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Case Report

Surgical, Dermatological, And Morphological Factors In The Diagnosis And Management Of Primary Cd4+ Cutaneous Lymphoproliferative Tumors.

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Abstract

A diverse category of T-cell (CTCL) and B-cell lymphomas (CBCL), primary cutaneous lymphomas form in the skin and are diagnosed without extracutaneous illness symptoms. Its indolent clinical behavior and unclear malignant potential led to the term "primary small/medium CD4+ T-cell lymphoma" being altered to "primary small/medium cutaneous CD4+ lymphoproliferative disorder." A uncommon example of small to medium CD4+ T-cell primary cutaneous lymphoma is presented in this research. A 37-year-old patient came in with a frontal tumor that had developed about 8 to 9 months prior. The tumor was round in shape, about 6–7 mm high, pink in color, firm in substance, painless to the touch, and had a diameter of around 8–9 mm. It was also well defined macroscopically.

The tumor was surgically removed deep to the level of the frontal muscle fascia, with an 8 mm margin of safety. The histological analysis confirmed the diagnosis of cutaneous lymphoproliferation, which is mostly made up of scattered medium-large lymphocytes, with a nodular distribution in the reticular dermis and extension around the follicular epithelia and sweat glands. More immunohistochemistry analysis was asked for. The diagnosis of "primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder" was validated by immunohistochemical analysis. Clinical dermatological controls were used to monitor the patients at 3, 6, and 12 months. A cranio-cerebral MRI was done a year later. An yearly dermatological check, blood count, lung X-ray, and craniocerebral MRI were advised for the next five years.

Keywords : *cutaneous lymphoma; immunohistochemistry; dermoscopy; cutaneous tumor.*

INTRODUCTION

A diverse range of T-cell (CTCL) and B-cell lymphomas (CBCL) that develop in the skin and do not exhibit any extracutaneous illness symptoms at the time of diagnosis are known as primary cutaneous lymphomas. About 75–80% of all primary cutaneous lymphomas are CTCLs, while 20–25% are CBCLs. A revised version of the WHO-EORTC (World Health Organization—European Organization for Research and Treatment of Cancer) was released in September 2018. It included a new section on cutaneous forms of chronic active EBV disease as well as new temporary entities for primary cutaneous CD8+ T-cell lymphoma and Epstein-Barr virus positive (EBV+) mucocutaneous ulcer. Because of its indolent clinical behavior and unclear malignant potential, the term "primary cutaneous small/medium CD4+ T-cell lymphoma" was modified to "primary cutaneous small/medium CD4+ lymphoproliferative disorder." According to WHO-EORTC, the CTCL group had a 6% frequency of primary cutaneous CD4+ small to medium T-cell lymphoproliferative disease.They were classified as lymphoproliferative illnesses rather than lymphomas because of their excellent prognosis and high healing rate (100% during a 5-year period).

Additionally, modifications were made to the lymphomatoid papulosis sections, resulting in the identification of two distinct subtypes and an expansion of the range of primary cutaneous lymphoma histological and genetic types in the marginal zone [1].

Other primary lymphomas with T- or B-cells, or those with deterministic effects on the skin, including Jessner-Kanoff lymphocytic infiltration, Lupus Tumidus, or pseudo-lymphomas, are used to make the differential diagnosis.

An incisional or excisional biopsy may be regarded as the initial step in treatment. Low-dose radiation therapy may be a therapeutic alternative in certain situations, but it has the drawback of potentially causing localized adverse effects. The dermatological technique is treated when folliculitis or other overlapping dermatoses are present. Another option

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is phototherapy or UVA and UVB light treatment.Since there is still much to learn about primary cutaneous lymphomas, especially in the area of immunohistochemistry, other methods used to examine malignant tumors may be used to this kind of tumor [2].

CASE REPORT

We describe the case of a 37-year-old woman who has a frontal tumor that developed 8–9 months ago and is asymptomatic. The tumor was roughly 8 to 9 mm in diameter, was round in shape, 6 to 7 mm tall, pink, firm to the touch, and not painful to the touch. It was also macroscopically well-defined. White-yellowish spicules were seen in the perilesional skin as well as subtly on the tumor's skin surface , and dermoscopy verified that they were Demodex tails from Demodex folliculorum.

After the dermatological evaluation, the decision was made to surgically remove the tumor for aesthetic reasons as well.

The tumor was surgically removed deep to the level of the frontal muscle fascia, with a safety limit of 8 mm. Two planes of sutures were applied to the wound: a 4.0 non-absorbable transcutaneous suture and a 3.0 deep absorbable suture, which were taken out after 14 days.

There were no problems and the postoperative course was positive.The diagnosis of cutaneous lymphoproliferation with nodular disposition in the reticular dermis and extension around the sweat glands and follicular epithelia was confirmed by the histopathological examination. It was primarily made up of medium-large lymphocytes that were dispersed and had vesicular nuclei; some of these were encircled by small lymphocytes that were arranged in a string of pearls on the periphery.

The supralesional epidermis was unaffected, but there were small intralesional clusters of epithelioid histiocytes as well as an infiltration of peripheral plasma cells and small reactive lymphocytes. In every plane that was inspected, the excision was complete. The request was made for additional immunohistochemistry analysis.

The diagnosis of "primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder" was validated by the immunohistochemistry analysis.Table 1 displays the immunohistochemistry markers.

The following immunohistochemistry markers were looked at:30–35% of infiltrate lymphocytes (B lymphocytes) are positive for CD20, and they are distributed reasonably uniformly (Figure 4). A member of the MS4A family of nonglycosylated phosphoproteins, CD20 is a B-cell marker that forms a tetraspan membrane-bound protein. Pre-B-cells exhibit CD20 expression, which vanishes when the cell differentiates into a plasma cell [3]. Although CD20 is confined to lipid rafts and functions as a calcium channel, its precise role is yet understood. A unique therapeutic target for B-cell malignancies, CD20 exhibits dynamic cellular activity [4]. Staining with CD20. 20x magnification.65–70% of infiltrating lymphocytes (T cells) are CD3 positive.This demonstrates how the infiltrate has spread around the appendages without exhibiting any signs of epidermotropism.All T-cell leukemias and lymphomas still contain the antigen, which is utilized to differentiate them from related B-cell neoplasms [5].Staining with CD3. 20x magnification.The majority of T helper cells (infiltrate lymphocytes) have CD4.The human immune system relies heavily on CD4+ T helper cells. They are frequently called T4 cells or T helper cells. For biopsy samples, CD4 immunohistochemistry is helpful in detecting peripheral T-cell lymphoma and other associated cancers. Autoimmune conditions like vitiligo and type I diabetes have been linked to the antigen [6]. In persistent infections and autoinflammatory disorders, CD4+ T helper cells play an important role [7].Staining with CD4. 20x magnification.In scattered T cells (T cytotoxic lymphocytes), CD8 is positive. Both tumor surveillance and immunological protection against intracellular infections depend on CD8+ T-cells, also known as cytotoxic T lymphocytes [8].

CD30 is a helpful marker for differentiating between these germ cell malignancies since it is expressed in embryonal carcinoma but not in seminoma, is positive in scattered activated lymphocytes, and is linked to anaplastic large cell lymphoma. Reed-Sternberg cells, which are characteristic of Hodgkin's lymphoma, also express CD30 [9].

Numerous infiltration cells, including T follicular helper lymphocytes, which are somewhat pleomorphic lymphoid cells with a hypertrophic nucleus, are positive for PD-1 (Figure 8). By encouraging the death of antigen-specific T cells in lymph nodes and inhibiting the death of regulatory T cells, PD-1 protects against autoimmunity in two ways [10]. Twenty percent of the infiltrate cells had positive Ki67.

Clinical dermatological controls were used to monitor the patients at 3, 6, and 12 months. A cranio-cerebral MRI was done at one year. An yearly dermatological check, blood count, lung X-ray, and cranio-cerebral MRI were advised for the next five years.

The sole treatment available in this instance is surgical excision, and the prognosis is favorable, as is the case with all solitary skin lesions.

DISCUSSION

According to the June 2018 publication of the European Society of Medical Oncology's Clinical Practice Guideline for Primary Cutaneous Lymphoma, CTCL accounts for 75–80% of all primary cutaneous lymphomas in the Western population, with mycosis fungoides (MF) being the most prevalent type, while CBCL accounts for 20–25%. Other regions of the world, however, experience it at a different rate. For instance, CBCLs

are far less common and CTCLs—aside from MF—much more common in Southeast Asia than in Western nations. The two most prevalent forms of CTCL are Sézary syndrome (SS) and MF. Other types of CTCL include subcutaneous T-cell lymphoma that resembles panniculitis, CD30+ primary cutaneous lymphoproliferative disorders,Primary cutaneous CD4+ small to medium T-cell lymphoma, primary cutaneous gamma/delta T-cell lymphoma, and primary aggressive cutaneous CD8+ cytotoxic epidermotropic T-cell lymphoma are uncommon forms of cutaneous T-cell lymphoma.

Solitary or multiple micro-papules, micro-nodes, or plaques may be the initial asymptomatic manifestation of primary cutaneous CD4+ small to medium T-cell lymphoma. These lesions are frequently purplishpink, lack unique clinical characteristics, and are challenging to distinguish from other similar incipient nodular lesions [11].The fact that cutaneous lymphoma's signs and symptoms vary from patient to patient and that some of them, particularly the milder ones, are frequently confused with psoriasis or eczema, fungal skin reactions (like ringworm), various skin reactions brought on by medications, specific substances, or allergies presents a challenge to accurately diagnosing the disease. Clinical terms for a variety of skin signs (sometimes called lesions) that may provide hints about a diagnosis include spots, plaques, papules, or tumors.

Children are more likely than adults to have those on the trunk and limbs, and those on the face have been mentioned seldom among the relatively few cases documented in the literature [12].

Burgdorferi, which is either unverified in our instance or consistent with post-vaccine responses or other autoimmune illnesses [13,14]. The majority of the time, lymphoproliferative cutaneous tumor CD4+ is asymptomatic; it changes, but its course is unpredictable. Indicators of Demodex folliculorum (DF) tails are the seemingly hyperkeratosis spicules that are infrequently reported in the literature, which we also detected clinically and during dermoscopy. Demodex tails can proliferate less directly on the skin layer covering the nodule and in regions where there may be perilesional immunosuppression. This is because underlying hypertension causes the follicular duct to shorten, preventing the development of DF; Tatu et al. have also described this occurrence.

There aren't many descriptions of dermoscopic imaging in lymphoproliferative cutaneous tumor CD4+ in the literature. In this case, the dermoscopy showed serpentine blood vessels and a salmon-colored backdrop, which led to the differential diagnosis of sarcoidosis, basal cell cancer, achromic melanoma, inflammatory intradermal nevus, insect bite reaction, etc. [16,17].Other diagnoses, such face granuloma, other primary T-cell or B-cell lymphomas, or cutaneous deterministic consequences, like Jessner–Kanoff lymphocytic infiltration, Lupus Tumidus, or pseudolymphomas, may be taken into consideration from a clinical standpoint [18–20].

The primary cutaneous CD4+ small to medium T-cell lymphoma accounts for 2% of all cutaneous T-cell lymphomas, making it a rare lymphoma according to immunohistochemistry. It is distinguished by the presence of small to medium-sized CD4+ pleomorphic T-cells in greater numbers than the usual MF plaques.

Rarely do patients' lower extremities become involved; instead, they arrive with a single plaque or nodule on the face, neck, or upper trunk. The sole clinical characteristic of these asymptomatic plaques is a tiny, isolated skin lesion.

The histological features of this type of lesion are represented by a dense, diffuse, or nodular infiltrate of the skin with a tendency to subcutaneous involvement. The infiltrate is formed by small to medium sized pleomorphic T-cells, sometimes with a small proportion of large pleomorphic cells. In addition, the infiltrate may contain reactive lymphocytes, histiocytes, eosinophils, or plasma cells [21]. In this instance, it was positive for CD3 and CD4. In terms of treatment, a positive prognosis and localized proliferation makes surgical treatment a good option, with complete excision followed by sutures and/or reconstructions possible, depending on the location and the particularities of the case. Although an exploratory incisional biopsy can be performed, we recommend complete excision per primam, followed by histopathological and immunohistochemical examinations.We do not consider useful the expectant attitude recommended by some authors, because the nodule often progresses in time and the excision area becomes wider (20). In specific cases, low-dose radiotherapy may be an alternative, but regional adverse reactions may limit this procedure. Local and intralesional treatments have not proven to be effective. In cases of folliculitis or other overlapping dermatosis, the dermatological procedure is addressed. In the particular case of this patient, topical treatment with Ivermectin-containing cream, following the healing of the post-excision scar, led to the disappearance of the DF spicules. This attitude is important, both from a curative and preventive perspective; especially since it has been recently described that Demodex folliculorum may be a factor in determining other viral infections, including SARS-CoV-2.This is not only from the perspective of chitin–lipid interactions but also of immunosuppression associated with lymphoma patients, as well as the activation of inflammatory, immunological and, possibly, proliferative phenomena by the endosymbionts attached to Demodex folliculorum [22,23]. In addition, and for further evolution, we consider the emotional factors that exist in patients with chronic diseases, and especially in those with aesthetic affectation [24]. The use of steroids, interferons, HDAC inhibitors, or chemotherapy can be a therapeutic option, but we do not consider it necessary in this type of cutaneous lymphoma at this stage.

CONCLUSIONS

A uncommon case of cutaneous T-cell lymphoma, more precisely primary cutaneous CD4+ small to medium T-cell lymphoma, with an obviously benign clinical history serves as the case report's unique example. The disorder responds well to skin-directed therapy and has a very good prognosis. In order to prevent severe systemic therapies, practitioners should be aware of this syndrome.

This lesion's histological characteristics include a nodular, diffuse, or dense skin infiltration. Small to medium-sized pleomorphic T-cells make up the infiltrate, with a tiny percentage of giant pleomorphic cells.The prognosis for isolated skin lesions is very good (surgical excision).This uncommon tumor kind serves as a representation of the case's uniqueness.

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