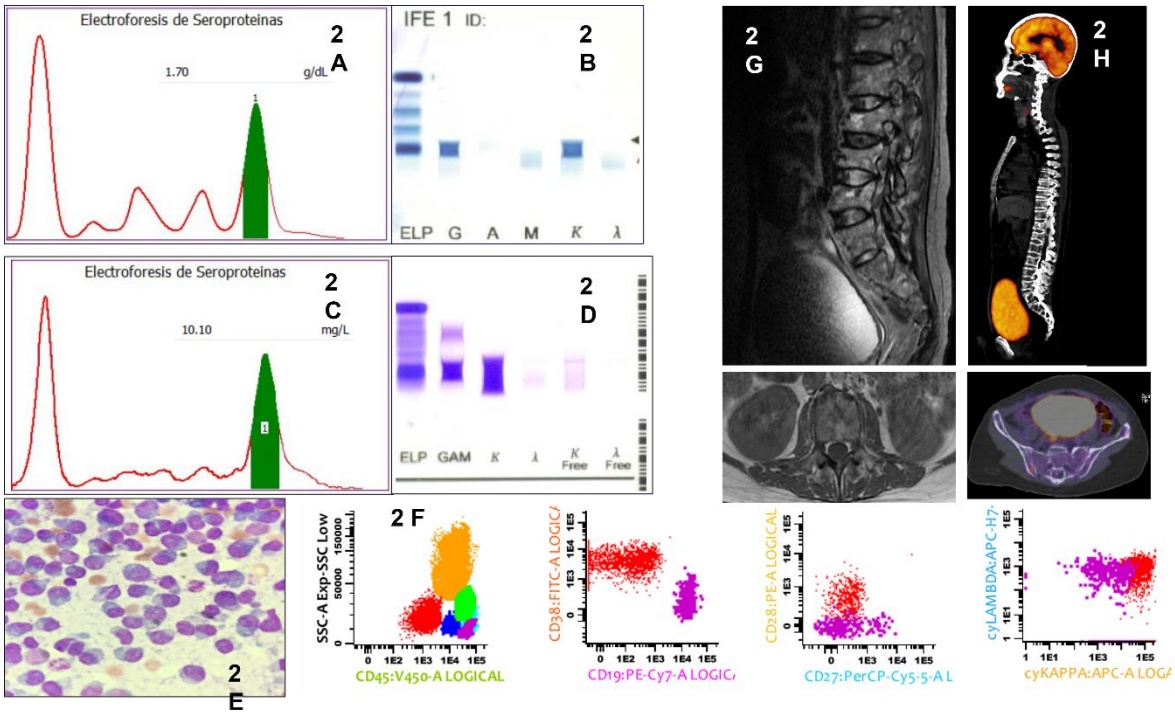

Figure 2. A). Protein electrophoresis with hypoalbuminemia as well as the persistence of the monoclonal peak at the beginning of the gamma region and few polyclonal immunoglobulins. identified as IgG Kappa by serum immunofixation technique (B). C) Protein electrophoresis in concentrated 24-hour urine. with evidence of proteinuria. because albumin and traces of the rest of the protein fractions are observed. as well as Bence Jones proteinuria in the center of the gamma region (D). Identified as monoclonal free Kappa light chains. by urine immunofixation technique. This last technique, in addition. detected the complete monoclonal immunoglobulin. Which suggests mixed proteinuria. F) PC with pathological

phenotype (CD45-; CD 19-; CD38+; CD 56+; CD138+; CD27-; weak CD28+), with Ig CL restriction. Kappa + lambda -.

The management was established based on the monthly CyBorD scheme, thalidomide 100 mg every 24 hours accompanied by acetylsalicylic acid 100 mg orally per day, as antithrombotic prophylaxis, and zoledronic acid 4 mg intravenously per month for bone disease. In addition to radiotherapy of 30 Gy to the dorsal column, kyphoplasty radiofrequency ablation of T12, L2, and L5. Performed during months 1 and 6 respectively. During the evolution and measurement of the responses (Figure 3.4), he achieved MBRP at month 3, managing to walk, and a CRE at month 6, which has been maintained to date. With this response, the patient received hematopoietic progenitor cell autotransplantation (ATCPH) which was given until month 14 due to problems that he presented for the mobilization and collection of progenitor cells, achieving in a second attempt to collect 2.1 million CD 34 cells per kg of body weight. weight (Figure 5) which were infused without problems at month 14. With hematological recovery on day + 11. Induction treatment was maintained until month 14 and after that, maintenance based on thalidomide dexamethasone was continued until month 24.

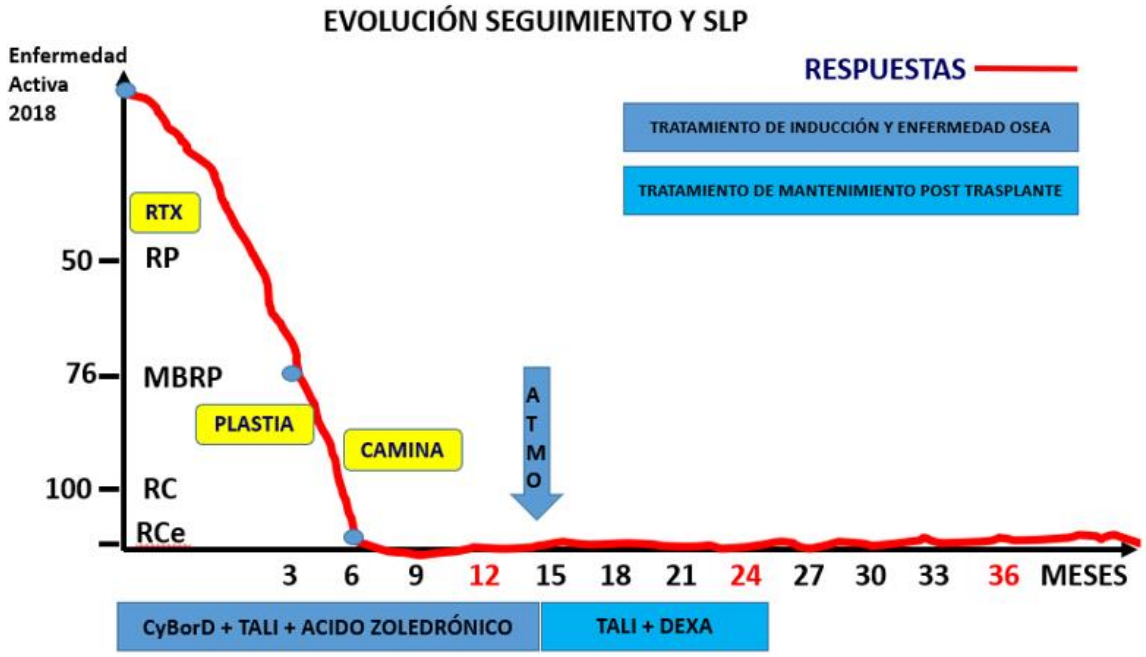

Figure 3. Evaluation of responses with PFS at 36 months. Duration of induction and maintenance.

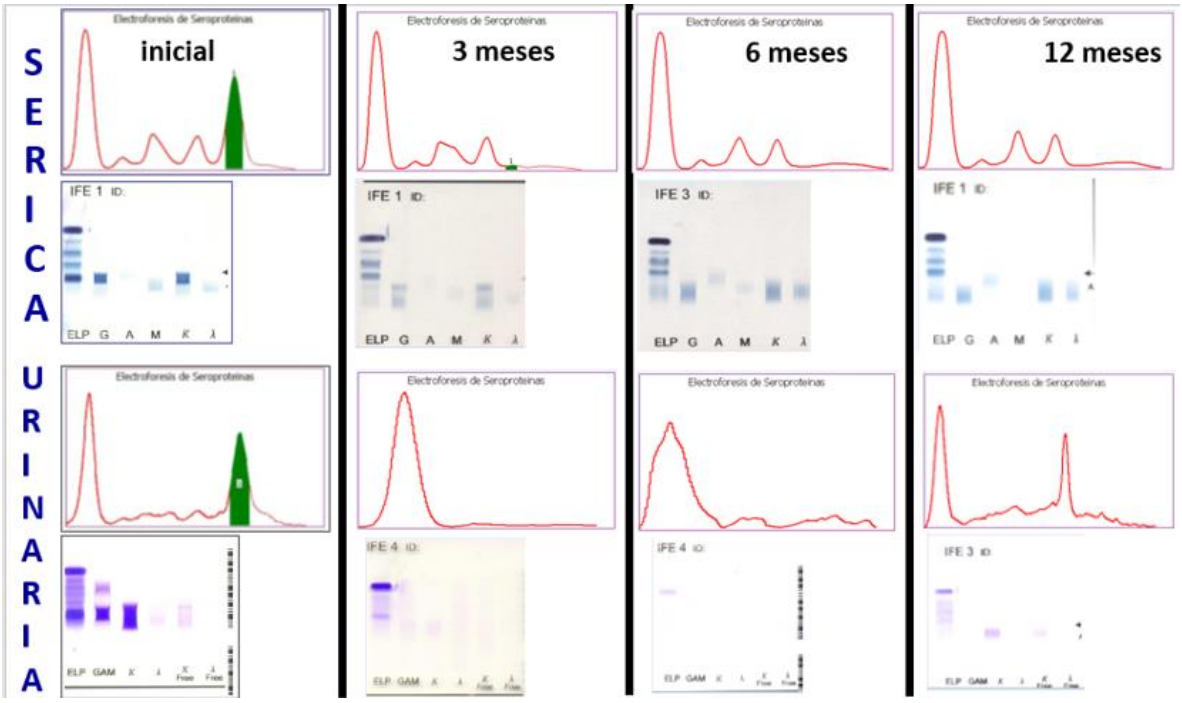

Figure 4: Evaluation of the response with EFP during the first year. At 3 months, serum PM persisted with positive serum If, without Urinary PM and negative PBJ. At Month 6, all parameters were negative.

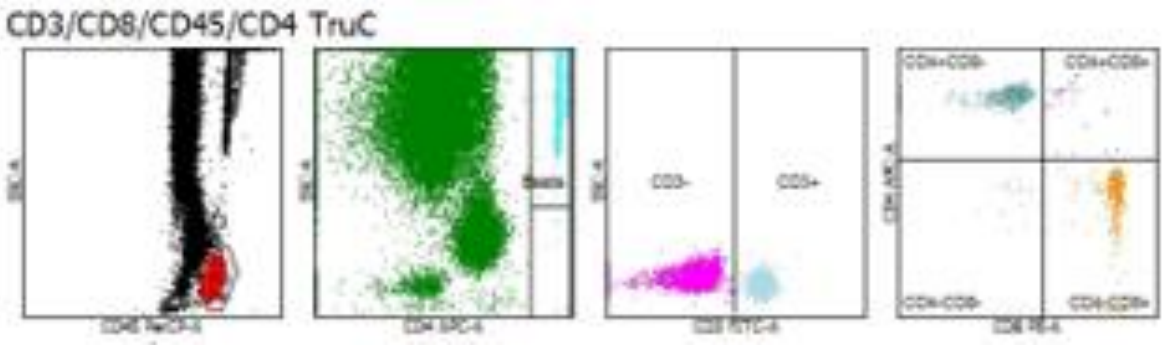

Figure 5. Collection of CD34 progenitor cells. Evaluation with flow cytometry.

Discussion

We present a case of multiple myeloma in a 17-year-old adolescent, the youngest reported in Mexico and most likely in Latin America, in which a correct appreciation of the integration of CRAB manifestations, morphology, and new molecular biomarkers made it possible. the diagnosis of multiple myeloma. This is perhaps the youngest case with MM in Mexico, in which proteasome inhibitors have

been successfully used, as well as immunomodulators for both induction and maintenance, and later consolidated with HPTA with favorable results. And perhaps the youngest with MM and PFS at 3 years, which places him as a unique case from which we have learned. The cases described in the literature for children and adolescents are very rare and appear to be the clinical presentation of myeloma. Seemed to be less aggressive than adults 6,7. Most of the world literature consulted showed cases of people over 18 years of age and only one of 8 years of age 6, None of whom had direct relatives with myeloma, and most of the published cases did not meet the full criteria for CRAB or MDE or much with documented PFS after autologous hematopoietic stem cell transplantation.

Conclusions

We present what appears to be the youngest multiple myeloma patient in the country reported in the literature, an exceptional case. In addition, the hereditary component is very important, which makes the case more interesting to follow its evolution and report the clinical evidence in this regard.

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