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Case report / Reporte de caso

Sarcoma of interdigitating dendritic cells. Case report

Sarcoma de células dendríticas interdigitantes. Reporte de caso

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ABSTRACT
Dendritic cells, essential in the immune response by presenting antigens to T and B lymphocytes, can develop extremely rare neoplasms, representing less than 1% of lymph node-originating tumors. We present a case of interdigitating dendritic cell sarcoma that, treated with chemotherapy, showed favorable progression and a good prognosis. Due to the rarity of this disease, it is crucial to consider it in differential diagnoses, as patient survival depends on the stage at which it is detected

Keywords: Case report, Immunohistochemistry, Dendritic cells, PET CT (F18-FDG).

RESUMEN
Las células dendríticas, fundamentales en la respuesta inmune al presentar antígenos a los linfocitos T y B, pueden desarrollar neoplasias extremadamente raras, que representan menos del 1 % de los tumores de origen ganglionar. A continuación, se presenta un caso de sarcoma de células dendríticas interdigitantes que al ser tratado con quimioterapia mostró una evolución favorable y un buen pronóstico. Debido a la rareza de esta enfermedad, es crucial considerarla en el diagnóstico diferencial, pues la supervivencia del paciente depende del estadio en el que se detecte.

Palabras Clave: reporte de caso clínico, inmunohistoquímica, células dendríticas, PET CT (F18-FDG).

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1. Introduction

Interdigitating dendritic cell sarcoma (IDCS) is a rare hematologic neoplasm with a complex diagnosis, often confused with other types of neoplasms, which leads to delayed diagnosis and an unfavorable prognosis for the patient. Here, we present a case of a 68-year-old female patient, initially suspected of having colon cancer. However, through histopathological studies, it was determined that she had a lymphoid neoplasm compatible with the disease described in this case report. This article details the diagnostic process, oncological management, treatment response, and current status, as well as a brief review of the topic to help readers understand the medical decisions made.

2. Case Report

A 68-year-old female patient with a history of hypertension, a colon tumor under investigation, and current pharmacological treatment with losartan. She also has a history of traumatic elbow fracture managed with a prosthesis and is a former smoker. She showed up at the emergency department with a two-month history of progressive abdominal pain associated with asthenia, adynamia, and pallor. Upon physical examination at admission, the abdomen showed no distension, positive peristalsis; it was soft, depressible, and tender to deep palpation in the left hemiabdomen. A palpable, hard, mobile mass was noted in the left hypochondrium without signs of peritoneal irritation. Hospital admission was decided for further studies. The patient provided a pathology report from a colonoscopy biopsy: "Distal ileum biopsies. Benign nodular lymphoid hyperplasia with focal villous atrophy and moderate chronic ileitis; ascending colon with polypectomy of a tubular adenoma with low-grade dysplasia." Contrast-enhanced abdominal and pelvic CT scan revealed retroperitoneal and mesenteric adenopathy suggestive of infiltrative neoplastic disease, along with thickening of the walls of the right colon. Based on these findings, inpatient management was deemed necessary. Additional laboratory tests documented elevated CA125, fibrinogen, and coagulation times. The infectious profile was negative, and results for folic acid, ESR, reticulocyte percentage, total proteins, and tumor lysis laboratory values were within normal ranges. Given these findings, an initial suspicion of lymphoproliferative disease with possible extranodal involvement was considered. Hematology was consulted, the initial clinical suspicion was confirmed and further extension studies were recommended, including:

- **July 22, 2021, PET-CT (F18-FDG):** Supra- and infra-diaphragmatic hypermetabolic lymphadenopathies, suggesting glycolytic tumor activity; consideration of lymphoproliferative disease, diffuse thickening of the right ascending colon wall, and diffuse FDG uptake in the axial skeleton (Figure 1).
- **July 29, 2021, Flow Cytometry on Bone Marrow:** No cell populations were identified that expressed immunophenotypes associated with hematologic neoplasms.
- **February 2022, Cytogenetics on Bone Marrow**:
    - Sample Results: 46, XX
    - Interpretation: No neoplastic clones were detected. This result does not exclude a hematologic neoplasm.
    - Observation: Occasional chromosomal breaks were noted. A metaphase 92, XXXX, -4, +6, -8, -11, +16, +17, -19, -19, +22 was observed. No translocations were described.
    - Cell Notes: Estimated resolution of banding: 475.

BONE MARROW BIOPSY

Pathology Report (September 4, 2021):

- **Macroscopic Description:** A paraffin block labeled as BR-1877-21 was received.
- **Microscopic Description:** The sections show a bone marrow core with an approximate cellularity of 40%, with megakaryocytes present and evidence of maturation across all cell lines. No blasts

are observed, and there is no abnormal presence of lymphoid or plasmacytic populations, which is confirmed by immunoperoxidase markers for CD34, CD20, CD3, and CD38.

- **Diagnosis:** Normal hematopoiesis of the three cell lines.

Immunohistochemistry Report (September 7, 2021):

- **Macroscopic Description:** Tissue embedded in paraffin, labeled #1453-21 A1, was received for study via immunohistochemistry.
- **Microscopic Description:** The problematic population is positive for CD45, VIMENTIN, S100, and CD20. It is negative for PANCYTOKERATIN and HMB45. These findings suggest a lymph node pathology compatible with interdigitating dendritic cell sarcoma of cervical lymph nodes. The case was reviewed in a pathology board, requiring an expanded marker panel to exclude other differential diagnoses. Metastases of epithelial and melanocytic origin were excluded.
- **Conclusion:** Block #1453-21 A1; Immunohistochemistry: Compatible with **INTERDIGITATING DENDRITIC CELL SARCOMA (IDCS).**

With these findings and the relevant clinical analysis, the diagnosis of IDCS was considered at the time, and treatment was initiated. The patient underwent 6 sessions of R-CHOP chemotherapy. Flow cytometry in the bone marrow showed aberrant plasma cells at 0.11%, and a PET-CT (F18-FDG), when compared to the initial study, reported resolution of supra- and infra-diaphragmatic adenopathy (See Figure 1). The scan also showed an iliac internal chain adenopathy with FDG uptake, surpassing liver uptake, which, based on Deauville criteria, scored a 4, thus indicating a partial response to treatment.

As a result, the treating hematologist recommended a second-line chemotherapy regimen (RICE) for 3 cycles. At the end of these sessions, a follow-up PET scan revealed the resolution of adenopathy in the obturator chain (Figure 3), demonstrating a complete metabolic response. Based on these findings, the patient was declared in remission. Given the favorable evolution, maintenance immunotherapy was initiated with a standard-dose Rituximab regimen for low-grade lymphoma, administered every 2 months for 2 years. As for the writing of this report, the patient has successfully completed 9 cycles and remains in remission.

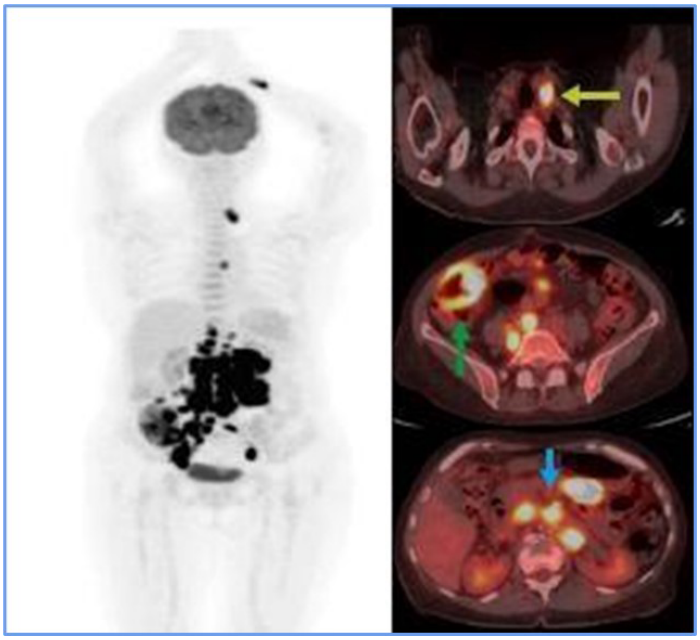

Figure 1. Initial PET CT. Hypermetabolic supra (yellow arrow) and infra diaphragmatic (blue arrow) adenopathy suggest tumor glycolytic activity. Diffuse mural thickening of the hypermetabolic ascending colon (green arrow) in the clinical context of suspected lymphoproliferative disease suggests extranodal involvement.
Fuente: Organización Clínica Bonnadona Prevenir, Barranquilla, Atlántico

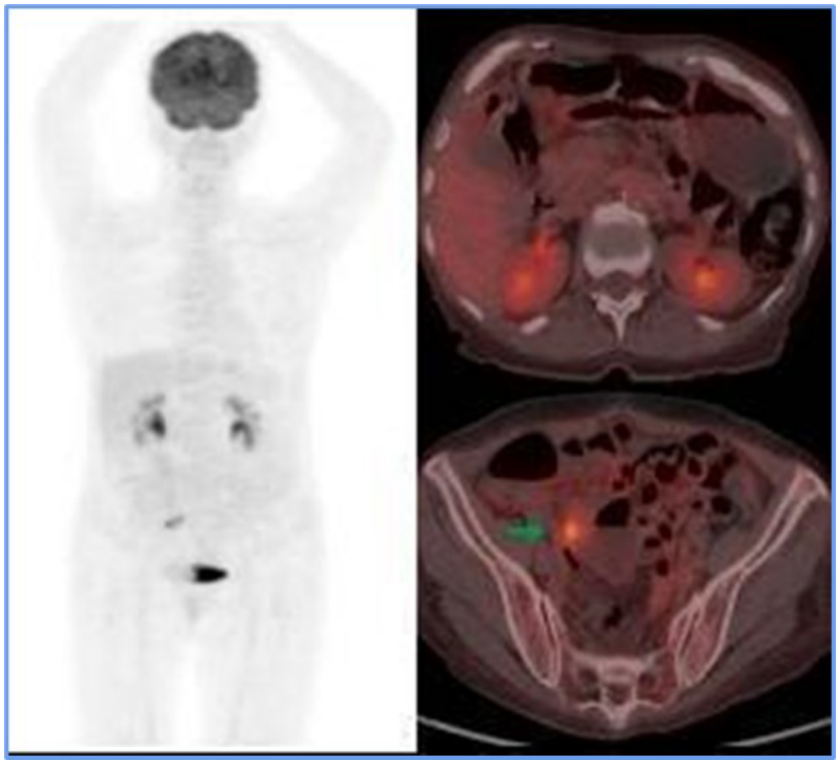

Figure 2. PET CT before ICE regimen. Only the right internal iliac chain adenopathy was evident (green arrow), which showed FDG uptake, exceeding hepatic uptake about score 4 of the Deauville criteria, suggesting a partial metabolic response to the medical treatment instituted.
Fuente: Organización Clínica Bonnadona Prevenir, Barranquilla, Atlántico

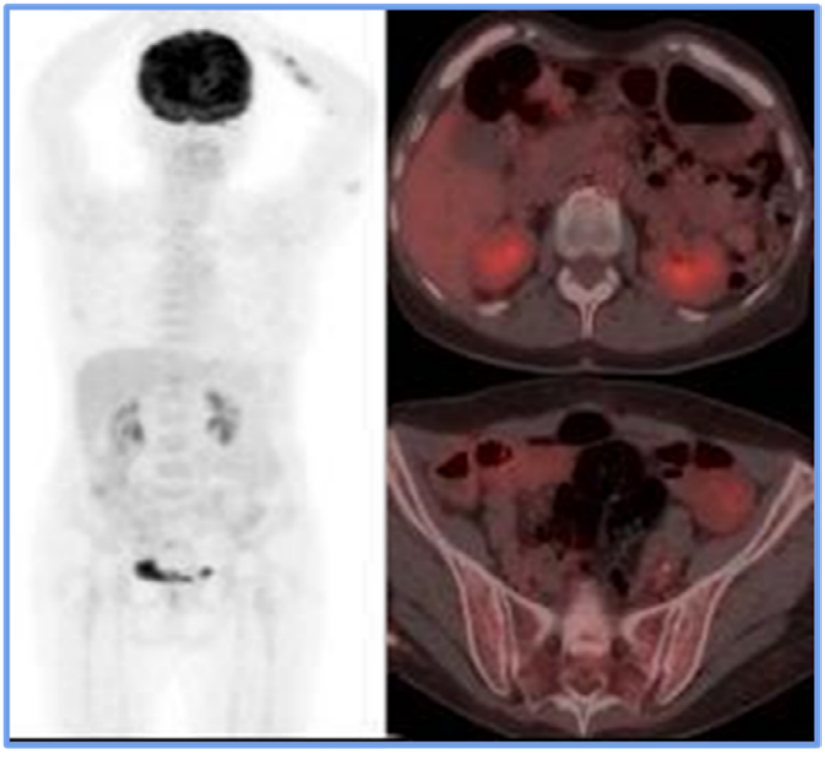

Figure 3. PET CT scan following the rescue scheme. It presents the resolution of adenopathy in the proper internal iliac chain, which is related to morphological and metabolic responses to medical treatment.
Fuente: Organización Clínica Bonnadona Prevenir, Barranquilla, Atlántico

3. Discussion

Dendritic cells are essential in the immune response, acting as a bridge between the innate and adaptive immune systems [1]. These cells are classified into follicular, Langerhans, fibroblastic, and interdigitating types [4]. They are typically found in lymph nodes, the spleen, tonsils, and mucosa-associated lymphoid tissues (MALT) [2]. Dendritic cells originate in the bone marrow or through migration from Langerhans cells [4].

Dendritic cell neoplasms (DCNs) are rare, representing less than 1% of lymphoid-origin tumors [1,6]. DCNs are classified into two main types: stromal dendritic cell neoplasms and myeloid-origin neoplasms, the latter being the focus of this clinical case [5]. Literature reports describe only about 100-127 cases, predominantly in men over 60 years of age, with high metastasis rates (39%) and an average survival of one year in advanced stages [2,3,4,5].

Interdigitating dendritic cell sarcoma (IDCS) typically presents as a painless lymphadenopathy, most commonly in the cervical region, but it has also been described in the axillary, mediastinal, abdominal, and inguinal regions [5]. The most frequent localization site is the lymph nodes, with a prevalence of 47%, and 25% of patients present extranodal involvement. Depending on the affected site, systemic symptoms may be present [2].

The diagnosis of IDCS is complex and requires pathology studies and immunohistochemistry. Due to its low prevalence, there are no established treatment guidelines. Treatment options include surgery, radiotherapy, and chemotherapy, depending on the disease stage [2].

The pathogenesis of IDCS has not been linked to a specific trigger. However, there have been reports of cases in patients who previously received treatments with Tacrolimus, suggesting a T-cell malignancy following its dysregulation, facilitating the development of this type of neoplasm [4]. Histologically, tumor cells are spindle-shaped or histiocytic, with irregular borders, eosinophilic cytoplasm, and enlarged nuclei. They resemble Langerhans cells microscopically but lack Birbeck granules and do not express CD1a or langerin [5].

Immunohistochemical studies typically express markers such as S-100, vimentin, HLA-DR, and CD68. Differential diagnoses include follicular dendritic cell sarcoma, indeterminate dendritic cell tumor, Langerhans cell sarcoma, anaplastic large cell lymphoma, and histiocytic sarcoma. One of the most challenging presentations to differentiate is follicular dendritic cell sarcoma, as both are hematologic neoplasms derived from similar precursors, sharing morphological and clinical features. However, immunohistochemistry can help differentiate these entities. Follicular dendritic cell sarcoma expresses CD21, CD23, and CD35, unlike IDCS. Furthermore, IDCS can mimic non-hematologic neoplasms, such as sarcomas, carcinomas, or melanomas. Metastatic melanoma, for instance, may be confused with IDCS due to expression of S-100 and CD68, but it expresses its own distinct immunohistochemical markers [4].

For staging, PET-CT (F18-FDG) is a crucial tool. Initially, it allowed for documentation of both nodal and extranodal involvement, establishing tumor viability and aiding in follow-up and evaluation of treatment response. The Deauville 5-point visual scale [7] was used to assess treatment response. In this case, the PET-CT documented persistent disease (Deauville 4), which influenced treatment decisions and led to escalation of the medical management. A subsequent PET-CT (F18-FDG) performed after rescue therapy demonstrated a complete metabolic response at the end of treatment [8].

There are no defined treatment guidelines for IDCS due to its low prevalence and unclear etiopathogenesis. For localized disease in early stages, surgery and/or targeted radiotherapy may be considered, although no significant survival differences have been found between surgical and conservative management [5]. In cases with metastatic disease, chemotherapy is usually preferred due to its systemic reach. Chemotherapy regimens used are typically those directed at non-Hodgkin lymphoma, though no regimen has been proven superior to others [4].

IDCS prognosis is directly related to the stage at diagnosis. Survival rates are lower in metastatic stages at the time of treatment initiation [3].

In the case presented here, the patient showed a favorable response to chemotherapy, achieving complete remission and surviving for two years to date. Lymph node and extranodal involvement, along with immunohistochemical findings, enabled the diagnosis and timely treatment initiation (Figure 1). The partial metabolic response observed in the post-treatment PET (Figure 2) led to the decision to

escalate the treatment to second-line RICE chemotherapy. Eventually, a new PET-CT (F18-FDG) post-treatment (Figure 3) confirmed a complete metabolic response.

4. Conclusion

Although IDCS is a very rare pathology due to its similarity to other hematological neoplasms, it should be considered as a differential diagnosis by exclusion, particularly when patients present with lymphadenopathy. It has been reported that 19.7% of cases occur in patients with a previous second malignancy, and in other cases, as a consequence of certain chemotherapy treatments for breast cancer or immunosuppressive therapies. However, due to the limited number of disease reports and the scarce information available, it is not currently possible to determine a clear etiology that explains its origin [4].

It is important to emphasize the critical role of studies such as histopathology and immunohistochemistry, which enable distinguishing among differential diagnoses. This is essential for the timely initiation of treatment, given the poor prognosis of the disease in advanced stages.

5. Abbreviations

TAC: Computed Axial Tomography

PET-CT (F18-FDG): Acronym in English: Positron Emission Tomography - Computed Tomography (Fluorodeoxyglucose 18 - FluoroDeoxyGlucose). In Spanish: Positron Emission Tomography - Computed Tomography (Fluorodeoxyglucose 18-Fluorodeoxyglucose)

ESR: Erythrocyte Sedimentation Volume

CA-125: Carcinoma Antigen 125. (Cancer Antigen 125)

R-CHOP: Rituximab - Cyclophosphamide, Hydroxy-Daunorubicin or Doxorubicin, Oncovin brand name for Vincristine and Prednisone

MALT: Mucosa Associated Lymphoid Tissue

CD: Cluster of Differentiation

HLA: Human Leukocyte Antigen

HMB: Human Melanoma Black

6. Administrative information

6.1 Additional files

None declared by the authors.

6.2. Acknowledgements and Authors' contributions

Rodriguez Orozco and Mojica Silva contributed to analyzing and interpreting the studies presented in this paper. Their knowledge and experience were essential for rigorous data analysis and for obtaining significant conclusions from the manuscript.

The other authors made a substantial contribution to the conception, design of the study, collection, analysis, or interpretation of the data; have participated in the writing of the article or the critical revision of its intellectual content; have approved the final version of the manuscript; and can respond to all aspects of the manuscript in order to ensure that questions related to the veracity or integrity of all its contents have been adequately investigated and resolved.

6.3 Limitation of Liability

The authors assume full responsibility for the opinions and conclusions presented in this article.

6.4. Financing

The authors did not receive any financial recognition for this work.

6.5. Statements

6.5.1. Declaration

Authors assume full responsibility for the opinions and conclusions presented in this article. The journal is not responsible for any errors or omissions, nor for the interpretations or applications derived from the information contained herein.

6.5.2. Consent for publication

The patient gave written informed Consent for this report.

6.5.3. Conflicts of interest

The authors declare that there are no conflicts of interest regarding this case report. All authors have independently participated in the development, analysis, and interpretation of the data, as well as in writing the article.

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