Original Article

Rare tumors of difficult initial diagnosis

María Inés Sanz[1], Daniel Feinsilber[2], Cristina Corbella[3], Roberto Schröh[3], Mercedes Lidia Hassan[4].

Abstract

Five rare tumors of difficult initial diagnosis are reported. In each case, several differential diagnoses were suggested and many supplementary exams were necessary. These 5 patients were studied at our hospital in a six-month period, with final diagnoses of skin and soft tissue angiosarcoma, peripheral primitive neuroectodermal tumor, plasmablastic lymphoma, amelanotic and desmoplastic polipoid melanoma, and nodular vulvar melanoma (Dermatol Argent 2009; 15(4):272-277).

Key words: *angiosarcoma, primitive neuroectodermal tumor, plasmablastic lymphoma, desmoplastic melanoma, vulvar melanoma.*

Introduction

Five cases of rare tumors of difficult initial diagnosis are reported. Many supplementary exams were necessary in order to rule out other possible diagnoses and decide on a suitable therapeutic approach.

Clinical cases

Case 1

A 52-year-old male patient, with a previously unremarkable medical history, consulted on February 2008 for a 7-month evolution tumor on right shoulder. He had noticed an increase in tumor size in the preceding month with functional disability of right upper limb.

Physical examination of anterior shoulder area evidenced a 7 × 7 cm subcutaneous tumor lesion, hard to elastic in consistency, painful on palpation, covered by apparently normal skin, with telangiectasias on lower half (**Figure 1**). No lymphadenopathies were identified.

Soft tissue ultrasonography evidenced a heterogeneous hypoechoic formation of solid appearance with poorly defined borders and calcifications within it. Shoulder magnetic nuclear resonance image (MRI) was performed and shows an extending 65 × 40 × 45 mm lesion on the anterior area with heterogeneous signal in T1 and T2 and hypointensive focal areas, attached to the coracoid process. Deltoid and pectoralis major muscles covered the surface of the lesion. No axillary lymphadenopathies were found.

The suggested differential diagnoses were leiomiosarcoma, angiosarcoma, dermatofibrosarcoma protuberans and myxoid metastasis of melanoma.[1]

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1. Dermatologist, chief Residents.
2. Staff Dematologist.
3. Dermatopathologists.
4. Professor Head of Dermatology Division.

All authors belong to the Dermatology Course and Division, Hospital General de Agudos "J.M. Ramos Mejía". Autonomous City of Buenos Aires, Argentine.

Correspondence
María Inés Sanz: Av. Callao 942 Piso 1º Autonomous City of Buenos Aires, Argentine Republic | isanz2002@hotmail.com

Losange biopsy reported vascular neoplasia with retiform hemangioendothelioma features. The patient was subjected to surgery, with complete excision of the tumor lesion and dissection of pectoralis major and minor, subscapularis, and part of deltoid muscles, and the clavicle. Histopathology of the specimen reported vascular neoplasia with morphological and immunohistochemical characteristics (positive Factor VIII and CD34, slightly positive Ki-67) of skin and soft tissue angiosarcoma, alternating with differentiated hemangiolymphangiomatous and other poorly differentiated areas separating soft tissues (**Figure 2**). There was no underlying bone involvement. Resection margins were scarce.

Chest, abdomen and pelvis computed axial tomography (CAT) did not evidence systemic involvement. The patient started radiotherapy and chemotherapy with doxorubicin and dacarbazine, but discontinued treatment after the second cycle. He consulted again 8 months after diagnosis for the presence of a 3-mm painful tumor mass on surgical site. He is currently undergoing a restaging program.

Case 2

An 82-year-old male patient consulted on July 2008 for a 4-month evolution tumor on the right foot.

Physical examination evidenced on the internal malleolar area a 5-cm purplish tumor of lobated surface, soft in consistency, friable, with superficial serosanguineous crust, slightly painful at palpation (**Figure 3**). Additionally, a right inguinal lymphadenopathy was found. Probable differential diagnoses were angiosarcoma, Merkel-cell carcinoma, and B-cell cutaneous lymphoma.

Losange biopsy reported blue-cell dermo-hypodermal tumor with morphology and immuhistochemistry suggesting peripheral neuroectodermal tumor. Routine laboratory test, dosage of 24-hour urine catecholamines, and chest and pelvis CAT were requested, with results within normal limits. Right foot MRI evidenced a 49-mm heterogeneous nodular formation in medial compartment involving subcutaneous cell tissue and contacting in depth with posterior tibial, flexor digitorum and flexor hallucis tendons. Needle aspiration punction was performed on palpable inguinal lymphadenopathy related to a reactive node.

After an interdisciplinary consultation with the Traumatology Department, it was decided to perform right infrapatellar amputation -due to the functional deficit of the foot which may result from simple excision of the tumor– and inguinal lymphadenectomy. Histopathology of the samples reported blue-cell dermo-hypodermal neoplasia consistent with primitive peripheral neuroectodermal tumor (**Figure 4**). Immunohistochemistry was positive for S100, neuron-specific enolase, vimentin and synaptophysin, and negative for CK20, ACL, Melan-A, HMB 45, and CD99. Neoplastic cells was found in the inguinal lymph node.

After surgery, the patient developed a rapidly growing, painful, stony hard right inguinal mass; thus, a superficial and deep inguinal lymphadenectomy was performed, with evidence of lym-

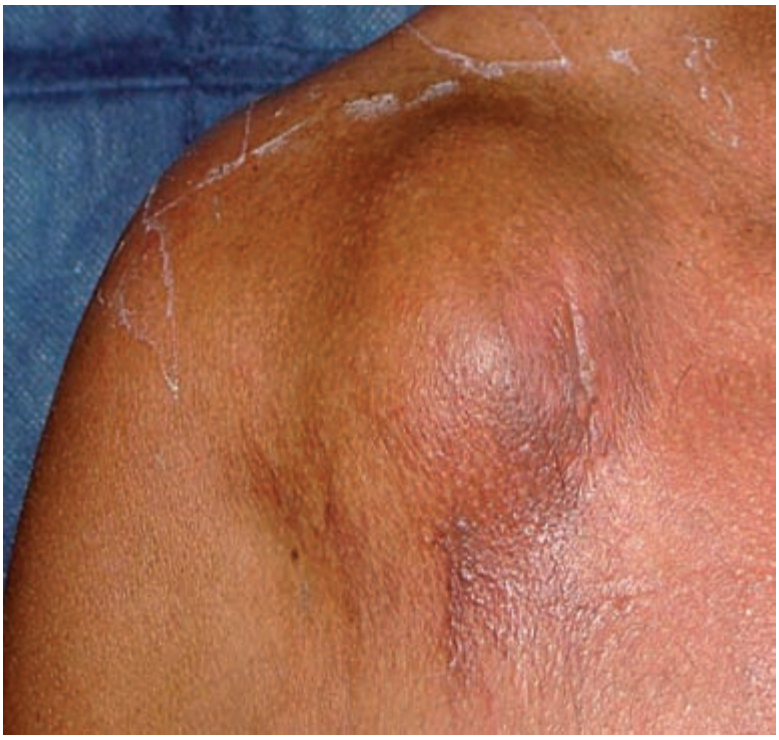

Figure 1. *Subcutaneous tumor, 7 × 7 cm, on right shoulder.*

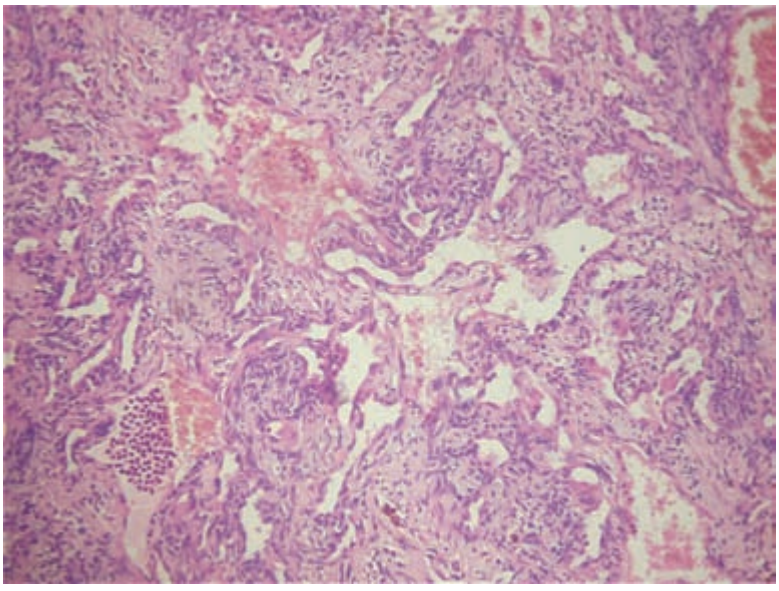

Figure 2. *Incomplete and anastomosed blood and lymphatic vascular structures.*

ph node involvement. A new CAT was performed three months after diagnosis, where images consis×tent with lung metastasis were identified. Currently, the patient undergoes a palliative radiotherapy and chemotherapy plan.

Case 3

A 61-year-old male patient, with no known history of pathologies consulted on July 2008 for a 7-month evolution purplish erythematous plaque on his left leg.

Physical examination evidenced a 7 × 13 cm purplish erythematous plaque with atrophic center on anterior aspect of the leg. When the patient undressed, multiple small wine red plaques were identified on abdomen, back, neck, thighs and palate. An asymptomatic 6 × 3 cm ulcerated exophytic tumor lesion with sanious base and raised erythematous borders was identified on the right lateral area of the hard palate, infiltrating the upper dental arch (**Figure 5**). No lymphadenopathy was identified.

Clinically, we suspected an HIV-positive patient with epidermal Kaposi's sarcoma; thus, differential diagnoses suggested for the oral lesion included plasmablastic lymphoma, squamous cell carcinoma, ulcerated Kaposi's sarcoma, CD30+ anaplastic T-cell lymphoma and deep mycosis. Numerous supplementary tests were performed, whereof the relevant ones were:

- Positive HIV serology (CD4: 135, viral burden: 178,644).
- Direct and culture of palate biopsy for AFB and fungi: negative.
- Serologies: Positive EBV and HHV-8; negative HCV, HBV and HTLV I/II.
- Helical CAT of facial bones, chest, abdomen, and pelvis: thickening of mucosa and moderate resorption of the right side maxillar sinus floor. Rest with no abnormalities discovered.

Biopsy of the leg plaque was consistent with Kaposi's sarcoma. Biopsy of the palate lesion was performed, reporting CD138+ plasmablastic lymphoma, MUM1+, Ki-67+; negative CD3, CD20, and bcl-6 (Dr. Narbaitz, Academia Nacional de Medicina) (**Figure 6**). In situ hybridization for EBERs was positive. Bone marrow biopsy reported 20 percent interstitial lymphocyte infiltration, with the presence of CD138+ plasma cells in 5 percent of the population.

The patient started antiretroviral therapy and EPOCH protocol chemotherapy (etoposide, vincristine, cyclophosphamide, doxorubicin, and prednisone) as continuous infusion for 6 cycles. Noticeable improvement of the tumor lesion was evidenced after the first cycle.

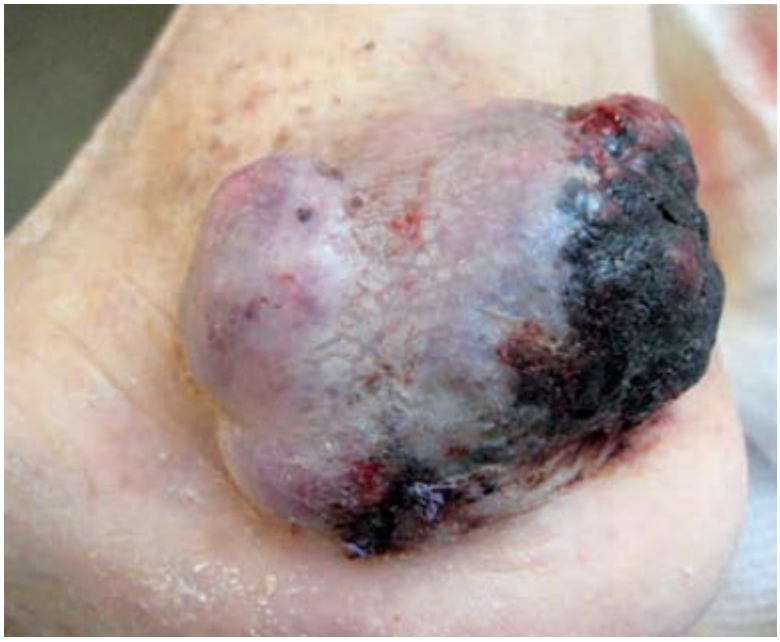

Figure 3. *Erythematous purplish, lobated tumor, soft in consistency, and friable.*

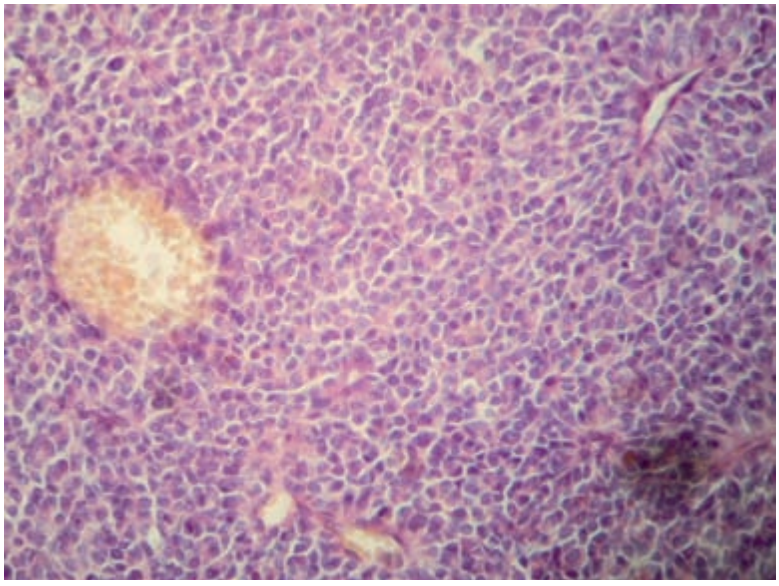

Figure 4. *Cells with irregular hyperchromatic nuclei, with scarse cytoplasm; Homer-Wright pseudorosettes.*

Case 4

An 87-year-old female phototype II patient consulted on March 2008 for a painful 5-month evolution tumor on her left leg. She produced a biopsy performed 1 month before reporting "micro-lobated and chorded malignant fibrohistiocytic proliferation (negative for cytokeratins and melanocytic markers)".

On posterointernal aspect of left leg, she had a tumor consisting of three erythematous, bright and erosive surfaced lobes hard-to-elastic

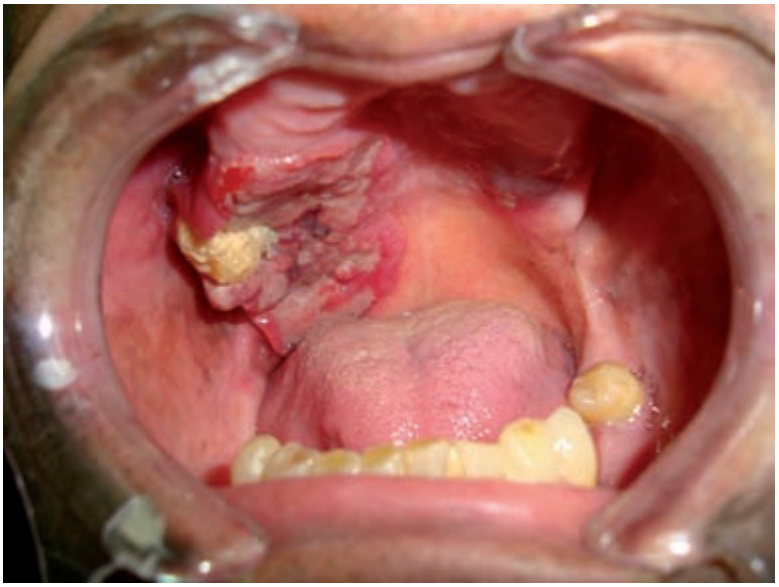

Figure 5. *Ulcerated exophytic palate tumor.*

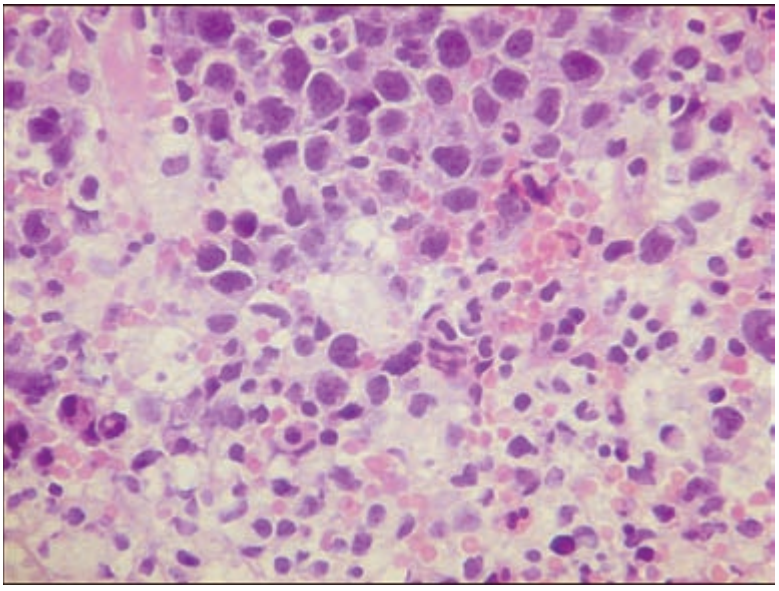

Figure 6. *Proliferation of atypical cells with broad cytoplasm and eccentric nuclei.*

in consistency, seated on a 15 × 10 cm indurated erythematous plaque (**Figure 7**). No lymphadenopathies were identified.

Suggested clinical differential diagnoses were amelanotic melanoma, dermatofibrosarcoma protuberans, cutaneous metastasis, B-cell cutaneous lymphoma, and basal cell carcinoma.

Three punch biopsies were performed, two from the lobes and one from the indurated plaque, which resulted in: lobated and ulcerated neoplasia; epithelioid sectors in both lobes; verticillated fusocellular sector (smaller lobe); intraepidermal activity (erythematous plaque). Immunohistochemistry was positive for S100 and vimentin; HMB45 and melan-A were positive in plaque only. Surgical excision with 3 cm safety margin and sentinel lymph node biopsy were decided, the latter reporting reactive lymphadenitis. Histopathology of the specimen was consistent with ulcerated and amelanotic polypoid melanoma with desmoplasia areas, 7.3 mm thick, predominance of fusiform cell type, high mitotic rate. Immunohistochemistry was positive for S100 and vimentin, and partially positive for HMB45 and melan-A. Supplementary tests were within normal ranges.

Taking into account the age of the patient, no adjuvant treatment was instituted. No relapses occurred in 8-months follow-up.

Case 5

A 46-year-old female phototype IV patient consulted on May 2008 for a 2-month evolution vulvar tumor. Physical examination evidenced a 12 × 9 mm polypoid tumor lesion on left labium minus (**Figure 8**). Ipsilateral inguinal lymphadenopathy was identified.

Suggested presumptive diagnoses were amelanotic melanoma, squamous cell carcinoma,[11] fibrosclerosing botryomycoma and adnexal carcinoma. Histopathology (punch) reported invasive nodal melanoma not less than 1.5 mm thick. Rapid growth and development of peripheral pigmented area with central ulceration was noted few days after hospitalization. Appropriate supplementary tests were within normal limits, and excision of left labium minus and inguinal lymphadenectomy were performed. The former evidenced invasive ulcerated 4.2 mm thick lymph node melanoma, epithelioid cell type, high mitotic rate, and free margins. Lymph node biopsy showed microscopic metastases. The patient currently undergoes the third cycle of dacarbazine and interferon chemotherapy.

Comments

The five tumors studied have low incidence in everyday dermatology practice.

Angiosarcomas account for only 1-2 percent of all sarcomas;[2,3] they are highly malignant, with a tendency to recur locally and highly metastazising.[3] In our case, it is important to highlight the unusual location and that although the incisional biopsy was consistent with retiform hemangioendothelioma –a low-grade angiosarcoma of benign evolution–[4] complete lesion excision demonstrated the presence of an aggressive tumor with radically different prognosis.

Peripheral primitive neuroectodermal tumor (pNET) is a rare small round cell-malignant tumor seated on soft tissues, bone and solid organs in children. Incidence has not been estimated in adult patients due to its extremely low frequency.[5]

Plasmablastic lymphoma is a recently described

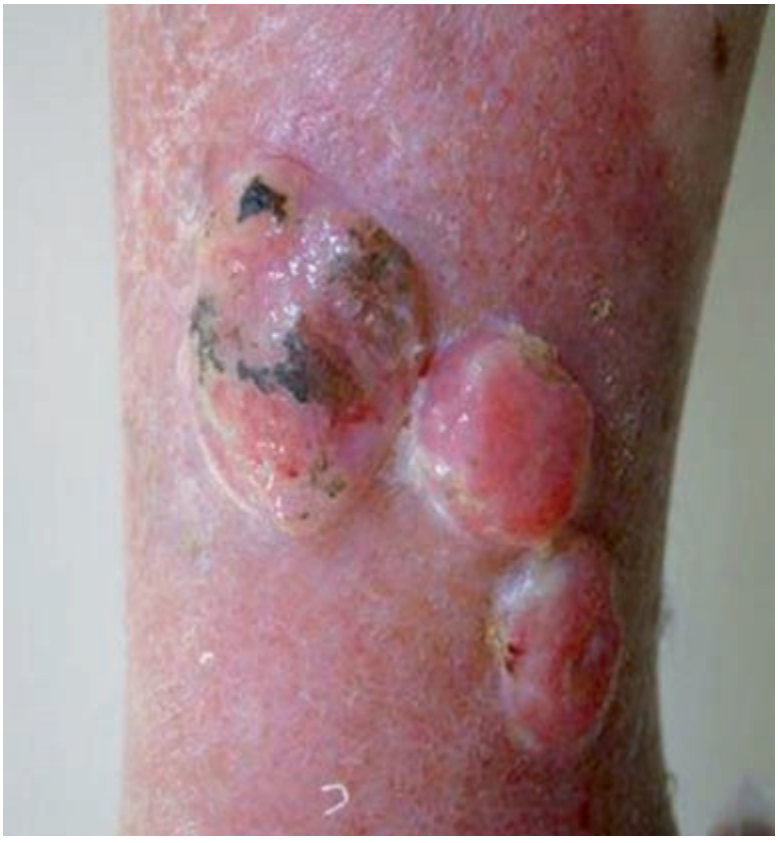

Figure 7. *Tumor constituted by three erythematous lobes seated on an indurated plaque.*

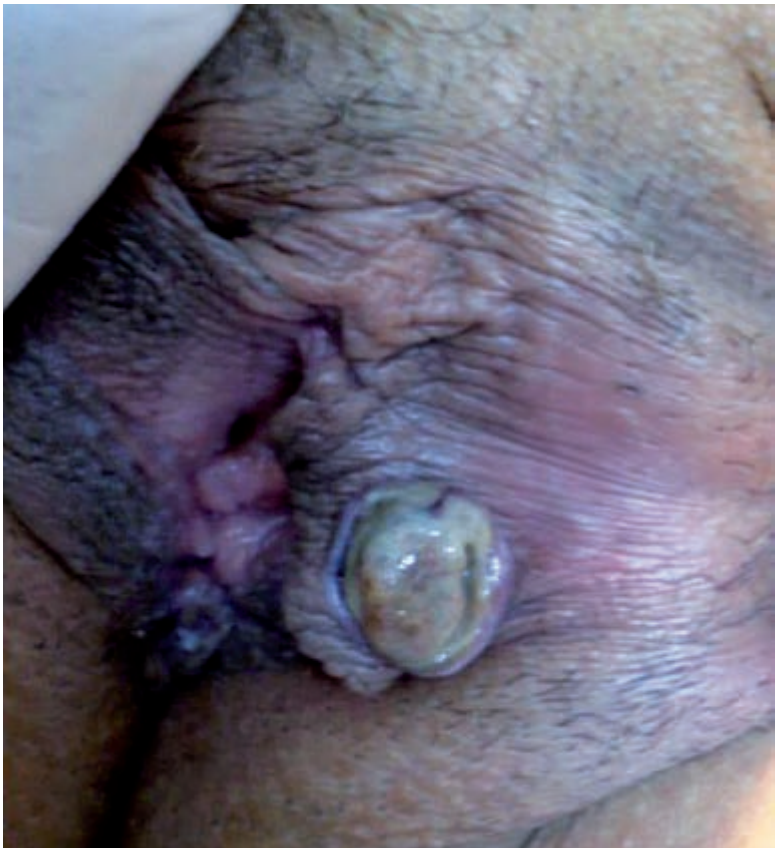

Figure 8. *Polypoid tumoral lesion on left labium minus.*

(1997) non-Hodgkin's B-lymphoma predominantly affecting HIV-positive individuals, with notorious preference for the oral cavity.[6,7] There are only 151 cases published in the literature.[8]

Desmoplastic melanoma is a rare melanoma variant characterized by the presence of fusiform melanocytes in a dense fibrous stroma. As in our case, it appears in older ages, compared to conventional melanoma, it usually develops on photoexposed areas of the head and neck, and tends to relapse locally.[9] Compared to a conventional melanoma of equal thickness, prognosis seems to be better, with lesser incidence of lymph node metastasis. However, diagnosis is often delayed.[9,10] In our case, we wish to point out the presence of a tumor in the shape of three lobes seated on an indurated plaque, with different histological aspect in each sector.

Although of low incidence, vulvar melanoma is the second most frequent invasive cancer of this area, after squamous carcinoma, accounting for 5-10 percent of vulvar neoplasias and 1.3-2.3 percent of female melanomas.[12] At our Department, of a total of 552 melanoma patients, only 6 vulvar locations were found (1.08 percent). Relevant to the reported patient was a history of gynecologic control 3 months before consultation, wherein no alteration was informed.

We wish to highlight the difficult initial diagnosis of these entities, which required numerous supplementary tests, and the request of interdisciplinary consulting in order to rule out other relevant differential diagnoses and define therapeutic approaches.

Likewise, it is appropriate to highlight the identification of these rare neoplasias at our Department in a less than 6 month-period of time.

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