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Case report

Association of multifocal Hodgkin's lymphoma and tuberculosis infection: A challenging entity

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ABSTRACT

The association of Hodgkin's lymphoma and Tuberculosis is a rare entity, resulting in misdiagnose or delay in diagnosis of both diseases, since they share similar signs and symptoms, laboratory tests results and imaging procedures.

We report the case of a 63 years old man who consulted for a clinical presentation of pulmonary and cervico-thoracic lymph nodes tuberculosis confirmed at the histopathological examination. The evolution after 5 months of antituberculous treatment was marked by the increase in size of the cervical nodes with a papular skin rash, diffuse abdominal pain and more weight loss. The FDG-PET-scan showed multiple confluent hypermetabolic lymphadenopathies on the whole upper body with cervical skin extension, next to hypermetabolic splenomegaly and focal liver hypermetabolism; next to a bilateral pleural effusion. The histopathological examination of the cervical lymph node specimen concluded to a Hodgkin lymphoma classified as Ann Arbor stage III. The chemotherapy protocol was started, while completing his antituberculous treatment. The patient passed away a few weeks later due to a septic shock.

We present this case to supplement the rare literature data concerning the association of Hodgkin's lymphoma and Tuberculosis, defining how they impact the prognosis of one another, in order to comfort the importance of tuberculosis screening in lymphoma patients, especially in endemic areas.

1. Introduction

The association of Hodgkin's lymphoma and Tuberculosis infection is a rare entity. Since they share similar signs and symptoms, laboratory tests and imaging results, concomitant occurrence leads to misdiagnose and delay in diagnosis and treatment of both diseases.

We present this case to supplement the rare literature data concerning this rare association, defining how they impact the prognosis of one another, in order to comfort the importance of tuberculosis screening in lymphoma patients, especially in endemic areas.

2. Presentation of the case

We report the case of a 63 years old man, with no medical history, who consulted for chronic coughing, with concomitant chest pain and expectorations, in a context of general fatigue, intermittent fever and night sweats. The clinical examination found enlarged bilateral cervical lymph nodes. The CT scan showed multifocal patchy consolidations with multiple nodules in bilateral lungs with bilateral cervical, paratracheal and hilar necrotic lymph nodes. The histopathological examination of the biopsied cervical lymph node revealed epitheloid cell granuloma with giant cells and enclosing caseating necrosis typically corresponding to Tuberculosis. And the tuberculinic skin reaction was positive with a dermal reaction diameter measured at 11 mm. The patient started then the antituberculous therapy based on Rifampicin, Isoniazid, Pyrazinamide and Ethambutol.

After 5 months of treatment, taken with strict adherence, the patient presented to our department for the persistence and increase in size of the cervical nodes with skin rash in the same area, diffuse abdominal pain and more weight loss. The clinical examination found multiple painless voluminous cervical lymphadenopathies, responsible of a drooping of the right corner of the mouth secondary to a lesion of the marginal mandibular branch of the facial nerve, covered with confluent erythematous papular skin lesions (Fig. 1). Also, palpation revealed

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bilateral axillary and inguinal lymphadenopathies, tender abdominal mass and enlarged spleen.

The abdominal CT scan showed an abdominal mass related to multiple enlarged lymph nodes fusing into lobular masses with heterogeneous enhancement, in addition to an enlarged spleen. The FDG-PET-scan showed multiple confluent hypermetabolic lymphadenopathies on the whole upper body with cervical skin extension (right cervical area: SUV max at 9,8; left cervical area: SUV max at 10; right axillary area: SUV max at 9,9; left axillary area: SUV max at 10,2; mediastinal area: SUV max at 11,5; right abdominopelvic area: SUV max at 11,7; left abdominopelvic area: SUV max at 12,1), bilateral hypermetabolic costodiaphragmatic lesions, hypermetabolic splenomegaly measuring 13,8 cm (SUV max at 3) and focal liver hypermetabolism between segment IV and V (SUV max at 4,17); next to a bilateral pleural effusion (Fig. 2)

The blood tests showed normocytic normochromic anemia with Hb at 9,9, increased LDH and CRP levels at 806 and 221 respectively and low amount of albumin at 20 g/L. Excision biopsy of a cervical lymphadenopathy was done and the specimen was subjected to histopathological examination, which revealed complete scattering with nodular lymphoid proliferation and fibrous strands on a background of lymphocytes, plasmocytes and Reed-Stenberg cells, positive for CD30 and CD15 antigens, corresponding to a nodular sclerosing type of a classic form of Hodgkin's lymphoma. The Reed-Stenberg cells were also found on biopsy of the skin lesion.

The patient was classified as stage III according to the Ann Arbor classification and was sent for exclusive chemotherapy based on ABVD protocol while completing the tuberculous therapy. The prognosis based on clinical and biological factors was considered poor regarding the age >60 years, the weight loss >10% in the last 6 months, the Ann Arbor stage, the number of affected lymph nodes territories, the volume of the cervical and abdominal mass, the anemia and increased level of LDH and the presence of a comorbidity represented by the bifocal recent underlying tuberculosis which delayed the diagnosis of the lymphoma. The patient passed away a few weeks later due to a septic shock.

This case has been reported in line with the SCARE 2020 criteria [1].

3. Discussion

With an incidence rate of 88 cases per 100,000 persons-year [2], Morocco is considered an endemic area for tuberculosis (TB); however, concomitant presentation of TB and lymphoma is not frequently reported. Indeed, this clinical association remains a rare entity [3].

In the large case series published by Kaplan et al. [4] describing 201 cases of malignancies complicated by TB, Hodgkin's lymphoma (HL) appeared as one with the most prevalence of TB infection (96/10,000 patients at risk), next to lung cancer et lymphosarcoma. Since HL is cell-mediated immunodeficiency, it may result in infections with several pathogens, such as Mycobacterium species. But, the presence of these pathogens can precede HL and some can contribute to HL development [5].

The hypothesis behind the pathogenesis of this association is related to the Mycobacterial tuberculous infection damages directly occurring on DNA, apoptosis inhibition and the inflammatory microenvironment rich in cell proliferation/mutation mediums, which promote mutagenesis, combined with angiogenesis favoring tumorigenesis. More specifically, multiple mycobacterial cell wall components are suggested to induce the production of nitric oxide and reactive oxygen species which are involved in mutagenesis [3,6]. In another hand, since immunity against TB demands induced cellular response mediated mainly by CD4 T-lymphocytes and HL causes a suppression of this cell-mediated immunity, which seems to become more impaired as the disease progresses, it predisposes to a concomitant TB infection/reactivation [3,4,6]. Also, the alteration of the antioxidative system in HL through depletion of glutathione (GSH) increases the risk for TB since GSH plays an important role in defending against mycobacterial pathogens [7].

The consequences can be misdiagnose or delay in diagnosis of both TB and HL since they both share similar signs and symptoms, laboratory tests results and imaging procedures [3,5]. Usually, TB accompanying malignant lymphomas is often characterized by an atypical clinical course, with unusual extrapulmonary localizations (lymph nodes, breast, spleen, liver, jejunum and skin) [5].

Tuberculin testing should be a routine test on patients with lymphoproliferative and lung cancers when the neoplasm is first diagnosed, since they are at such increased risk [4]. Moreover, in endemic areas of

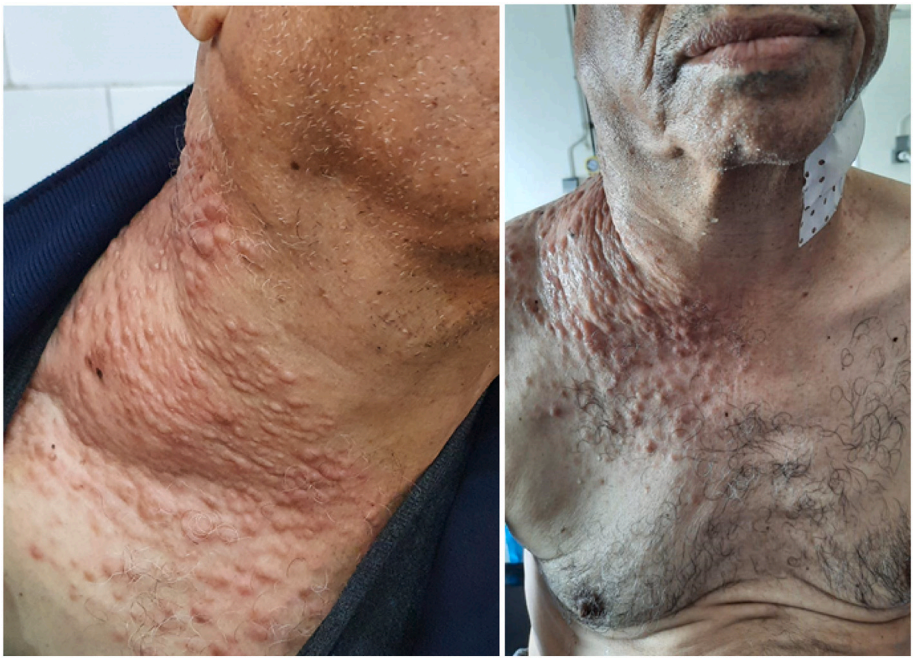

Fig. 1. Multiple voluminous cervical lymphadenopathies, responsible of a drooping of the right corner of the mouth, with a skin rash made of confluent erythematous papular lesions.

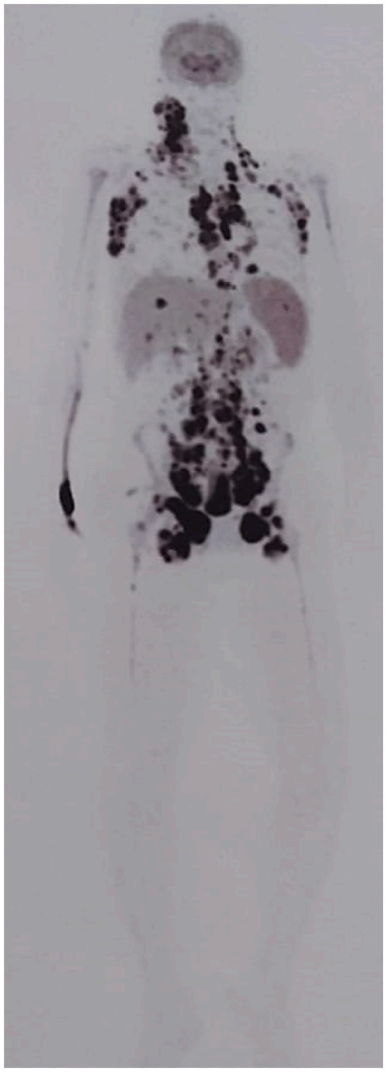

Fig. 2. FDG-PET-scan showing multiple confluent hypermetabolic lymphadenopathies on the whole upper body with cervical skin extension, hypermetabolic splenomegaly and focal liver hypermetabolism.

TB, TB screening should be routinely done for any cancerous patient, including those with HL [8]. However, regarding the underlying immune suppression in the background of a malignancy, diagnostic utility of tuberculin skin test is very low [3].

CT imaging and Positron Emission Tomography (PET) scan are not always specific for the differentiation between TB and lymphoma [5]. In fact, hypermetabolic lesions can be observed in malignant tissues as well as in inflammatory process [9].

Biopsy with histopathological examination remains the most specific and sensitive diagnostic tool. However, TB typical caseating or necrotizing granulomatous lesions can also be found in HL and non-Hodgkin's lymphomas (NHL). Thus, an immunostaining assay is requisite in order to determine the expression of CD15 and CD30 antigens on Reed-Sternberg cells [3,5]. At last, further differential diagnosis by PCR tests with mycobacterium-specific primers can be used to confirm infection [5].

The principle of management of these cases is treating TB simultaneously with HL after multidisciplinary discussion [3,9]. No drug interaction between anti tuberculous treatment and HL chemotherapy was reported, these concomitant treatments has been proved effective and safe [8].

The "International Prognostic Factors Project on Advanced Hodgkin's Disease" suggested 7 significant prognostic parameters: age, sex, stage IV disease, low albumin level (<4.0 g/dL), anemia (<10.5 g/dL), leukocytosis (>15,000/mm^3) and lymphopenia (<600/mm^3) [10]. Also, the presence of co-morbidity was associated with a decreased overall survival within the first 4 months after diagnosis in HL. And TB was considered in several studies, such as Vas Spronsen et al. study [11] which evaluated the prognostic effect of co-morbidities in lymphoma patients, as a co-morbid condition with potentially negative prognostic effects next to connective tissue diseases, chronic infections and cardiovascular diseases.

4. Conclusion

The coexistence of HL and TB infection is a rare entity than can mislead and delay the diagnosis and treatment of either disease. Thus, in front of a patient diagnosed with TB with no response to regular treatment, next to atypical mycobacteria and drug-resistant TB, a concomitant malignancy should be considered starting with lymphomas and lung cancer, especially in TB endemic areas.

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Ethical approval

Obtained.

Informed consent was obtained from the patient's family for publication of this case report.

Consent

Written informed consent was obtained from the patient's family for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

El Bouhmadi Khadija: Corresponding author and writing the paper
Oukessou Youssef: Study concept
Sami Rouadi: study concept
Abada Reda: study concept
Roubal Mohamed: correction of the paper
Mahtar Mohamed: correction of the paper

Research registration

N/a.

Guarantor

El Bouhmadi Khadija.

Declaration of competing interest

None.

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