

Not all that shines is cancer: pulmonary cryptococcosis mimicking lymphoma in [(18)] F fluoro-2-deoxy-D-glucose positron emission tomography

Nem tudo o que brilha é câncer: criptococose pulmonar mimetizando linfoma na tomografia por emissão de pósitrons com [(18)] F fluoro-2-desoxi-D-glicose

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ABSTRACT

We report of a case of pulmonary cryptococcosis mimicking lymphoma in a positron emission tomography (FDG-PET) scan. A 62-year old man with diffuse large B-cell lymphoma had complete resolution of abdominal and pulmonary lesions after three cycles of rituximab-based chemotherapy (R-CHOP). However, FDG-PET showed new pulmonary nodules, suggesting active lymphoma. Chronic inflammatory granuloma was seen in the histopathological exam, with round-shaped structures compatible with fungus, later identified as *Cryptococcus neoformans* on culture. The lesions disappeared after 6 weeks of fluconazole therapy, and the patient could continue chemotherapy without further infectious complications.

Keywords: Positron-emission tomography; Lymphoma, non-Hodgkin; Cryptococcosis; Lung diseases; *Cryptococcus neoformans*; Case reports

RESUMO

Relato de caso de criptococose pulmonar mimetizando linfoma num exame de tomografia por emissão de pósitrons (PET-scan). Homem de 62 anos com resolução completa, ao PET-scan, de seu linfoma não Hodgkin de células B, lesões abdominais e pulmonares, após três ciclos de quimioterapia baseada em rituximabe (R-CHOP). Entretanto, o mesmo exame mostrou também novos nódulos pulmonares, sugestivos de lesões do linfoma. Granuloma inflamatório crônico foi observado no exame anatomopatológico, com estruturas circulares compatíveis com fungo. Cultura revelou *Cryptococcus neoformans*. As lesões desapareceram após 6 semanas de fluconazol, e o paciente pôde continuar a quimioterapia sem complicações infecciosas.

Descritores: Tomografia por emissão de pósitrons; Linfoma não Hodgkin; Criptococose; Pneumopatias; *Cryptococcus neoformans*; Relatos de casos

INTRODUCTION

[(18)] F fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) is an imaging modality based on the Warburg effect, the propensity of cancer cells to maintain elevated glycolysis in the presence of oxygen⁽¹⁾. It has shown great value in distinguishing between benign and malignant lesions⁽²⁾, and has emerged as the gold standard technique for staging both Hodgkin's and aggressive non-Hodgkin's lymphomas (NHL)^(3,4).

Several reports describe pitfalls in FDG-PET imaging diagnosis. Benign inflammatory/infectious lesions can have increased metabolic rates and can be misclassified as malignant lesions. Single pulmonary nodules imaging by FDG-PET may be particularly difficult to evaluate, since *Mycobacterium* or fungal granulomas can resemble lung cancer⁽⁵⁾. The standardized uptake value (SUV max), a calculated measure of contrast uptake, has been used in an attempt to differentiate the underlying etiology of such lesions. Low SUV values (up to 2.5) are seen more frequently with benign lesions and high uptake values (over 2.5) are more frequent with

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malignant lesions⁽⁶⁾. Clinical judgment and a complete laboratory evaluation can help establishing the correct diagnosis, although biopsy is usually necessary.

CASE REPORT

A 62-year old man was referred to the institution due to weight loss, fever, abdominal pain and jaundice. Computerized tomography (CT) of the abdomen revealed 6-cm infiltrative perihepatic mass, liver nodules, splenomegaly and periaortic enlarged lymph nodes. CT of the thorax revealed multiple pulmonary nodules and enlarged axillary, cervical and mediastinal nodes. Biopsy of the hepatic mass diagnosed CD20+ diffuse large B-cell lymphoma (DLBCL).

After three cycles of rituximab-based chemotherapy (R-CHOP), the patient complained of daily fever, up to 38°C. Extensive laboratorial and imaging workup for infectious disease was inconclusive. FDG-PET study revealed complete resolution of previous abdominal and pulmonary lesions. However, new pulmonary nodules, up to 2.5cm large, with a SUV max of 13.6 were observed on the right posterior lobe of the lung, suggesting active lymphoma (Figure 1).

An open lung biopsy was performed to elucidate the diagnosis. A chronic inflammatory granuloma was observed in the histopathological exam with round-shaped structures compatible with fungus (Figure 2). Culture of the pulmonary tissue revealed *Cryptococcus neoformans*. Fluconazole (150mg daily) was started, 6 weeks later the pulmonary lesions had disappeared and the patient was asymptomatic. He was able to continue chemotherapy without further infectious complications.

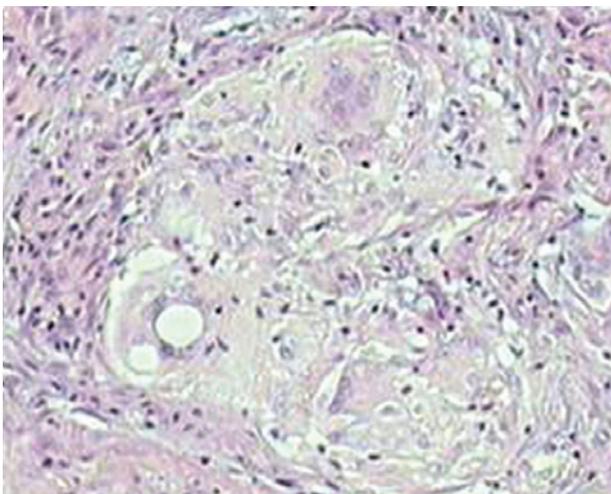


Figure 1. [(18) F] fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) showing pulmonary nodules in the right posterior lobe, suggestive of active lymphoma lesions

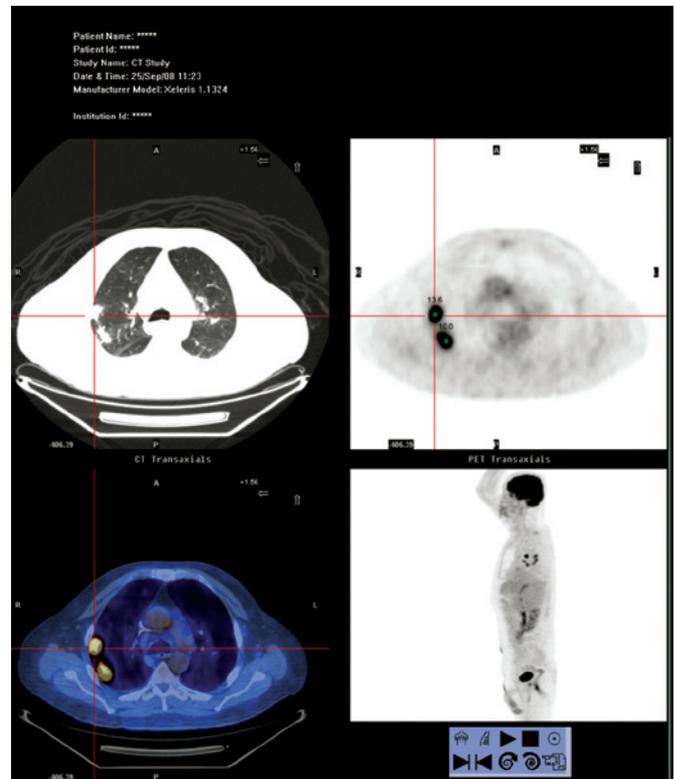


Figure 2. Histologic section from open lung biopsy showing chronic inflammatory granuloma and round-shaped structures compatible with fungus (hematoxylin-eosin, 100 X)

DISCUSSION

Pulmonary cryptococcosis (PC) is an infectious fungal disease often seen in immunocompromised hosts. Several risk factors have been described including HIV infection, malignancies, stem cell and organ transplantation, and they are treated with glucocorticoids or tumor necrosis factor antagonists^(7,8). In the case described here, both malignancy and chronic use of glucocorticoids imposed a risk for fungal infection.

FDG-PET is very sensitive and accurate in NHL staging and reevaluation. However, it is known that immunocompromised patients may have atypical clinical presentations of infectious diseases and biopsy may be necessary for a correct diagnosis. The use of SUV for discrimination between benign and malignant disease has been extensively studied and the majority of studies establish a SUV of 2.0 to 5.0 as a rational cutoff⁽⁹⁾. Particularly in cryptococcosis, few reports have been conclusive. Huang et al.⁽⁶⁾, for example, observed a SUV max ranging from 2.2 to 11.6. In the patient studied, a SUV of 13.6 was highly suggestive of active NHL. However, with the impressive clinical and radiological response observed in other affected areas and after a judicious evaluation of the pulmonary

nodules, the different diagnosis of fungal infection was suspected. This report highlights the importance of histopathological diagnosis before initiating/changing a treatment.

REFERÊNCIAS

1. Kelloff GJ, Hoffman JM, Johnson B, Scher HI, Siegel BA, Cheng EY, et al. Progress and promise of FDG-PET imaging for cancer patient management and oncologic drug development. *Clin Cancer Res*. 2005;11(8):2785-808.
2. Collins CD. PET/CT in oncology: for which tumours is it the reference standard? *Cancer Imaging*. 2007;7 Spec No A:S77-87.
3. Buchmann I, Reinhardt M, Elsner K, Bunjes D, Althoefer C, Finke J, et al. 2-(fluorine-18)fluoro-2-deoxy-D-glucose positron emission tomography in the detection and staging of malignant lymphoma. A bicenter trial. *Cancer*. 2001;91(5):889-99.
4. Sasaki M, Kuwabara Y, Koga H, Nakagawa M, Chen T, Kaneko K, et al. Clinical impact of whole body FDG-PET on the staging and therapeutic decision making for malignant lymphoma. *Ann Nucl Med*. 2002;16(5):337-45.
5. D'Souza MM, Tripathi M, Shrivastav M, Sharma R, Mondal A. Tuberculosis mimicking malignancy. *Hell J Nucl Med*. 2009;12(1):69-70.
6. Huang CJ, You DL, Lee PI, Hsu LH, Liu CC, Shih CS, et al. Characteristics of integrated 18F-FDG PET/CT in pulmonary cryptococcosis. *Acta Radiol*. 2009;50(4):374-8.
7. Finke R, Strobel ES, Kroepelin T, Guzman J, Klein PJ, Schaefer HE, et al. Disseminated cryptococcosis in a patient with malignant lymphoma. *Mycoses*. 1988;Suppl 1:102-8.
8. Arend SM, Kuijper EJ, Allaart CF, Muller WH, Van Dissel JT. Cavitating pneumonia after treatment with infliximab and prednisone. *Eur J Clin Microbiol Infect Dis*. 2004;23(8):638-41.
9. Kishi K, Homma S, Kurosaki A, Kohno T, Motoi N, Yoshimura K. Clinical features and high-resolution CT findings of pulmonary cryptococcosis in non-AIDS patients. *Respir Med*. 2006;100(5):807-12.