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Research Article

CUTANEOUS T-CELL LYMPHOMA WITH BILATERAL ADRENAL METASTASIS

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Abstract

Adrenal involvement without lymph nodes infiltration secondary to cutaneous T-cell lymphoma is very rare. Large anaplastic T cell lymphoma originating from the skin and metastasizing to bilateral adrenal glands are uncommon occurrence without similar cases founded in the review of the literature. We present a case of a 67 year-old African man who presented with skin lesion diagnosed as large anaplastic T cell lymphoma metastasized to bilateral adrenal glands. Hormonal analysis didn't found adrenal insufficiency however, endogenous hypercorticism was observed. The patient was treated by chemotherapy. Prognosis was considered as poor.

Keywords: Adrenal lymphoma, Cutaneous lymphoma, Anaplasic lymphoma.

INTRODUCTION

Cutaneous T-cell lymphoma (CTCL) is defined by monoclonal T-cell proliferation involving the skin (Pulitzer, 2017). According to the 2017 revised WHO classification of tumours of haematopoietic and lymphoid tissues, the most common subtypes of cutaneous lymphoma were mycosis fungoides, Sezary syndrome and the CD30 lymphoproliferative disorders including primary cutaneous anaplastic large cell lymphoma (Swerdlow *et al.,* 2017; Swerdlow *et al.,* 2016). Primary cutaneous anaplastic large cell lymphoma was generally described as solitary or localized nodules. These lesions may show spontaneous regression, and frequently relapse in the skin. Extracutaneous dissemination occurs in about 10% of patients, and mainly involves the regional lymph nodes (Swerdlow *et al.,* 2017; Swerdlow *et al.,* 2016). Adrenal metastasis without lymph nodes involvement is uncommon and didn't been reported in the literature. Similar lymphoma originating from the skin and metastasizing to bilateral adrenal glands was an exceptional occurrence. Diagnosis is difficult and requires biopsy of lesions with immunohistochemistry analysis. We report a case of cutaneous lymphoma with bilateral adrenal lymphoma metastases.

CASE REPORT

A 67 year- old man, with medical history of hypertension, diabetes and coronary artery disease was hospitalized in Endocrinology department of Hedi Chaker hospital in Sfax, Tunisia on November 2020 for exploration of bilateral adrenal masses. He presented six months before his admission, scaly round patches on his leg with recent infiltration and epidermal necrosis with ulceration. The lesion is shown in Figure 1. The patient suffered from general weakness, excess of sweating and skin fragility. He had no lymph nodes in his physical examination. Fasting of Ramadan was well tolerated. His blood pressure was normal at 120/80 mmHg. He had no signs of acute adrenal insufficiency. He had clinical euthyroidism.

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In his biological analysis we found: Na^+= 137/ K^+= 4, 1 mmol/L, blood count: WBC= 4180 10^3/uL, lymphocytes= 600 10^3/uL, hemoglobin=11.9g/dL, Platelet: 226000 10^3/uL. Histopathological examination of the skin biopsy revealed the presence of a diffuse dense lymphoid proliferation in the dermis, without epidermotropism (Figure 2). The tumour cells were large with abundant cytoplasm and vesicular nucleus. Immunohistochemistry showed strongly positive expression of CD3, CD4, granzyme B, CD10 and CD7 (Figure 3). Tumor cells were negative for CD56 and CD20. Clinical, histopathological and immunohistochemical findings were compatible with the diagnosis of Primary cutaneous anaplastic large T-cell lymphoma. Computed Tomography found bilateral adrenal large masses (Figure 4). The right one measured 118* 74*79 mm involving the inferior vena cava and the upper kidney including renal artery and had tissular density with heterogeneous contrast enhancement. Left adrenal was the site of voluminous mass 94*77*110 mm involving the upper pole of ipsilateral kidney with polycyclic contours and heterogeneous enhancement. No lymph nodes were revealed on imaging (Figure 4). Bone marrow biopsy didn't show lymphoma infiltration. Adrenal mass biopsy was indicated. Microscopically, the latter was formed by a diffuse lymphoid proliferation. This proliferation was composed of anaplastic cells with abundant eosinophilic or amphophilic cytoplasm and irregular nucleus. Immunohistochemical study showed a positive staining for CD3 and a negative staining for CD20. The diagnosis of cutaneous anaplastic large T cell lymphoma with adrenal metastasis was retained. Hormonal analysis didn't found adrenal insufficiency (basal cortisol concentration: 182nmol/; stimulated cortisol concentration: 202 nmol/L). (cortisol=37 nmol/L after low doses dexamethasone suppression test / cortisol=31 nmol/L after high doses dexamethasone suppression test). Basal adrenocorticotropic hormone (ACTH) level was in the upper limit of normal at 71 ng/mL. Samples of plasma aldosterone and rennin were in within the normal range (adosterone=30,22ng/L, Renin=4, 1ng/L Aldosteron /renin= 7,37). 11desoxycorticosterone (DOC) was also in the normal range (DOC= 0,53pmol/ml) Evaluation of catecholamines excess was performed by measuring free plasma level and normetanephrine after 30 mn

derivatives were normal (metanephrines = 39ng/L, normetanephrines= 71 ng/L). Endogenous hypercorticism was retained. Pituitary MRI didn't show adenoma. (18) FDG-PET scan showed pleural and peritoneal thickening. The patient received the first cure of chemotherapy based on CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide and prednisone). He presented fever and neutropenia at the 20th day of cure. He was also treated by radiotherapy of the skin lesion. Prognosis was considered as poor.

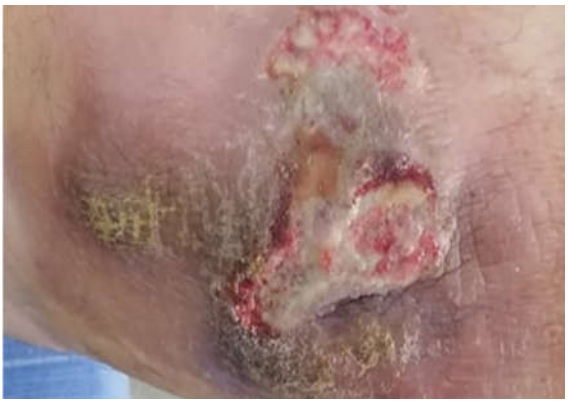

Figure 1. Cutaneous lesion

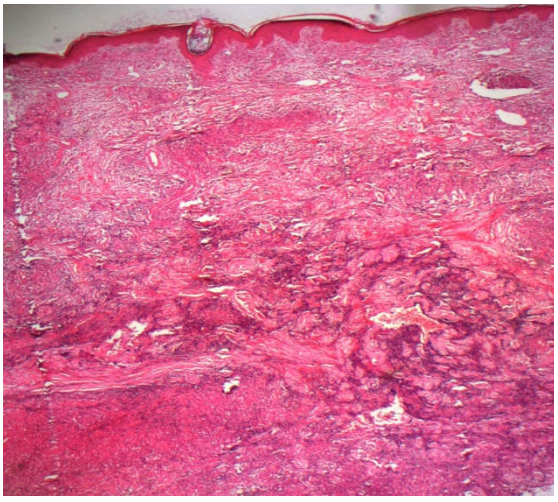

Figure 2. Presence of a diffuse lymphoid proliferation in the dermis, without epidermotropism (hematoxylin eosin × 25)

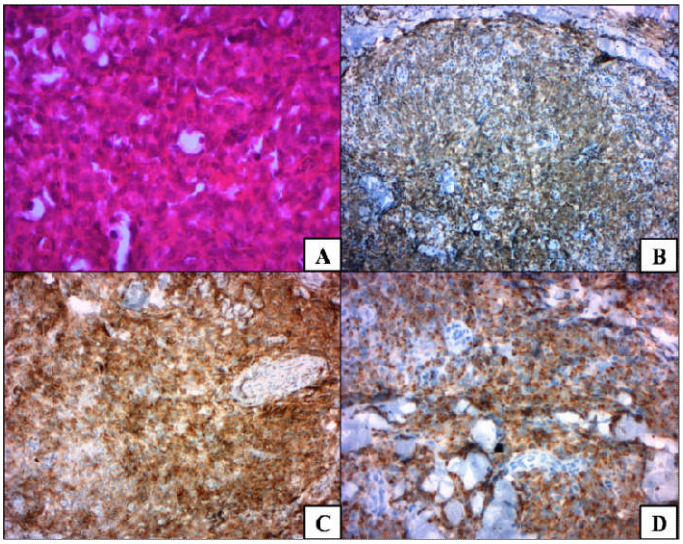

Figure 3. (A) Large tumour cells with abundant cytoplasm and vesicular nucleus (hematoxylin eosin × 400). Positive immunostaining for CD3 (B) (×100), CD4 (C) (×200) and granzyme B (D) (×200)

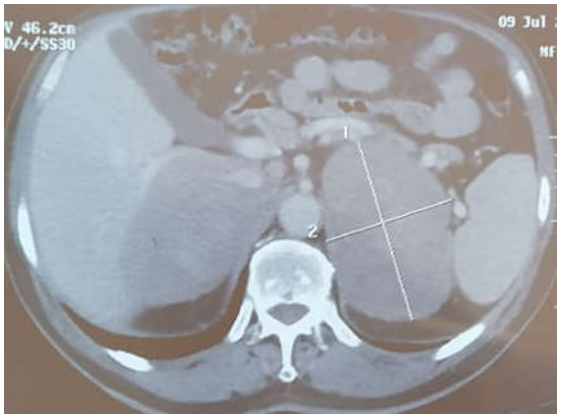

Figure 4. Axial sequence of abdominal computed tomography revealing the bilateral adrenal masses

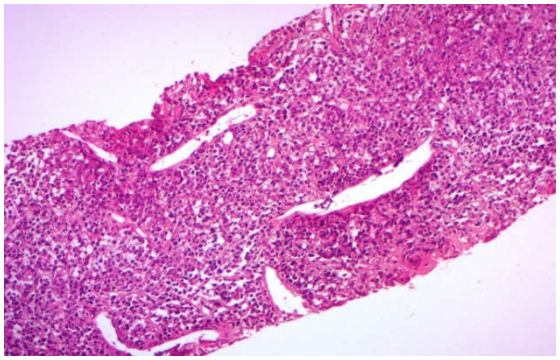

Figure 5. Adrenal mass biopsy formed by a diffuse lymphoid proliferation. (hematoxylin eosin X100)

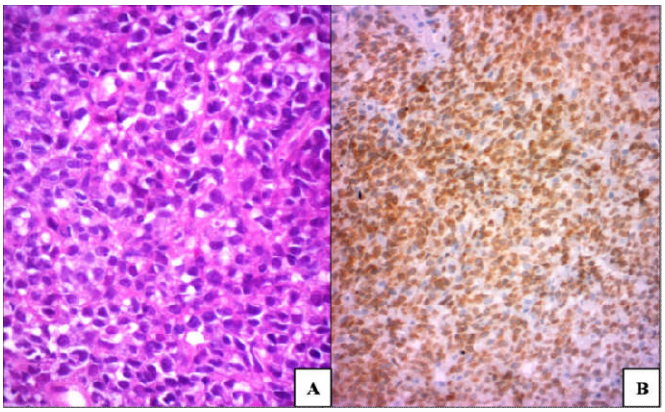

Figure 6. (A) Anaplastic tumour cells with abundant eosinophilic or amphophilic cytoplasm and irregular nucleus (hematoxylin eosin × 400) (B) Positive staining for CD3 (×200)

DISCUSSION

Cutaneous T-cell lymphomas (CTCL) were dominated by mycosis fungoides and CD30+ lymphoproliferative disorder (LPD). CD30+ LPD comprise approximately 25-30% of primary cutaneous lymphomas. It include Primary cutaneous anaplastic large cell lymphoma (PC-ALCL) which had relatively good prognosis on early stage (Bekkenk *et al.,* 2000). Typical presentation was as a single nodule with central ulceration that affects the head and limbs (Brown *et al.,* 2017). In PCALCL, histopathologic features are characterized by absence of epidermotropic or dermal aggregates of CD30+ tumor cells which occurs more frequently in mycosis fungoides (Fauconneau *et al.,* 2015). Involving lymph nodes was uncommonly described (Pulitzer *et al.,* 2017). Extracutaneous involvement was observed in 10% of cases

(Koestinger *et al.,* 2012). Visceral metastasis has been documented between 2 months to 10 years from initial diagnosis. The development of metastatic disease is not always associated with progression to a higher T category (Benner *et al.,* 2009). Adrenal were unusually the site of secondary localization in lymphoma. It was estimated less than 0.2 % (Hassan *et al.,* 2019). Amongst the few cases of adrenal lymphoma documented, there is none reported in association with primary or secondary cutaneous infiltration (Rakheja *et al.,* 2020). Adrenal lymphoma with primary cutaneous infiltration wasn't been reported previously and this is the first case in this context. However, adrenal glands are one of the most common sites for metastasis due to their high vascular supply (more than 90%). Originating cancers were frequently type carcinoma (lungs, stomach, oesophagus and liver) (Hassan *et al.,* 2019). Adrenal lymphoma metastases appeared like masses greater than 3 cm hypodense homogeneous and well limited (Hassan *et al.,* 2019; Alshahrani *et al.,* 2019; Herndon *et al.,* 2018). However in our case, masses were heterogenous and irregularly limited. Face to bilateral adrenal metastases, adrenal insufficiency should be rule out because destruction of more than 90% of cortex of both glands may lead to adrenal insufficiency. The prevalence of adrenal insufficiency was estimated to be very low (3-8%) (Tallis *et al.,* 2019; Gamelin *et al.,* 1992). Basal cortisol levels were more than 140 nmol/L in the most cases with bilateral adrenal metastases (Tallis *et al.,* 2019). In our case, we didn't objectified primary adrenal insufficiency. In basis on few studies, there were no significant correlations between cortisol or ACTH concentrations and the total size of the adrenal metastases on radiology (Tallis *et al.,* 2019). In the other hand, hypercorticism in neoplasic context results from ectopic extrapituitary corticotropic secretion. Paraneoplasic Cushing syndrome (PCS) due to non-pituitary tumors, were mostly caused by neuroendocrine tumors such as bronchial carcinoid tumor, small cell lung cancer, medullary thyroid carcinoma, thymic carcinoidtumors, gastroenteropancreatic neuroendocrine tumors (GEP-NETs), and genitourinary tumors (Ejaz *et al.,* 2011). Some ectopic ACTH secretion remained with unknown primary origin despite extensive investigations. Clinical presentation in Cushing syndrome may be masked by symptoms of the underlying tumor. Thus, the diagnosis can be challenging, and the source of ACTH production can be difficult to identify. Histology confirmed the diagnosis. It revealed tumor cells stained positive for ACTH, CD56, Chromogranin and synaptophysin. As particular finding observed in our case, extra pituitary hypercorticism with inappropriate normal ACTH level. Ectopic Cushing's syndrome caused by an ACTH secretion wasn't been described with anaplasic large cell lymphoma. Clinical courses of adrenal lymphoma was aggressive with mostly poor prognosis (Laurent *et al.,* 2017). Adrenelectomy was recommended for unilateral adrenal insufficiency with suspicious malignant lesion on imaging as well as tumors with overt hormonal secretion (Tabarin *et al.,* 2009). However patients with adrenal lymphoma don't undergo adrenelectomy.They are treated by systemic chemotherapy. Many factors are predictors of prognosis. In fact: hormone secretion, high morning cortisol, higher tumor grade were correlated with shorter over all survive and bad prognosis (Lase *et al.,* 2020).

Conclusion

This case illustrates the dilemma between the need for morphological diagnosis of the ectopic ACTH source and control of the life-threatening hypercortisolism. (18) FDG-PET scan and (18) DOPA-PET scan should be considered early as a secondary diagnostic tool when conventional imagery fails to show any tumor. It is desirable to have a greater number of cases in the literature in order to protocolize its diagnosis, treatment and monitoring.

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