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ABSTRACT

BACKGROUND

The association of Chronic Lymphocytic Leukemia (CLL) and melanoma have been studied in the last years. The immunosuppression caused by the treatment of CLL seems to be the major factor of increasing patients' susceptibility to the development and spread of skin cancer.

CASE REPORT

This case report describes a 53-year-old male patient, in CLL treatment since 2018, already submitted to many cycles of chemotherapy with fludarabine. History of an exeresis of epithelioid nodular melanoma of the scalp in 2019, which was removed with a clear margin. One year later, he presented with a poor general condition with hospitalization indication. Additional investigation revealed metastatic lesions in lungs, liver, kidneys, stomach, central nervous system, and lymph nodes. Histopathologic analysis positive for melanoma. The possibility of treatment was discarded by the Oncology team, which suggested palliative care.

DISCUSSION

One of the most discussed mechanisms to explain this cancer association is the immunosuppression developed during the treatment of CLL, increasing patients' susceptibility to the development and spread of melanoma. In addition, the use of fludarabine, a chemotherapy commonly used in relapsed CLL, is known to deplete T-helper cells and has been described as a cofactor of this process. The association of leukemia and cutaneous melanoma has been reported in the last years, yet there is no surveillance protocol.

INTRODUCTION

Chronic Lymphocytic Leukemia (CLL) is the most common leukemia in adults and previous studies have reported that the imune deficits caused by CLL are (connected with an increased risk of developing melanoma[2] and other solid tumors, especially within the first 5 years of diagnosis[1]. Other factors such as chemotherapy and UV radiation via sun exposure may also contribute to worse prognosis[4].

Different types of Non-Hodgkin's Lymphoma show an association with a greater predisposition to the appearance of skin cancers compared to the general population[2]. However, it is known that in CLL patients the incidence and mortality are significantly higher[2,3].

The progress achieved in CLL treatment has allowed a better prognosis, with increased survival in the last decades. In this context, it is worth noting that it is an indolent disease, more common in older age groups (> 60 years), which coincides with the stage of higher incidence of several types of cancer, including melanoma[1,2, 5]. Doctors, patients, and caregivers should be aware of the data in the medical literature regarding the association of CLL and skin cancer.

CASE REPORT

A 53-year-old Caucasian male patient, a farmer, in CLL treatment since 2018. He had already been submitted to five cycles of chemotherapy, the first four cycles of combined fludarabine and cyclophosphamide, followed by one cycle of a second-line treatment – due to a relapse – with fludarabine, cyclophosphamide and rituximab. History of an exeresis of epithelioid nodular melanoma of the scalp in 2019, biopsy indicated Breslow thickness 12 mm, mitotic rate 4 mitoses/mm^2, Clark Level V and a clear margin. He was admitted to this Hospital with a dry cough, tiredness, pyrosis, abdominal distension, and a weight loss of almost 20 kg in 2 months. At physical examination, patient in poor general appearance, emaciated, bilateral cervical enlarged lymph nodes; respiratory auscultation with diffuse rhonchi and reduced murmur in both pulmonary bases; pain upon palpation of the epigastrium. Chest and abdominal CT scans revealed moderate bilateral

pleural effusion and pulmonary atelectasis; multiple pulmonary, hepatic and renal nodules suggesting secondary nature; and abdominal and pelvic enlarged lymph nodes. Bronchoscopy pointed a left bronchial tree with extrinsic compression of the air passage, without possibility to progress the device from the left carina. Clear right bronchial tree. Bronchoalveolar lavage performed in the right lower lobe didn´t found neoplastic cells. Cranial tomography described hyper-attenuating areas in the right cingulate gyrus, upper frontal gyrus and left insular subcortical region. Those findings suggested infiltrative lesions with high cellularity and without an expansive effect or midline deviation. Upper Digestive Endoscopy showed severe erosive gastritis and histopathologic analysis compatible with metastatic melanoma. Fine needle aspiration of a cervical lymph node also found melanocytic cells. We decided to suspend hematological treatment and evaluate the possibility of treating metastatic melanoma, which was discarded by the Oncology team. At the moment, the patient is in palliative home care.

DISCUSSION

The association of leukemia and cutaneous melanoma has been reported since 1960[1]. A study conducted in the United States revealed that the risk of developing skin cancer in patients with CLL is high, especially in the first five years of diagnosis and in white men between 45 - 64 years[2]. Another American study published in 2015 described that the association of melanoma with LLC or Non-Hodgkin's Lymphoma (NHL) is almost 107 cases / 100,000 inhabitants, while the statistics for the general population is 25.9 cases / 100,000 inhabitants[3]. One of the most discussed mechanisms to explain this cancer association is the immunosuppression developed during the CLL treatment, increasing patients' susceptibility to the development and spread of melanoma.

Fludarabine, a chemotherapy commonly used in relapsed CLL, is known to deplete T-helper cells and has been described as a cofactor of this process[4]. The patient reported in this communication was submitted to five treatment cycles, all including fludarabine. Other potential risk factors are exposure to

ultraviolet radiation, genetics, fair skin, and advanced age[5]. In this case, the patient's labor activity as a farmer, without adequate sun protection, may also have contributed to the onset of skin cancer. Mortality in melanoma associated with CLL is 2.46 times higher than expected for patients without this hematological neoplasia[3].

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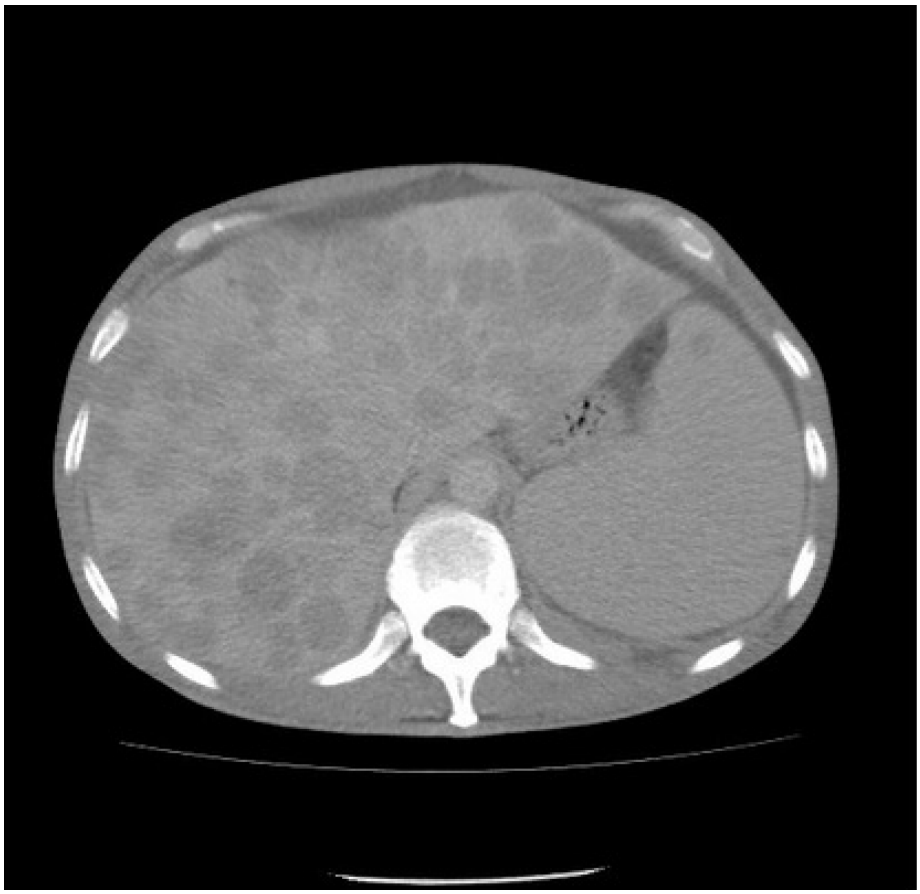
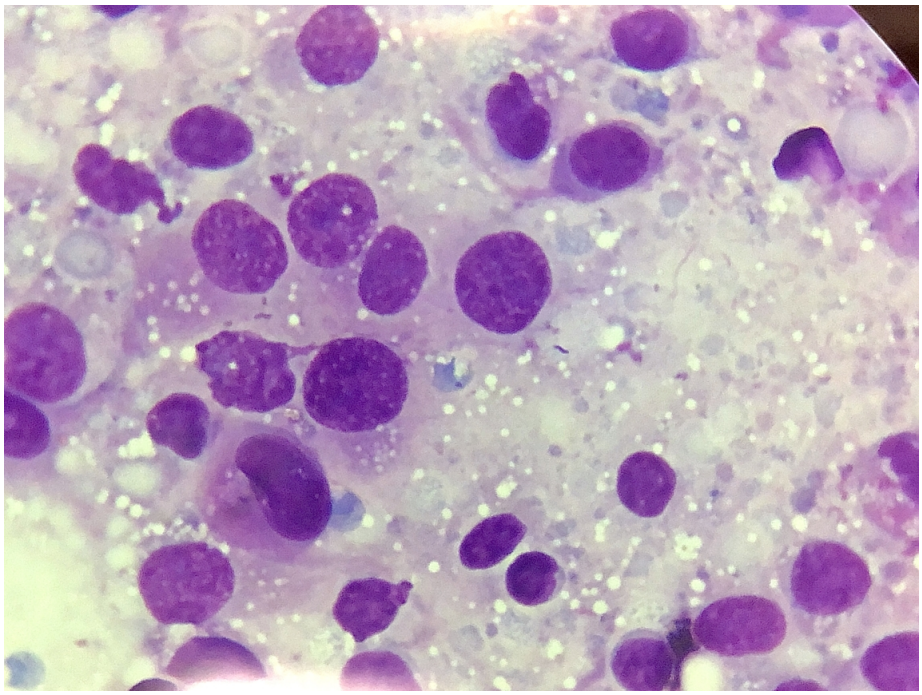
pulmonary metastatic lesions



liver metastatic lesions

abdominal metastatic lesions



microscopic image of cutaneous melanoma metastatic cells in stomach biopsy

1422x1066mm (72 x 72 DPI)