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Diagnostic challenge: cardiac myeloid sarcoma in a patient with acute myeloid leukemia

Reto diagnóstico: sarcoma mieloide cardiaco en un paciente con leucemia mieloide aguda

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Keywords: cardiac myeloid sarcoma, imaging studies, cardiovascular imaging, cardiac granulocytic sarcoma, cardiac chloroma.

Palabras clave: *sarcoma mieloide cardiaco, estudios de imagen, imagen cardiovascular, sarcoma granulocítico cardiaco, cloroma cardiaco.*

ABSTRACT

Introduction: myeloid sarcoma, also known as granulocytic sarcoma or chloroma, is a malignant neoplasm resulting from the infiltration of immature myeloid cells into extramedullary tissues, with an estimated incidence of 2.5-9.1% in patients with acute myeloid leukemia (AML). The heart is an uncommon site of occurrence (< 1%). Currently, there are no firmly established diagnostic or treatment guidelines for this condition. **Case report:** a 21-year-old female patient with a history of acute myeloid leukemia (translocation 9:11), diagnosed at age 16. After receiving chemotherapy, she achieved remission in October 2019. She was referred for follow-up in December 2021, presenting with wasting syndrome, palpitations, and dyspnea (NYHA II). **Conclusions:** this case highlights the rarity of cardiac myeloid sarcoma and underscores the need for the use of multimodal imaging in diagnosis and follow-up. Additionally, it emphasizes the importance of establishing specialized care pathways with a cardio-onco-hematological perspective in Mexico.

RESUMEN

Introducción: *el sarcoma mieloide, también conocido como sarcoma granulocítico o cloroma, es una neoplasia maligna resultante de la infiltración de células mieloides inmaduras en tejidos extramedulares, con una incidencia estimada de 2.5-9.1% en pacientes con leucemia mieloide aguda (LMA). El corazón es un sitio poco común de aparición (< 1%). Actualmente, no existen pautas diagnósticas ni de tratamiento firmemente establecidas para esta condición.* ***Caso clínico:*** *paciente femenino de 21 años con antecedente de leucemia mieloide aguda (translocación 9:11), diagnosticada a los 16 años. Tras recibir quimioterapia logró la remisión en octubre de 2019. Fue referida para seguimiento en diciembre de 2021, presentando síndrome consuntivo, palpitaciones y disnea (NYHA II).* ***Conclusiones:*** *este caso resalta la rareza del sarcoma mieloide cardiaco y subraya la necesidad de utilizar imagenología multimodal en el diagnóstico y seguimiento. Además, destaca la relevancia de establecer rutas asistenciales especializadas con una perspectiva cardio-onco-hematológica en México.*

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Abbreviations:

AML = Acute Myeloid Leukemia
CMS = Cardiac Myeloid Sarcoma
MRI = Magnetic Resonance Imaging
MS = Myeloid Sarcoma
NYHA = New York Heart Association
PET = Positron Emission Tomography
PET-CT = Positron Emission Tomography-Computed Tomography scan

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INTRODUCTION

Myeloid Sarcoma (MS) is associated with childhood Acute Myeloid Leukemia (AML) and may appear before AML is diagnosed, during its course, or even in isolation without bone marrow involvement (Primary or Isolated Myeloid Sarcoma).[1] Additionally, the expression of this pathology has been linked to Myeloproliferative Disorders or Myelodysplastic Syndromes during adulthood. The presentation of MS in cardiac localization, as in this case, is uncommon and accounts for < 1% of cases, so a high index of suspicion in the clinical context is warranted.[2]

There are multiple risk factors for developing this condition, including chromosomal aberrations (monosomy 7, trisomy 8, and rearrangement of the MLL gene) or manifestation of subtypes of promyelocytic and myelomonocytic leukemia (according to the French-American-British [FAB] classification for AML),[3] and the expression of Auer rods in leukemia cells has been described as a risk factor associated with the presentation of myeloid sarcoma.[4]

Due to the extremely rare presentation of Cardiac Myeloid Sarcoma (CMS), there are no well-established guidelines or consensus on the diagnosis, management, and treatment of this disease.

CASE PRESENTATION

This is a 21-year-old female patient, native and resident of Mexico City, with a history of acute myeloid leukemia with translocation (9:11), diagnosed at the age of 16 (February 2019). Initially managed and treated at the *Hospital Infantil de México*, where she received chemotherapy *(Table 1)*, and complete remission by bone marrow aspiration (BMA) was documented in October 2019. Consequently, she was referred to our center, *Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán* in December 2021, upon reaching adulthood for follow-up. This month, the patient presented with wasting syndrome, palpitations, and dyspnea (NYHA II).

Consequently, an electrocardiogram was conducted, and an echocardiogram was scheduled. A 12-lead electrocardiogram performed in December 2021 showed a First-degree AV Block, with a PR interval of 240 milliseconds *(Figure 1)*. An echocardiogram performed in January 2022 reported an infiltrating mass of 49 × 26 mm in the lower two-thirds of the interatrial septum, with retro-aortic infiltration and at the base of the anterior leaflet of the aortic valve. A decreased global longitudinal strain of -17% and an ejection fraction of 45% were reported *(Video 1 https://www.medigraphic.com/videos/cardiovascuar/cms252v_1)*.

Differential diagnosis. Clinically, there are multiple conditions that need to be differentiated from cardiac myeloid sarcoma, because they present with a very similar clinical picture. For example, benign cardiac tumors, any type of cardiac metastasis, or even some cardiomyopathies. Additionally, we should also consider cardiac lymphomas. Due to this clinical mimicry, it is crucial to

Table 1: First chemotherapy regimen targeted for myeloid leukemia.

Phase	Chemotherapy regimen	Drugs used
Induction	ATEDox regimen	Cytarabine + mercaptopurine + etoposide + doxorubicin
Reinduction	AM regimen	Cytarabine + mitoxantrone
Consolidation	First cycle	Cytarabine + mitoxantrone
	Second cycle	Cytarabine + etoposide
	Third cycle	Cytarabine
	Fourth cycle	Cytarabine + etoposide

Note: Abstract of the chemotherapy regimen targeted for myeloid leukemia in February 2019.

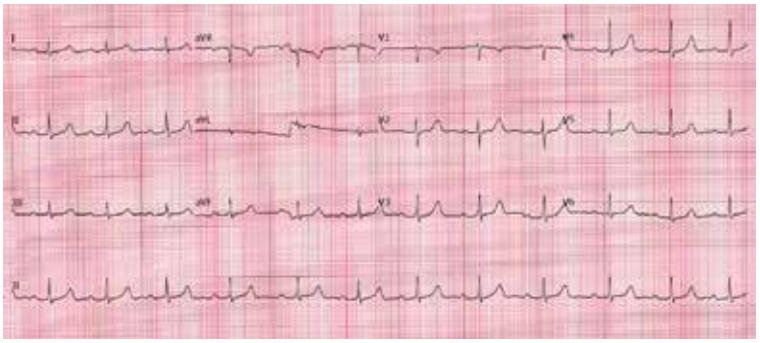

Figure 1: A 12-lead EKG is performed with the unique finding of a First-degree AV Block, with a PR interval of 240 milliseconds.

Table 2: Treatment for heart failure prescribed (January 2022).

Carvedilol 6.25 mg orally every 24 hours
Dapaglifozin 5 mg orally every 24 hours
Sacubitril/valsartan 50 mg orally every 12 hours

This table summarizes the medical treatment provided after the patient's symptoms and echocardiogram indicated heart failure with reduced ejection fraction and altered global longitudinal strain.

perform immunohistochemical characterization of the lesions.

Investigations. Based on the previous findings, she was referred to the cardiology service to start treatment for heart failure *(Table 2)* and also a cardiac magnetic resonance imaging (MRI), Positron Emission Tomography (PET), and bone marrow aspiration (BMA) with immunofixation, cytogenetics were requested.

Magnetic Resonance Imaging was performed in January 2022, and an infiltrating mass of the interatrial septum was identified, with invasion of the anterior atrial wall and the upper third of the interventricular septum *(Video 2 https://www.medigraphic.com/videos/cardiovascuar/cms252v_2)*.

PET-CT (Positron Emission Tomography-Computed Tomography scan) performed in February 2022 reported irregular solid tissue in the interatrial septum with an SUV of 7.0 and extension surrounding the ascending aorta, as well as focal metabolism in fatty tissue of the aortopulmonary window with an SUV of 4.8; these findings are compatible with neoplastic activity *(Figure 2)*.

Bone Marrow Aspiration, performed in February 2022, demonstrated decreased cellularity. No blasts, 6% eosinophils. Macrophages without hemophagocytosis. Additionally, immunofixation showed weak CD45, CD117+, CD34+, CD13+ and

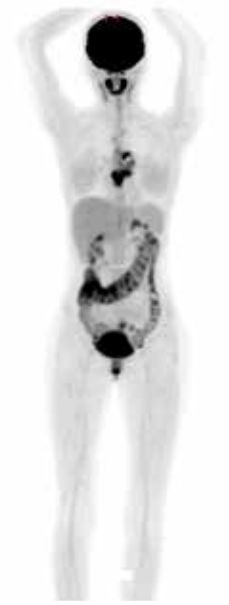

Figure 2: PET-CT performed in February 2022.

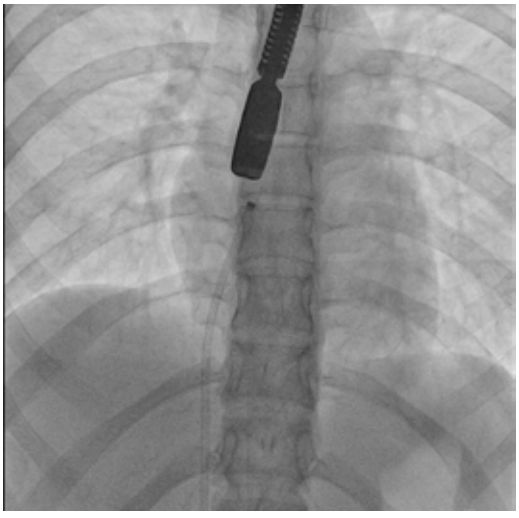

Figure 3: Biopsy performed by catheterization and guided by transesophageal echocardiography (TEE).

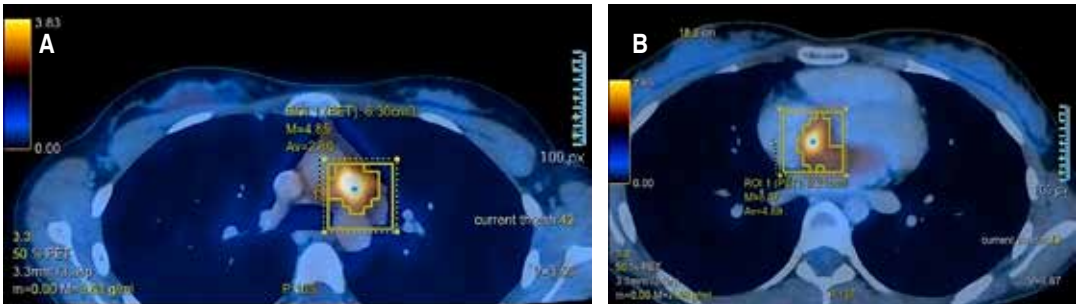

Figure 4: A) PET-CT performed in April 2022. **B)** PET-CT performed in April 2022.

Table 3: Second chemotherapy regimen.

Cycle	Drugs used	Dosage regimen (mg/m^2)
First	Azacitidine	75
	Venetoclax	100
Second	Azacitidine	75
	Venetoclax	100
Third	Azacitidine	75
	Venetoclax	100

CD33+. Bone biopsy showed hypocellular (50%) bone with adequate maturation without infiltration or presence of blasts.

Consequently, to characterize this lesion histopathologically, a first biopsy of the mass was performed, in march 2022 via right femoral venous catheterization guided by transesophageal echocardiography (TEE) *(Figure 3)* in which it was reported myocardium with CD45+ lymphocyte foci, MPO−, calretinin−, and S100−. These results were not conclusive for determining a tumor of myeloid origin.

A follow-up PET-CT was performed in April 2022, showing increased lesion activity (SUV 8.8) *(Figure 4)*. Thus, probable disease recurrence with CMS was suspected despite the initial biopsy result. Consequently, it was decided to initiate second-line chemotherapy *(Table 3)*.

During treatment, PET-CT follow-up in June 2022 showed reduced metabolic activity (SUV 5.6) with no changes in dimensions. Consequently, in August 2022, increased uptake despite treatment was reported (SUV 8.8), leading to a determination of refractory disease.

Afterwards, a second biopsy was performed in September 2022 to determine the histopathological origin of the mass. The reported results were as follows; MPO+, CD68+, CD4+, TdT-, HLA-DR+, lysozyme+. Therefore, these findings were consistent with the diagnosis of cardiac myeloid sarcoma. The histological sections obtained are included in the image *(Figure 5)*.

Management and follow-up. Due to refractory disease, a rescue regimen of FLAG-IDA-VEN. Idarubicin was excluded due to the high risk of cardiotoxicity in October 2022. Afterward, three consolidation cycles of this same regimen were administered in December 2022, January 2023, and May 2023 *(Table 4)*.

Subsequently, in February 2023, imaging studies were conducted, including a transthoracic echocardiogram, PET-CT *(Figure 6)*, and cardiac magnetic resonance imaging, revealing persistence of the mass. However, a decrease in uptake in the PET-CT was observed, with an SUVmax of 2.5.

Due to the patient's refusal to enroll in a hematopoietic stem cell transplantation protocol and also decline in continuing chemotherapy treatment, it was decided to initiate a plan of radiation therapy sessions. It is important to note that better therapeutic outcomes have been documented with radiotherapy; therefore, this type of therapy was chosen.

A PET-CT imaging study was conducted in February 2024 *(Figure 7)*, which showed a much more pronounced decrease in metabolic activity (1.8 SUV), compared with previous studies that showed higher metabolic activity *(Figure 8)*. Additionally, a new echocardiogram reported an ejection fraction of 60% and a

global longitudinal strain of −19%, attributed to treatment for heart failure.

We have attached an abstract image that provides a clearer view of the case and its evolution over time *(Figure 9)*.

DISCUSSION

In the case presented above, both the patient's initial manifestations and her hematologic/oncologic history guided the search for underlying cardiovascular pathology, employing an initial approach with echocardiography that identified the interatrial mass. Available literature highlights the importance of conventional imaging techniques (Computed Tomography and Magnetic Resonance Imaging) as pillars in the non-invasive diagnosis of CMS,[5] which help conduct a deeper investigation into the layers, chambers, and valves involved. Similarly, other imaging methods such as echocardiography or Positron Emission Tomography (PET) play crucial roles.[6] In the presented case, an approach through MRI was decided upon, corroborating the infiltrating mass of the interatrial septum with malignant characteristics and delineating its extension. Additionally, an initial PET-CT was performed, which showed increased metabolic activity, guiding diagnostic suspicion toward malignant neoplastic etiology; PET-CT also played a key role in patient follow-up, guiding the diagnostic approach to the mass and assessing response to chemotherapy (refractory to second-line regimen but with partial response to the rescue regimen).[7]

Other studies such as histopathological, immunohistochemical, and molecular analyses help stratify risk and make therapeutic decisions.[8] Typically, histopathological examination reveals an infiltrate of myeloid cells at various stages of maturation, which may exhibit granulocytic or monocytic maturation, sharing similarity with the histological appearance of Acute Myeloid Leukemia.[9]

In the presented case, although the first biopsy obtained by intervention was inconclusive, the findings of PET-CT and the t(9;11) translocation in peripheral blood guided the initiation of treatment. Subsequently, due to a lack of response to the second-line treatment regimen, a second biopsy was performed,

Table 4: FLAG-IDA-VEN regimen for refractory disease.

Fludarabine: 30 mg/m^2 IV daily for five days
Cytarabine (Ara-C): 2 g/m^2 IV daily for five days
Idarubicin: 12 mg/m^2 IV daily for three days (excluded due to high risk of cardiotoxicity)
Venetoclax: 100 mg orally daily for the first seven days, escalating to 200 mg daily for the next seven days, up to a maximum of 400 mg daily.

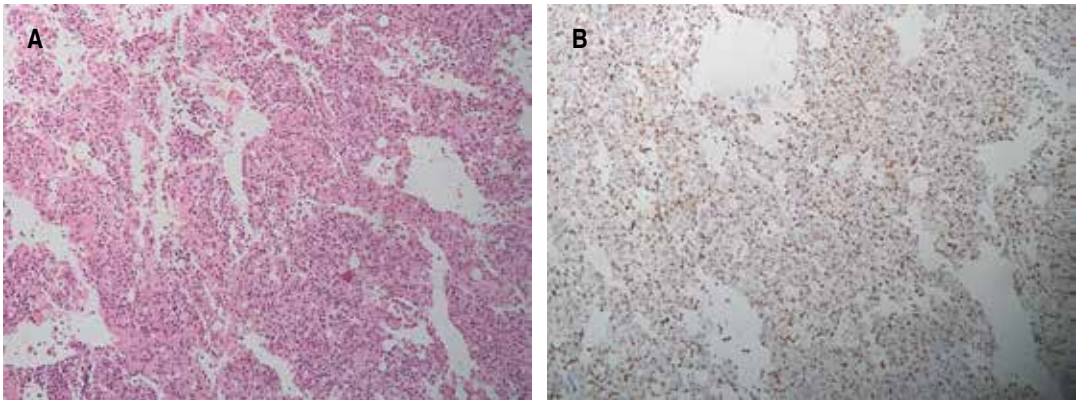

Figure 5: A) Histological section stained with hematoxylin-eosin (H&E) showing abundant infiltrate composed of small-sized cells with clefted nuclei and scant cytoplasm. **B)** Diffuse staining is observed with the myeloperoxidase (MPO) reaction.

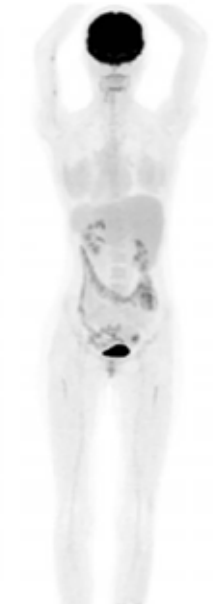

Figure 6: PET-CT performed in February 2023.

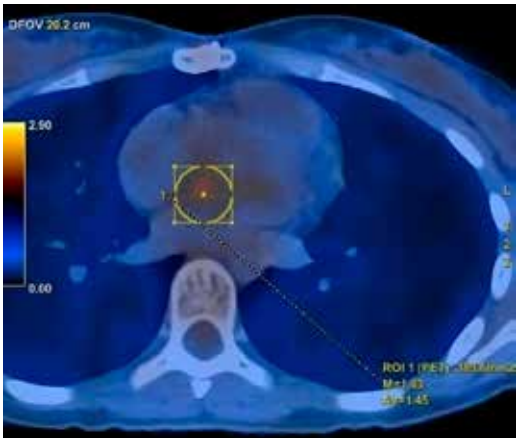

Figure 7: PET-CT performed in February 2024.

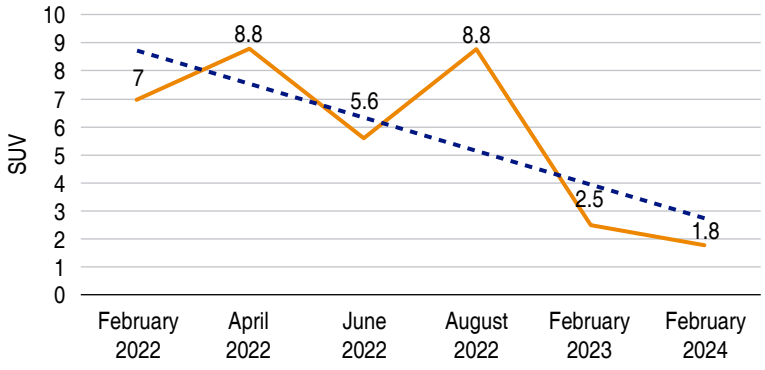

Figure 8: Changes in PET-CT standardized uptake value (SUV).

which was positive for MPO, CD68, CD4 and HLA-DR, confirming the myeloid origin of the tumor. In conjunction with the patient's clinical context, set the basis for initiating rescue therapy.

Anthracyclines were not used in Acute Myeloid Sarcoma, despite being of myeloid origin, due to their association with chemotherapy-associated cardiac dysfunction. However, better therapeutic outcomes have been documented with radiotherapy, so this type of therapy was opted for, achieving follow-up for resolution of Cardiac Myeloid Sarcoma with preservation of cardiac function.[10]

CONCLUSIONS

1. **Rarity of the condition:** this case report underscores the rarity of cardiac myeloid sarcoma and encourages physicians to consider similar diagnoses in patients presenting with cardiac masses.
2. **Role of multimodal imaging:** this case highlights the crucial role of multimodal imaging in both diagnosing and monitoring cardiac masses, providing valuable insights for effective treatment.
3. **Collaborative approach:** the collaborative approach between hematology and cardiology services was essential in guiding the diagnosis and initiating the appropriate treatment.
4. **Need for specialized pathways:** this case emphasizes the importance of establishing and promoting healthcare pathways with a cardio-onco-hematologic perspective in Mexico to improve patient care for complex conditions.

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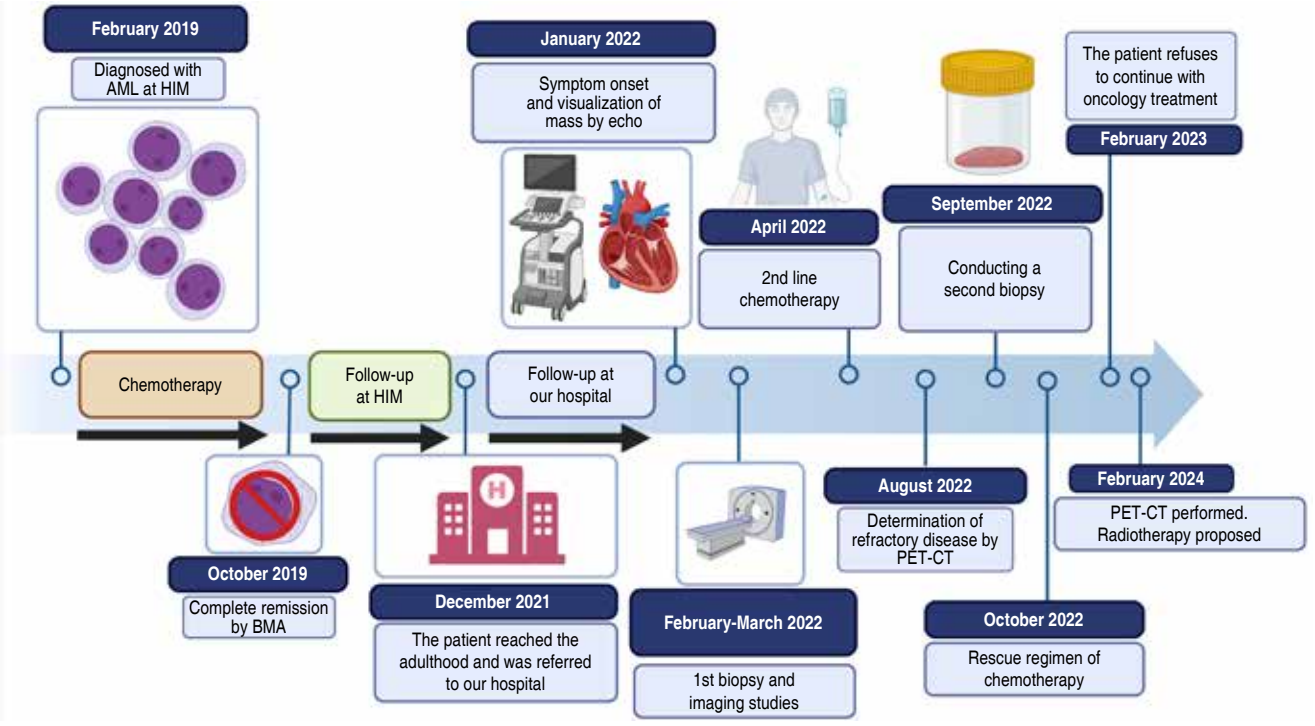

Figure 9: Abstract image that provides a clearer view of the case and its evolution over time.
AML = Acute Myeloid Leukemia. BMA = Bone Marrow Aspiration. HIM = *Hospital Infantil de México.* PET-CT = Positron Emission Tomography-Computed Tomography scan

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