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Case Report: Multiple Myeloma (Kahler's Disease - Mm) At "San Juan" General Hospital In The City Of Riobamba

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ABSTRACT

Multiple myeloma (MM) or also known as Kahler's disease is a pathology of plasma cells (plasmocytomas) at the level of the bone marrow or extramedullary sites, characterized by inappropriate multiplication of a monoclonal protein (IgA or IgG). It was described for the first time between the years 1844 to 1850, in 1889 it was given the eponym of Kahler's disease. The disease presents as a tumor (abnormal accumulation of cells within the bone marrow) that causes destruction and invasion of the bone surrounding the bone marrow cavity (multiple lytic bone lesions), the patient's response causes various symptoms such as bone pain , fractures, renal failure, predisposition to infections, anemia, hypercalcemia and coagulation disorders. It is a frequent pathology in the United States, in Latin America the highest incidence rate was in Colombia and Ecuador. Black people are affected twice as much as whites, likewise it affects more men than women (1:4 ratio). It evolves in several phases: initial, activity and terminal. Diagnosis is based on invasive and non-invasive methods. At the moment, multiple myeloma is an incurable disease, but with the improvement and combination of treatments, a stable remission of several has been achieved; early intervention improves survival.

Key Words: *multiple myeloma, Kahler's disease, dyscrasia, bone pain, fractures, renal failure, infection, anemia, tumor, bone marrow, lytic lesions, survival.*

1. INTRODUCTION:

Multiple myeloma is a dyscrasia of plasma cells at the level of the bone marrow or extramedullary sites called plasmacytomas, characterized by inadequate proliferation of a monoclonal protein, immunoglobulin IgA or IgG, measurable in blood or urine. At the same time a particula[1]r element of these immunoglobulins light chains (kappa or lambda) that will be detectable in urine and are associated with renal impairment (1), (2).

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Multiple myeloma is attributed as a disease since the ancient era, first described between 1844 - 1850 scientists Solly, Dalrymple, Bence-Jones and Macintyre described the characteristics of the disease then known as "Mollities ossium" and later called by von Rustizky multiple myeloma. In 1889 Otto Kahler described a patient with bone pain and proteinuria giving him the eponym of Kahler's disease, from this they continue to make multiple discoveries about their pathogenesis, molecular biology and treatment however so far their origin is a mystery (3), (4).

This disease presents as a tumor and the response of the host to them causes various organic functional disorders and symptoms such as bone pain or fractures, renal failure, predisposition to infections, anemia, hypercalcemia and sometimes coagulation disorders (5).

2. METHODS:

The present work is a review of primary sources obtained from the databases: C. Med Mastercl, Medscape, New England Journal of Medicine, Multiple Myeloma Oncoguide, Brain Chain Magazine, Colombian Journal of Cancerology, Journal of the Faculty of Medical Sciences, Journal of the Medical Body of the HNAAA, Journal of Hematology. Mexicana., Revista Médica Chile, Revista Médica de Costa Rica y Centroamérica, Revista Cubana Hematología e Inmunología, Revista Médica Electrón, Revista Sanitaria de Investigación, Sociedad Argentina de Hematología, etc., with research articles in specialty journals, which address a wide variety of hematological and oncological pathologies and especially neoplastic diseases, prevention measures, evolution, complications and treatment. Multiple myeloma (MM) or Kahler's disease is a neoplastic pathology, chronic and progressive, of different etiological causes not yet well known, characterized by a dyscrasia of plasma cells at the level of the bone marrow or extramedullary sites; the same that presents as one or multiple tumors.

3. RESULTS:

Epidemiology:

This disease is a frequent pathology in the United States, being the second hematological neoplasm representing 10% of these and with an incidence of 4 per 100,000 inhabitants, at the level of Ecuador there are no data on the prevalence and incidence of this pathology (6).

In Latin America, between 1990 and 2007 it was reported that the highest incidence rate of myeloma was in Cali (Colombia) and Quito (Ecuador), especially affecting the group of patients over 60 years of age, with rates ranging between 14.2/100000 and 12.8/100000 for men and women, respectively (7)(8).

Black people are affected twice as much in relation to the white race, as men versus women speak of a 1:4 ratio, the median age for diagnosis is 65 years with less than 3% in children under 40 years (9), (10), (11).

Aetiology:

Although at present a precise etiology of Kahler's disease has not been found, there is talk of different causes including genetic, environmental or occupational, radiation, chronic inflammation and infection.

At the genetic level, it is known to evolve from premalignant and subsequent disease states to primary genetic events such as chromosomal translocations involving heavy immunoglobulin, secondary genetic events involving include copy number abnormalities, DNA hypomethylation and mutations leading to tumor progression (12).

The place where chromosomal abnormalities, most commonly related to the heavy chain change region of immunoglobulin have been identified are on the long arm of chromosome 14, although these alone do not appear to be sufficient to give rise to multiple myeloma (13), (10).

In addition to genetic instability, events such as RAS mutation, p16 methylation, alterations of the MYC oncogene, secondary translocations, p53 mutation and alterations of the microenvironment, such as induction of angiogenesis, suppression of immunity, increase of IL-6 and VEGF, increase of the receptor of the activator of nuclear factor KB ligand (RANKL) and decrease of osteoprotegerin that will lead to the destruction and invasion of bone (14).

Also in certain case-control studies there is talk of an increased risk in patients with significant exposures in the agricultural and petrochemical industry as well as herbicides and insecticides. Radiation can be a risk factor in some cases, although there are no studies to corroborate it, as well as states of persistent chronic inflammation.

Physiopathology:

Multiple myeloma (MM) is a clonal acquired disease that affects the B lymphocyte plasmacytes that are at the end of their differentiation. It is considered as a pathology that evolves in several phases:

- Initial phase: plasmocytes are immortalized, but accumulate in the marrow without proliferating;
- Activity phase: a small fraction of the cells becomes proliferating, acquires plasmablastic cytological characters and special phenotypic characteristics, to which oncogenic processes are added;
- Terminal phase: it is characterized by the presence of extramedullary locations and by the expansion of the plasmablastic component.

Multiple myeloma is often preceded by a non-malignant tumor process, known as monoclonal gammopathy of undetermined significance, which is a group of pathologies derived from plasma cells that have recovered their ability to replicate and that clinically range from asymptomatic to states of destruction of healthy tissue (15). It has a medullary plasmocytosis of less than 10% and becomes a true multiple myeloma expressing the same clonotype and immunoglobulin isotype.

Epidemiological studies suggest that about 30% of multiple myeloma may be preceded by monoclonal gammopathy of this type (16).

One of the main features of the pathophysiology of myeloma is the abnormal accumulation of cells within the bone marrow, producing alteration of normal function, causing the appearance of anemia, decrease in the number of leukocytes or platelets or both, destruction and invasion of the bone surrounding the bone marrow cavity (multiple bone lytic lesions) (14). Also the most common mechanisms of kidney injury are tubular injury, amyloidosis or plasmacytoma involvement.

Clinical Manifestations:

The presenting signs and symptoms of multiple myeloma include a variety of occurrences (17):

Table 1: Incidence of signs and symptoms of multiple myeloma.

Signs and symptoms	**Incidence**
Bone pain (especially back pain)	58%
Fatigue (typically caused by anemia)	32%
Pathological fractures	26 – 34%
Weight loss	24%
Paresthesias	5%
Fever	0,7%
Asymptomatic	34%

Fuente: American Family Physician (17)

About 30% of patients are diagnosed through routine blood tests for unrelated problems, and one-third are diagnosed after a pathological fracture involving the axial skeleton (18).

- Bone pain: it is the most typical and frequent symptom at the time of diagnosis, appearing in the spine at the lumbar level, also sternum ribs or proximal area of the extremities (18).

- Pathological fractures and bone lesions: Their origin is bone lesions that, by radiology, usually correspond to typical osteolytic images in "punches" without peripheral sclerosis, but can also manifest as severe osteoporosis or pathological fractures.

- Osteolysis is located mainly in bones with a large amount of bone marrow, that is, in order of frequency: skull, spine, ribs, pelvis and proximal epiphyses of long bones (19).

- Anemia: due to a decrease in the number of blood progenitors, followed by an erythropoietin deficiency that is secondary to concomitant kidney disease, as well as a depletion of iron stores (1).

- Renal insufficiency: this appears between 25-30% of patients, its origin is multifactorial being the most frequent cause the renal elimination of light chains (Bence Jones protein) whose presence tubular level is named as "myeloma kidney"

- Infection: infections are the leading cause of mortality with an incidence of 0.8-2.2 episodes per patient/year, usually bacterial due to monoclonal hypogammaglobulinemia (19)

- Hypercalcemia: this complication may be present in 30% of patients at the time of diagnosis, presents with confusion, drowsiness, bone pain, constipation

- Hyperviscosity: manifests with generalized malaise, fever, paresthesia, mental slowness and sensory loss.

- Neurological symptoms: Most cases present with dysesthesias and paresthesias in the hands and feet, to a lesser extent hyperesthesia or muscle weakness, and a minority of cases report autonomic neuropathy, also carpal tunnel syndrome is a frequent complication (17) (20).

- Abnormalities in hemostasis: as in other tumors there is a high risk of thrombosis, probably due to the secretion of tissue growth factors that interact with circulating neutrophils and cause endothelial damage favoring thrombosis (1)

Diagnosis:

The studies listed below should be performed at initial diagnosis in patients with suspected multiple myeloma:

1. Medical history and physical examination.

2. Blood count and peripheral blood smear.

3. Serum biochemistry: Mandatory: creatinine and urea, calcium and phosphorus, total proteins and albumin, LDH and beta-2 microglobulin (β2m). Recommended: liver function tests and screening for anemia (metabolism of iron, vitamin B12, folic acid and thyroid hormones) or hyperparathyroidism (PTH) if appropriate.

4. Protein study:

   - In serum: electrophoresis with quantification of the monoclonal component in serum and immunofixation to confirm monoclonality; immunoglobulin dosage (Igs); Level and ratio of free light chains in serum (Kappa/Lambda) perform them in nonsecretory multiple myeloma and amyloidosis (21).

   - In 24-hour urine: total proteinuria, electrophoresis to quantify the monoclonal component in urine by Bence Jones proteinuria, and immunofluorescence to confirm monoclonality (21).

5. Viral serologies: hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV).

6. Immunohematological study: extended erythrocyte phenotyping or genotyping. Recommended at diagnosis or prior to the first transfusion; mandatory prior to initiation of treatment with anti-CD38 monoclonal antibodies (21).

7. OM study (aspirate and/or biopsy):

   - Cytomorphology: percentage and morphology of plasma cells

   - Inmunofenotipo.

   - Cytogenetic studies

8. Imaging tests (21):

- Bone X-ray (skull, spine, pelvis, femurs and humerus).
- When clinical suspicion of other bone lesions: Rx of compromised bones.
- ECG and echocardiogram to determine left ventricular function.
- In special circumstances (22) :

  - MRI (vertebral injury, spinal canal compression, CNS or meningeal involvement or with doubtful bone X-rays or suspected injury in special areas rib, sternum, scapular.
  - CT scan (without contrast) or suspected extra-bony lesions or for biopsy guidance in lesions that require it.
  - PET/CT scans in suspected extra-bone lesions, solitary plasmacytomas and/or whether to be used to evaluate response to treatment.
  - Bone densitometry in the absence of lytic imaging and if used as a criterion for the use of bisphosphonates.
  - Serum viscosity (with high concentration of monoclonal gammopathy IgA or if hyperviscosity syndrome is suspected).
  - If amyloidosis is suspected: investigate amyloid in BMO, abdominal fat puncture or rectal biopsy if these are negative biopsy of the involved organ
  - If cryoglobulinemia is suspected: investigate them in serum.
  - Typing: HLA of the patient and siblings in cases of probable allogeneic transplantation of CPH in the evolution.
  - Fine needle aspiration (FNA) of abdominal fat: if amyloid is suspected

Diagnostic Criteria: for the diagnosis, the presence of ≥ 10% of plasma cells in bone marrow or a confirmatory biopsy of bone plasmacytoma or extramedullary plasmacytoma and the presence of at least one event that defines Myeloma is required, such as (21):

- Hypercalcemia: Serum calcium > 0.25 mmol/L (> 1 mg/dL) above the upper limit of normal or > 2.75 mmol/L (> 11 mg/dL).

- Renal impairment: creatinine clearance < 40 mL/min or serum creatinine > 177 μmol/L (> 2 mg/dL).

- Anaemia: decrease in haemoglobin (Hb) > 20 g/L below the lower limit of normal or Hb < 100 g/L.

- Bone lesions: ≥ 1 osteolytic lesions by conventional radiology, CT (computed tomography) or PET-CT (positron emission tomography-computed tomography).

- Biomarkers high risk of progression (one or more of the following) (23):

  - Clonal plasma cells in bone marrow ≥ 60%.
  - Altered/unchanged free light chain (CLL) ratio ≥ 100 (in addition the CLL of the altered chain must be ≥ 100 mg/L).
  - Magnetic resonance imaging (MRI) with > 1 focal lesion (>= 5 mm).

Treatment:

Although multiple myeloma is an incurable disease so far, over the years treatments have improved immeasurably, with many patients now able to achieve a stable multi-year remission through treatment combinations (24).

The literature mentions that, despite being diagnosed with quiescent multiple myeloma, it is recommended to start treatment as soon as possible, this being beneficial since it delays the time of progression to symptomatic disease and increases survival (25).

In a study published by the New England Journal of Medicine on August 1, 2022, it is mentioned that:

"After a median follow-up of 40 months, the median time to disease progression was not reached in the treatment group and was 21 months in the observation group ($p < 0.001$). The 3-year survival rate was also higher in the treatment group (94% vs. 80%; risk ratio, 0.31; $P = 0.03$)." (26)

Thus demonstrating that early intervention improves survival and the rate of progression to symptomatic disease.

Chemotherapy: chemotherapy treatment, in combination of corticosteroids is the mainstay of treatment in newly diagnosed patients, large combinations have been made including the use of antiangiogenic drugs such as thalidomide and lenalidomide, in addition bortezomib which is a proteasome inhibitor, however these drugs produce adverse effects including peripheral neuropathies and thromboembolic events that in some cases produce states of hyperviscosity and can lead to the death of the patient. There is talk of a high response rate with many patients in remission but they will gradually relapse (2)

Autologous stem cell transplant: for this treatment young people are eligible, those under 65 years of age it is also required to induce complete remission and then proceed to the transplant, all this depends on the general condition of the patient.

Allogeneic stem cell transplantation: the use of a healthy source of progenitor cells with the ability to have a graft effect against myeloma is very attractive, especially after a good remission with a previous autologous transplant. However, given the age of presentation of myeloma and the difficulty of finding a donor, this therapeutic option is restricted to few patients (5-10%). Response rates are high but relapse is common.

Supportive Therapy: The use of bisphosphonates should be continued monthly, as they are said to reduce bone disease and modulate the disorder. The use of erythropoietin in anemic patients, the use of kyphoplasty or vertebroplasty in severe vertebral lesions and vigorous antibiotic treatment in case of infections (27).

4. DISCUSSION:

Multiple myeloma (MM) is a chronic and progressive neoplastic disease with different etiological causes that are not yet well understood. It is characterized by a dyscrasia of plasma cells at the level of the bone marrow (or extramedullary sites); the same that presents as one or multiple tumors (plasmacytomas).

According to F. Samaniego et al. (2022), the mean age at diagnosis was 58 and 62 years and 52.5% and 51.5% were male, respectively (6). Although studies conducted by Suárez González and collaborators (2018) conclude that in general it occurs at advanced ages (at least 65 years of age), with the average age at the time of diagnosis of 65 years and in less than 15% of cases they occur below 50 years. They also state that it affects more men than women (28).

Ramón Rodríguez LG et al. (2013) state in their study that the symptoms and signs presented by patients with MM are bone pain, thirst, weight loss, weakness, fatigue and mucosal skin pallor (29). According to the research of Silva-Flores GA and collaborators (2021) it is known that more than 85% of patients will present skeletal damage and the primary symptom will be bone pain, sometimes misinterpreted by both the patient and medical personnel. Bone pain in patients with MM is caused by increased intraosseous pressure, increased osteoclast activity, and increased hypoxia within bone tissue. The lytic lesions presented by patients with MM can cause pathological or compression fractures being a source of intense pain, which could be disabling. There are few reports in the medical literature regarding the association between low back pain as a suspicious symptom of MM (30).

Approximately 1% to 2% of patients have extramedullary disease at the time of initial diagnosis, while 8% develop later in the course of the disease (31); as stated by Aliaga-Chávez and collaborators (2022).

5. CONCLUSIONS:

Multiple myeloma is a dyscrasia of plasma cells at the level of the bone marrow or extramedullary sites called plasmacytomas, characterized by inadequate proliferation of a monoclonal protein, immunoglobulin IgA or IgG, measurable in blood or urine (1), (2). This disease presents as a tumor and the response of the host to them causes various organic functional disorders and symptoms such as bone pain or fractures, renal failure, predisposition to infections, anemia, hypercalcemia and sometimes coagulation disorders (5). This disease is a frequent pathology in the United States being the second hematological neoplasia, at the level of Ecuador there are no data about the prevalence and incidence of this pathology (6). Black people are affected twice as much as whites, as are men compared to women (1:4), the median age for diagnosis is 65 (9), (10), (11). Although at present a precise etiology of Kahler's disease has not been found, there is talk of different causes including genetic, environmental or occupational, radiation, chronic inflammation and infection. Certain case-control studies speak of an increased risk in patients with significant exposures in the agricultural and petrochemical industry as well as to herbicides and insecticides. Radiation can be a risk factor in some cases, although there are no studies to corroborate it, as well as states of persistent chronic inflammation. An acquired clonal disease that affects the plasmacyte B lymphocytes at the end of their differentiation. It is often preceded by a non-malignant tumor process of undetermined significance, clinically ranging from asymptomatic to states of destruction of healthy tissue (15). One of the main features of the pathophysiology of myeloma is the abnormal accumulation of cells within the bone marrow, producing alteration of normal function, causing the appearance of anemia, decrease in the number of leukocytes or platelets or both, destruction and invasion of the bone surrounding the bone marrow cavity (multiple bone lytic lesions) (14). Diagnosis is based on invasive (biopsy and bone marrow aspiration) and non-invasive (laboratory studies and imaging) methods. Although multiple myeloma is an incurable disease so far, over the years treatments have improved immeasurably, with many patients now able to achieve a stable multi-year remission through treatment combinations (24). It is recommended

to start treatment as soon as possible and this is beneficial since it delays the time of progression to symptomatic disease and increases survival (25).

CONFLICT OF INTEREST:
The group responsible for the article, declares not to have any conflict about the content, opinions that cause diversion of information, plagiarism, or other situation that threatens the intention of the research and the presentation of magisterial articles.

CASE PRESENTATION:

MULTIPLE MYELOMA (KAHLER'S DISEASE **- MM)**
MLTIPLE MYELOMA (KAHLER'S DISEASE - MM)

Male patient, 50 years old, born and resides in Riobamba, education: superior, occupation: teacher, ethnicity: mestizo, religion: Catholic, blood group: unknown. Source of information: direct.

- Personal Pathological History:
  - Clinical: does not refer.
  - Surgical: does not refer.
  - Allergies: does not refer.
  - Vaccines: 3 doses for COVID-19.
- Family Pathological History: does not refer.
- Psychological Background: does not refer.

Reason for Consultation:
- Abdominal pain
- Low back pain.

Current Disease: patient reports that, for approximately 24 hours, presents pain at the level of the abdominal region. Located in the left hypochondrium, of great intensity (VAS 10/10), continuous type and radiating towards the dorsolumbar area; without apparent cause. He goes to a health institution where they administer analgesics, however discomfort does not subside and 12 hours ago he goes to the doctor who performs paraclinics of image and laboratory ruling out pathology of abdominal origin and indicates intravenous analgesia based on opiate and NSAIDs; with which symptomatology partially subsides. Picture is exacerbated 2 hours ago as estimated time, with a considerable increase in pain at the cervical, dorsal and lumbar level that hinders mobility and is accompanied on this occasion by paresis and paresthesias in both lower limbs. Reason why he goes to our health establishment and after assessment his admission is decided (23/11/2022).

Physical Exam:

TA: 110/65 MMHG FC: 71 LPM FR: 19 RPM SAT O2: 91% (FIO2: 21%) T°: 36.5 °C

Conscious patient, oriented in: time, space and person, hydrated afebrile, algic to a large extent (VAS 10/10).
Head: normocephalic, not masses.
Eyes: isochoric pupils, normorreactive to light and accommodation. Anicteric sclera, pink conjunctiva.

Nose: permeable nostrils.
Mouth: semi-moist oral mucous membranes.
Oropharynx: in erythematous, in congestive.
Thorax: symmetrical, decreased expandability.
Heart: normophonetic, rhythmic heart sounds in synchrony with the pulse. No blows.
Lungs: preserved vesicular murmur. No overadded noise.
Abdomen: soft, depressible, painful on palpation at the level of left hypochondrium (areas of dermatome T2 to T4), no signs of peritoneal irritation. Hydroaerial noises present.
Dorsolumbar: acupressure pain at T2, T3 and T4. Negative Lasègue sign.
Inguinogenital: male external genitalia.
Extremities: symmetrical, mobility, tone, strength and preserved sensitivity, not edema. Preserved distal neurovascular.

Diagnostic Impression:

- Thoracic vertebra fracture.
- Rib fracture.

Evolution Summary:

Evolution: neurosurgery (24/11/2022): patient with no history of importance, who was admitted due to abdominal and lumbar pain due to fracture of the thoracic vertebra. He reports low back pain to mobility (VAS 6/10), which has improved compared to his admission with prescribed analgesia. Vital signs within normal parameters. As there is no traumatic history for diagnosis, complementary imaging tests are requested.

Dorsolumbar corset is used, but pain worsens after its placement; so it is decided to retire.

Interconsultation: internal medicine (24/11/2022): patient with weight loss without apparent cause and cough of several months of evolution. In analytical with elevation of TSH. Therefore, imaging tests (neck ultrasound and simple and contrasted tomography of the chest, abdomen and pelvis) are requested to rule out the presence of masses. Hormone replacement therapy with levothyroxine is initiated.

Evolution: neurosurgery (25/11/2022): patient during the night refers pain of great intensity (VAS 10/10) in the thoracic region, with irradiation towards hypochondrium, so an opioid pump and portion of buprenorphine patch are placed, with which symptoms partially subside and he manages to rest. Hemodynamically stable, there is evidence of decreased thoracic expandability secondary to pain.

Results were obtained from imaging studies that reported lytic lesions in thoracic vertebrae and left rib cage mass suggestive of chondrosarcoma, in addition to diffuse lytic lesions in pelvis and iliac bones. Evaluation by oncology is requested.

Interconsultation: oncology (25/11/2022): patient who presents lytic lesions at the level of thoracic vertebral bodies (T6, T9, T10, T11) with pathological fracture at the level of T8, lytic lesions in the left femoral neck, in addition to L1, L5 and S1. With this background we are in the presence of investigating the origin of these lesions, focusing on their age we could think about ruling out bone metastases of origin to be determined vs. multiple myeloma. In this virtue with the imaging extension examinations has ruled out possible visceral origins that could

cause these lesions (thyroid, prostate, lung, kidney) studies have been carried out to identify if the cause of these lesions is multiple myeloma so it has been requested skull x-ray and laboratory tests in search of findings that guide its diagnosis (complete blood count, calcium, LDH, renal function tests, albumin, beta2 microgobulin, serum and urine protein electrophoresis, bone marrow biopsy), with the result of the requested studies a diagnostic analysis will be performed.

Evolution: neurosurgery (26/11/2022): patient rests peacefully during the night and remains calm during the day, with good analgesic management with prescribed medication. Vital signs within normal parameters. Evaluated by oncology after the results of tomography that report lytic lesions and chondrosarcoma, in addition in skull radiography it is reported finding of myeloma and confirmation of diagnosis of multiple myeloma by simple tomography of the skull. Surgical resolution for dorsal vertebra fracture is scheduled and preoperative check-up is requested.

Interconsultation: internal medicine (26/11/2022): patient diagnosed with multiple myeloma and fracture pathology of secondary thoracic vertebra. So he will be surgically operated. We proceed with assessment prior to surgery not contraindicating it. Clinical risk: Lee II, Goldman: I, ASA: 1, ACC/AHA: low, Gupta: 0.01%, PET/DVT: intermediate. Surgical risk: intermediate. Isocoagulation and anti-embolic measures are recommended.

Evolution: neurosurgery (27/11/2022): patient on his third day of hospitalization. Hemodynamically stable, with adequate pain control at the moment (VAS 2/10). He presents episodes of acute intermittent urinary retention (autonomic symptomatology) so it is indicated that urgent surgical management is required by posterior vertebrectomy, plus intracorporeal box placement and posterior thoracic fixation.

Postsurgical note: neurosurgery (27/11/2022):

Under rules of asepsis and antisepsis, after general anesthesia and with the use of image intensifier, we proceed to perform: posterior vertebrectomy, plus placement of intracorporeal box and posterior chest fixation with osteosynthesis material. Having as findings: infiltrative osteolytic lesion of violet color and great vascularization at the level of T8, with lytic pedicles in anterior and posterior segment of vertebral body; Friable fibrous ring and nucleus pulposus. Resection of tumor lesion is performed at T8 and lesion sample is sent for histopathological study. Approximate time of surgical intervention 8 hours.

Conclusion**:** patient with imaging finding of lytic lesions compatible with diagnosis of Multiple Myeloma, the same located at the level of skull, dorsal and lumbar spine, costal arch, pelvis and femur.

Complementary Exams:

Laboratory:

24/November/2022:

Haematology:

- Leukocytes: 9,150, Neutrophils: 57.9%, Hematocrit: 33%, Hemoglobin: 12.6 g/dl, Hematocrit: 34%, Platelets: 266,000.

Chemistry:

- ALT/TGP: 52 u/l, AST/TGO: 35 u/l.

Endocrinology:

- FT4: 1.64 ng/ml, TSH: 11.38 ulu/ml.

26/November/2022:

Chemistry:

- Creatinine: 1.39 mg/dl, Albúmina: 3.40 g/dl

27/November/2022:

Electrophoresis:

- Capillary Protein Electrophoresis: gamma band, elevation at the level of the gamma zone of monoclonal origin.
- High Resolution Electrophoresis in Urine: monoclonal proteins are not observed, proteinuria with the presence of albumin region is observed.

Pathology:

- Medullary tissue consisting of cell proliferation of monotonous arrangement of hyperchromic nuclei, which tend to polarize, with abundant cytoplasm, show a mild pleomorphism; They are accompanied by occasional bi- and multinucleated cells. Descriptive diagnosis: vertebral body consistent with plasmacytoma.

Conclusion: patient without evidence of alterations in blood count. With increase in value of stimulating hormone of the thyroid gland; as well as elevation of azoados and slight decrease of albumin. Histopathological result of lytic lesion of thoracic vertebra compatible with plasmacytoma was received.

Image:

24/November/2022:

Standard chest x-ray: no signs of active pleuropulmonary lesion are observed. Cost angles and free cardiophrenics. Cardiac silhouette within normal limits. Aortic button and cone of the normal lung. Normal caliber mediastinum. Configuration threads, topography and normal dimensions. **Bone structures with image suggestive of lytic lesion of the sixth left rib.** Soft tissues of the chest wall without alterations. Conclusion: rib injury.

Cervical Ultrasound (Thyroid-Parathyroid): symmetrical thyroid gland, normal shape, size and echostructure. The signal to the color doppler application is preserved. Right lobe measures 34 x 7 x 14 mm, with an approximate volume of 2.1 ml. Left lobe measures 28 x 8 x 12 mm with an approximate volume of 1.6 ml. No focal occupative lesions of solid or cystic type are observed. Homogeneous isthmus measures 1.9 mm. **The different cervical levels were explored, observing lymph node images that preserve ovoid morphology and fat center that measure 10 mm in the right level II and 4 and 6 mm in the left level II.** Conclusion: thyroid gland without focal lesions, bilateral cervical nodes.

25/November/2022:

Simple and Contrasted Thoracic Tomography: andmediastinal vascular structures of normal caliber and regular contours. Trachea and main bronchi permeable and normal caliber. Lobar and segmentar bronchi of normal caliber. There are no adenomegaly, heart normal dimensions. Pulmonary hila of normal configuration and dimensions. Pulmonary parenchyma with mild interstitial fibrosis, bulla of 10 mm and 11 mm in the apical region of the right upper lobe, bullah of 13 mm and 14 mm subpleural in the left upper lobe, apical fibrosis in the right upper lobe, calcification of 4 mm in the right lower lobe, basal laminar atelectasis in the bilateral lower lobe. Pulmonary vascularization of adequate distribution and caliber. Pleura without pathology data. Fracture and lytic injury of the T8 process decreased intervertebral spaces, bone fragment and intervertebral disc projects to the spinal canal. Aorta of normal caliber and path, regular contours, no signs of dissection. **Lytic lesion of vertebral body of T6, T9, T10, T11. Sixth rib on the left side is mass of 53 x 20 mm that captures contrast and produces lytic lesion in the anterior arch. Lytic lesions in the bilateral scapulas.** Conclusion: Chondrosarcoma.

Simple and Contrasted Tomography of the Abdomen and Pelvis: with the administration of 100 ml of water-soluble contrast medium IOPAMED is observed in the Abdomen: stomach of adequate repletion, thin-walled without image inside. The liver of regular contours and parenchyma of homogeneous density, portal vein and hepatic of normal caliber, without space-occupying lesions; Dilatation of intra- and extrahepatic bile ducts. Thin-walled distended gallbladder with no images inside. Pancreas of normal shape and size, normal Wirsung duct. Spleen of normal dimensions, regular contours and parenchyma of homogeneous density. **Horseshoe kidneys of normal dimensions and regular parenchyma contours with usual attenuation coefficients without evidence of lithiasis or dilation of collecting systems.** Adrenal glands of normal dimensions. Abdominal aorta of normal caliber. No retroperitoneal and peritoneal lymphadenopathy is observed. There is no free liquid. In Pelvis: prostate of 50 x 37 x 50 mm, homogeneous. Bladder of smooth external contour, with adequate filling, normal wall thickness, without space-occupying injuries. Vessels of the pelvis of normal path and caliber. Correct representation of perirectal fatty tissue. Muscle planes with normal attenuation coefficients. Visible intestinal loops, without thickening of the wall or pathological dilations or stenosis. Ascending and transverse cecum with abundant amount of fecal matter. **Lytic lesion of 16 mm in the neck of the left femur. Left iliac bone with lytic lesion of 12 mm. L5 with lytic lesion of 14 mm. S1 with lytic lesion of 13 mm. Lytic lesions in the spinous process of L1.** Conclusion: Lytic lesions.

Anteroposterior and Lateral Skull X-ray: digital impressions of normal characteristic. **Multiple lytic lesions in the skull shell suggestive of myeloma.** There are no calcifications. Normal sphenoid sinus. Turkish sella of normal shape and diameters. There are no supra or intrasellar calcifications. Conclusion: myeloma.

26/November/2022:

Skull tomography: brain parenchyma of homogeneous texture. Symmetrical cisternoventricular system, normal size. Interhemispherical fissure in central position. Normal-sized convolutions and grooves. Posterior fossa, pontocerebolous angle without pathological findings. The gray-white substance ratio is adequate, the density of the brain parenchyma is preserved. Base cores, talamos, symmetrical internal capsule, normal. **Cranial bone window with multiple lytic lesions, the largest measuring 22 mm in the right parietal region with**

soft tissue density inside. Maxillary anthros with formation of hydro-aerial levels. Ethmoid cells partially opacified suggestive of acute sinusitis. Conclusion: multiple myeloma.

Patient with lytic lesions at the level of skull (right parietal region), scapulae, dorsal spine (D6 - D11), lumbar (L1 and L5) and sacral (S1), costal arch (sixth left costal arch), pelvis (left iliac bone) and femur femoral neck (left). Findings compatible with the diagnosis of Multiple Myeloma.

Conclusion: patient with evidence in imaging study of lytic lesions located at the level of skull, scapules, dorsal, lumbar and sacral spine, left costal arch, iliac bone and ipsilateral femur. Compatible with diagnosis of Multiple Myeloma. In addition, in the results of laboratory tests there is an elevation of azoates, in capillary protein electrophoresis there is an elevation at the level of the gamma zone of monoclonal origin and in high resolution electrophoresis in urine proteinuria is observed with the presence of albumin region. The result of histopathological study is compatible with plasmacytoma. So you get the diagnosis of: Multiple Myeloma (Kahler's Disease).

BIBLIOGRAPHY:

1. Madera-maldonado C, Olarte-carrillo I, Collazo-jaloma J. Revista Colombiana de Cancerología. 2021;25(2):93–102.

2. A MM contributors; edited by JF. ORIGINAL Haematology : multiple myeloma. C Med Mastercl. 2019;19:58–60.

3. Escalona-gonzález SO, González-milán ZC, Vázquez-gonzález LA. CASE PRESENTATION Multiple myeloma as a presentation of end-stage chronic kidney disease. 2020;2(1).

4. Hidalgo CO. Original article From plasma cells to multiple myeloma. A brief historical perspective. Patol Rev Latinoam. 2011;49(2):120–31.

5. Weber N. Review of pathophysiology, clinical and diagnosis of multiple myeloma. Rev medica Costa Rica and Centroam. 2012;(603):343–9.

6. Samaniego F, Bull L, González N, Araos D, Rojas H, Donoso J, et al. Multiple myeloma in Chile. Novel drug use in two national centres. 2022;331–8.

7. Garrido D, Granja M. Limitations in the management of Multiple Myeloma in Ecuador. Rev Fac Medical Sciences. 2019;44(2):5–9.

8. Leone P (REDIMM). Mieloma multiple en America. 2022.

9. Carlos J. Multiple myeloma in hospitalized patients in Pinar del Rio provincial hospital. 2020;24(1).

10. Raúl de Castro Arenas José. MULTIPLE MYELOMA Diagnosis, Study and Treatment. Man Medical Practices- Hosp Hermanos Ameijeiras MYELOMA [Internet]. 2013; Available from: http://www.sld.cu/galerias/pdf/sitios/hematologia/mmarreglado.pdf

11. Lujan, M(USFQ); Salazar, G(USFQ); Paez J. Multiple myeloma at the Carlos Andrade Marin Hospital, clinical status at diagnosis and survival. 2014.

12. Castaneda O, Baz R. Multiple Myeloma Genomics – A Concise Review. 2019;48(1):57–67.

13. Alvarado-Ibarra M, Luis Álvarez-Vera J, Anaya-Cuéllar I, De La Peña-Celaya A, García-Fernández L, Hernández-Ruiz E, et al. First National Consensus of Multiple Myeloma by ISSSTE Hematologists. article Espec Rev Hematol Mex. 2015;16:306–32.

14. Martínez-cornejo TL, Nájera-martínez J, Torres-alarcón CG, Iván A, García-castillo C, Campos-cortés Á, et al. Prevalence of multiple myeloma in a national hospital of reference of Mexico City from 2011 to 2016 . 2020;21(1):32–40.

15. Peña-celaya JA De, Aguilar-luevano J, Alcivar-cedeño LM, Álvarez-vera JL. Mexican Consensus on Multiple Myeloma. 2020;157(Suppl 1).

16. Bouscary D, Roux C, Ravaud P. Mieloma múltiple. EMC - Apar Locomot [Internet]. 2003;36(4):1–10. Available from: http://dx.doi.org/10.1016/S1286-935X(03)72291-6

17. Nau KC. Multiple Myeloma: Diagnosis and Treatment. 2008;

18. Shah D, Editor C. Multiple Myeloma. Medscape. 2023;1–55.

19. Garcia-sanz R, Victoria M, Fernando J, Miguel S. Multiple myeloma. 2007;129(3):104–15.

20. Rodriguez, To; Waters, F; García L, Band L. Posterior antler involvement, initial manifestation of multiple myeloma. Med Interna Mex. 2022;38:942–7.

21. Ge's Myeloma. Guide to Multiple Myeloma. 2021. 4-94 p.

22. Curutchet, M; Cusminsky, G; Labanca V et all. Multiple myeloma. Soc argentina Hematol. 2012;

23. Cooperative Group for the Study of Monoclonal Gammopathies of Castilla y León. Summary Multiple Myeloma Oncoguima. 2014;134. Available from: http://www.sehh.es/images/stories/recursos/2014/documentos/guias/resumen_oncoguia_v2_1.pdf

24. Nelson R. High-Risk Smoldering Myeloma Benefits From Early Treatment. Medscape [Internet]. 2013;23–4. Available from: http://www.medscape.com/viewarticle/808778

25. Grobman AB, Vivero RJ, Campuzano-Zuluaga G, Ganjei-Azar P, Rosow DE. Drug Shows Promise in Slowing Progression of Smoldering Myeloma to Cancer. Case Rep Oncol Med. 2019;1–3.

26. Mateos M-V, Hernández M-T, Giraldo P, de la Rubia J, de Arriba F, Corral LL, et al. Lenalidomide plus Dexamethasone for High-Risk Smoldering Multiple Myeloma. N Engl J Med. 2013;369(5):438–47.

27. Chimbo R. Vertebroplasty in patients with multiple myeloma. Rev Sanit Investig. 2021;

28. Suárez González A, González Gil A, García Menéndez R, Álvarez Vega N, Estrada Vaillant A, Hernández Ugalde F. Behavior of immunoglobulins in the follow-up of patients with multiple myeloma. Comandante Faustino Pérez University Hospital. Matanzas. Rev Méd Electron [Internet]. 2018 Feb [cited 23/06/2019]; 40(1): 69-80. Available in: http://www.revmedicaelectronica.sld.cu/index.php/rme/article/view/2501/3691

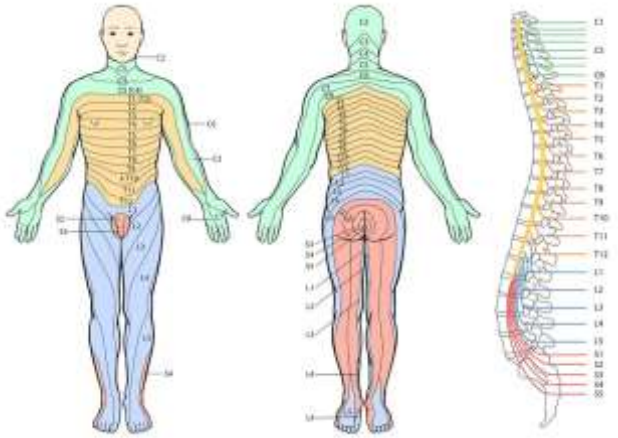
29. Ramón Rodríguez LG, Rivera-Keeling C, Arencibia-Núñez A. Clinical and laboratory characterization of multiple myeloma at the Institute of Hematology and Immunology. Rev

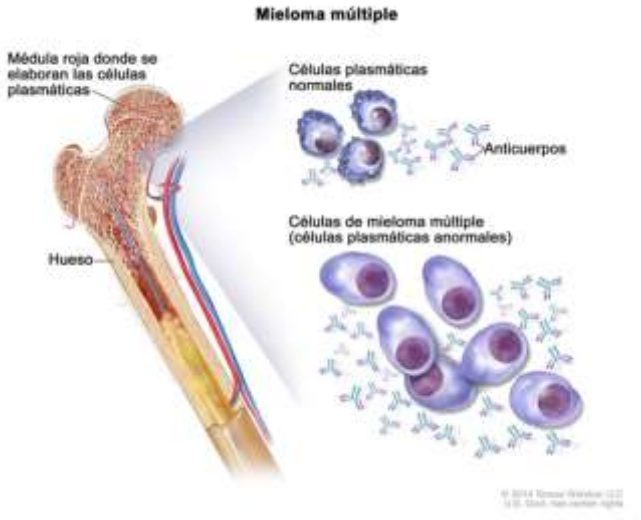
Cubana Hematol Inmunol Hemoter [Internet]. 2013 Dec [cited 29/05/2019]; 29(4): [approx. 15 p.].

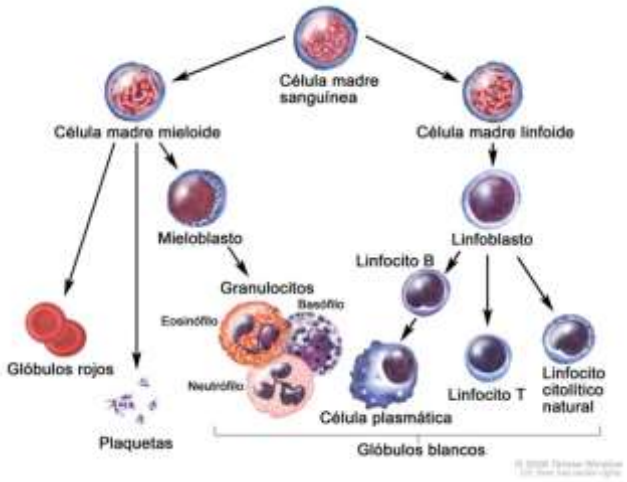
30. Silva-Flores GA, Vidals-Sánchez M. Case report: Isolated low back pain as an atypical presentation of multiple myeloma. Rev Cadena Cereb. 2021; 5(1): 78-81. DOI: 10.5281/zenodo.4435342

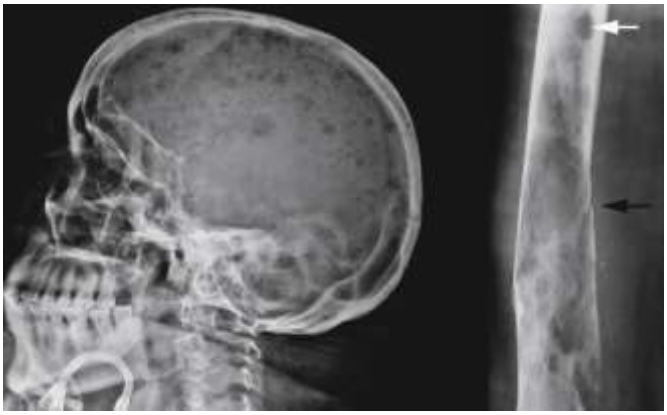
31. Rolig A. Aliaga-Chávez, Luis E. Bendezú-Huasasquiche, Diego A. Crisol-Deza. Case Report Atypical histopathological presentation in bone marrow of multiple myeloma. Journal of the Medical Corps of the HNAAA, Vol 15 (1) - 2022. DOI: https://doi.org/10.35434/rcmhnaaa.2022.151.1016

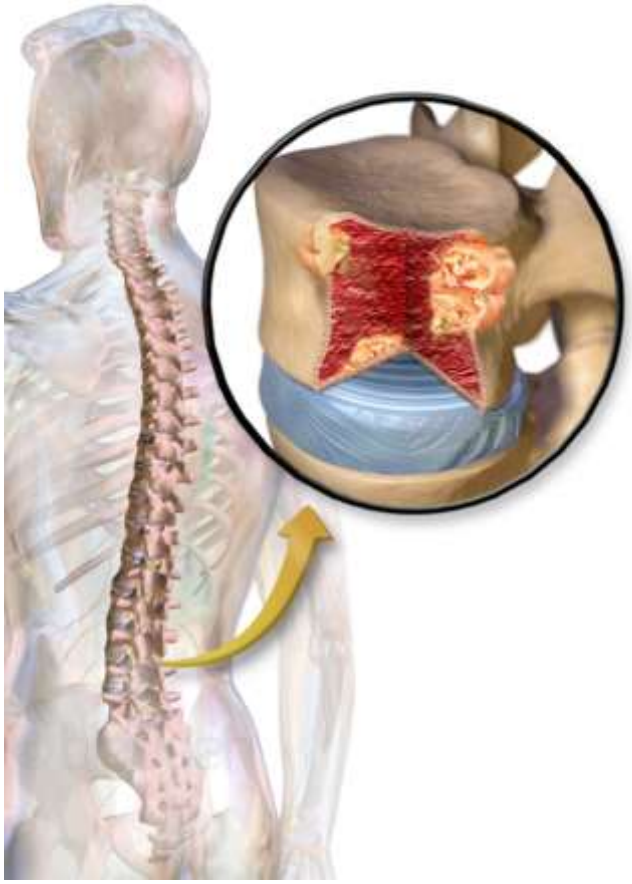
32. **ANNEXES:**

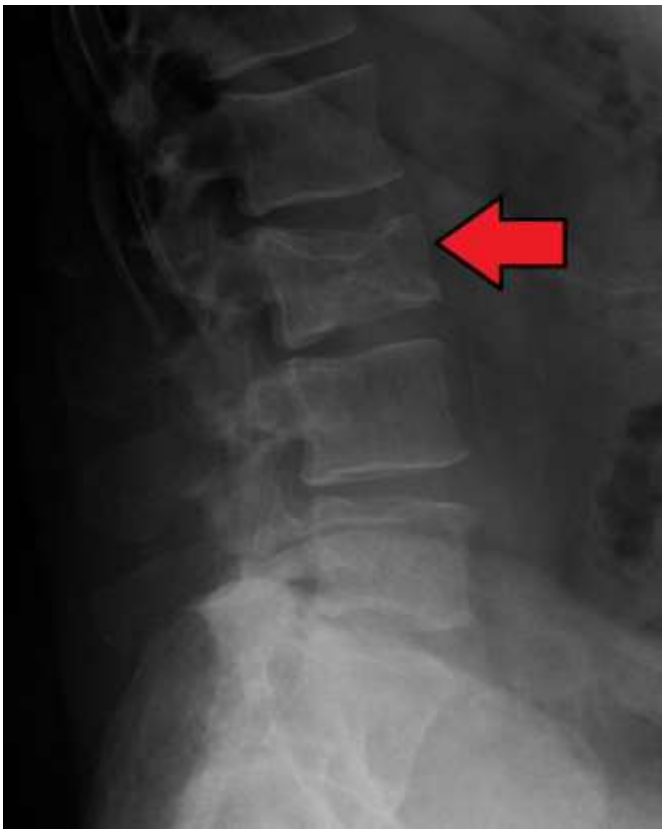


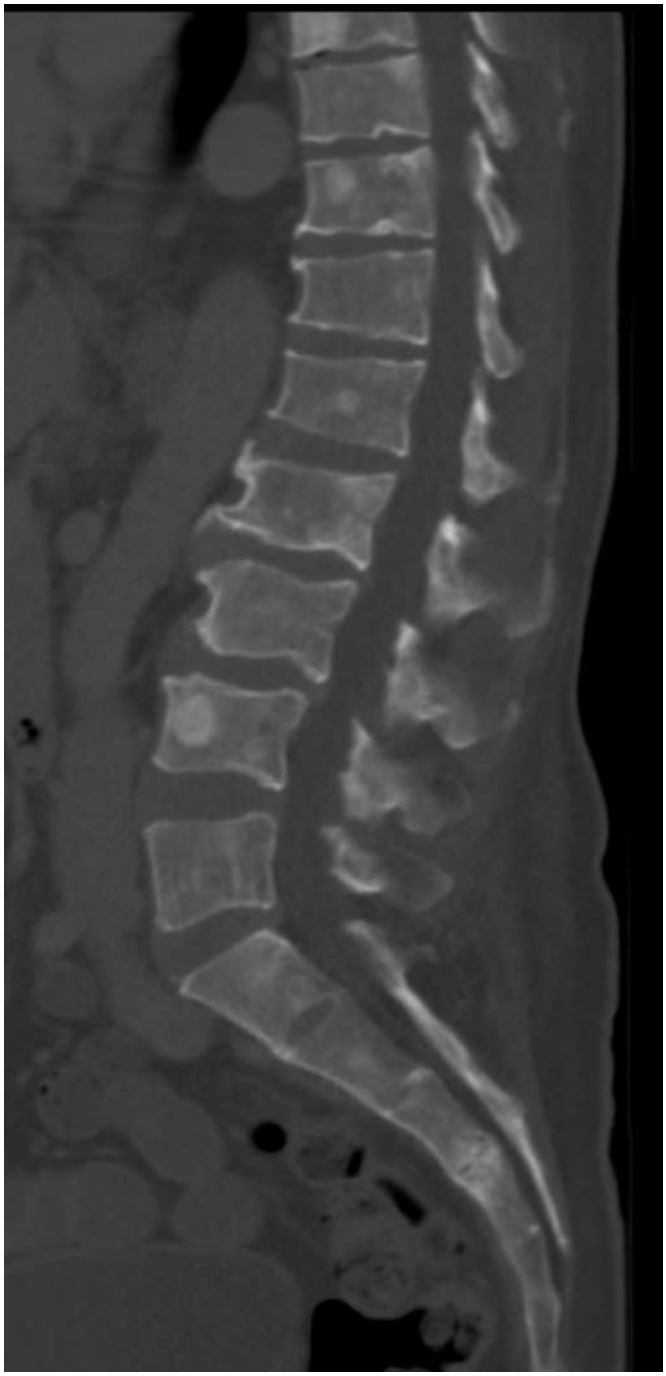


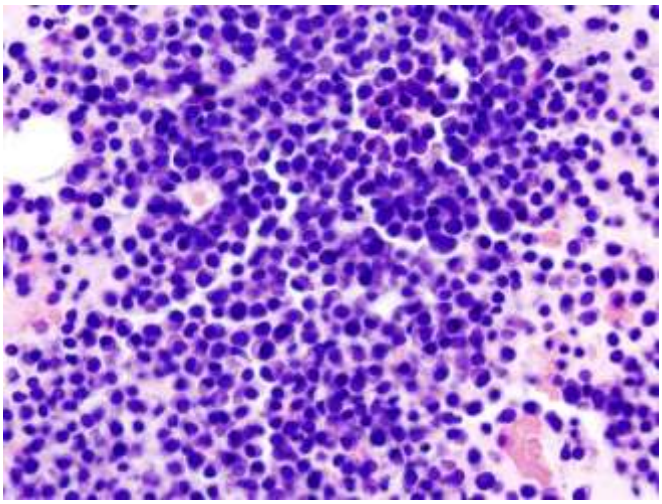

Célula madre sanguínea
Célula madre mieloide
Célula madre linfoide
Mieloblasto
Linfoblasto
Linfocito B
Granulocitos
Basófilo
Eosinófilo
Neutrófilo
Glóbulos rojos
Plaquetas
Célula plasmática
Linfocito T
Linfocito citolítico natural
Glóbulos blancos

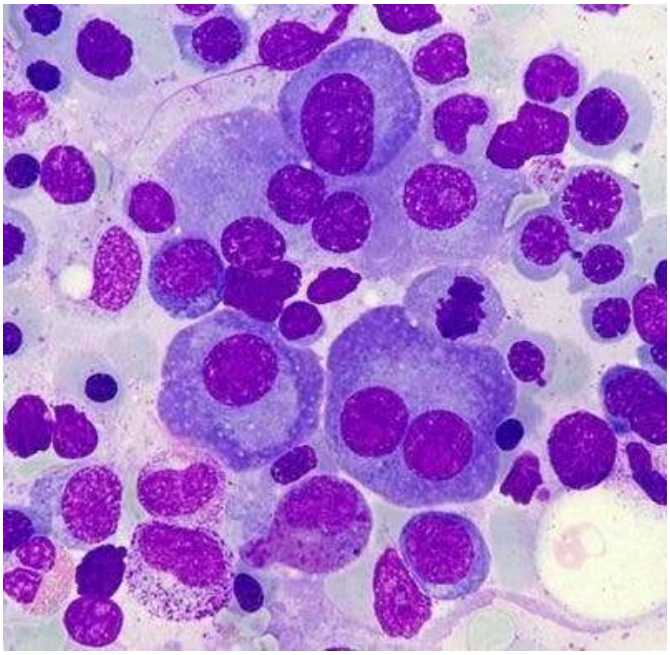


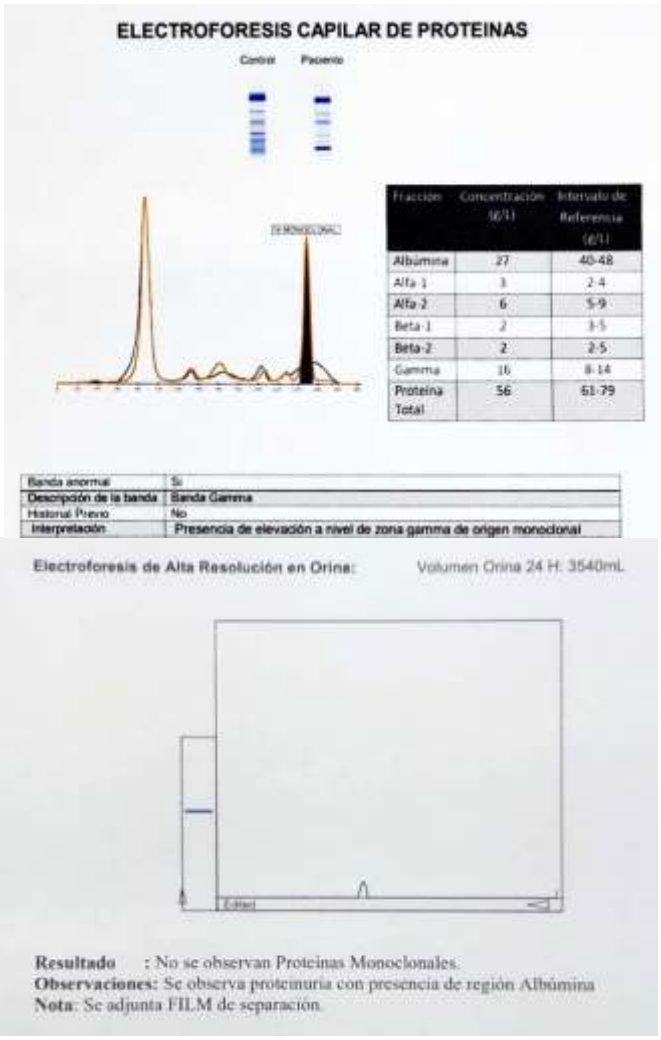












ELECTROFORESIS CAPILAR DE PROTEINAS

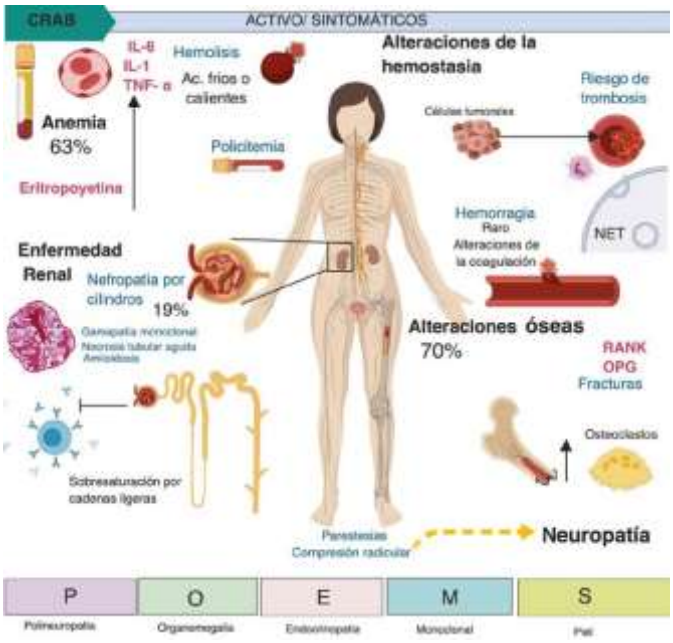
Control Paciente

Fracción	Concentración (g/L)	Intervalo de Referencia (g/L)
Albúmina	27	40-48
Alfa-1	3	2-4
Alfa-2	6	5-9
Beta-1	2	3-5
Beta-2	2	2-5
Gamma	16	8-14
Proteína Total	56	61-79

Banda anormal	Si
Descripción de la banda	Banda Gamma
Historial Previo	No
Interpretación	Presencia de elevación a nivel de zona gamma de origen monoclonal

Electroforesis de Alta Resolución en Orina: Volumen Orina 24 H: 3540mL

Resultado : No se observan Proteínas Monoclonales.
Observaciones: Se observa proteinuria con presencia de región Albúmina
Nota: Se adjunta FILM de separación.


CRAB
ACTIVO/ SINTOMÁTICOS
IL-6
IL-1
TNF- α
Hemolisis
Ac. fríos o calientes
Alteraciones de la hemostasia
Riesgo de trombosis
Anemia
63%
Eritropoyetina
Policitemia
Hemorragia
Raro
Alteraciones de la coagulación
NET
Enfermedad Renal
Nefropatía por cilindros
19%
Alteraciones óseas
70%
RANK
OPG
Fracturas
Osteoclastos
Sobresaturación por cadenas ligeras
Parestesias
Compresión radicular
Neuropatía
P
O
E
M
S
Polineuropatía
Organomegalia
Endocrinopatía
Monoclonal
Piel