Clinical note

Sarcoidosis mimicking metastatic gynaecological malignancies: A diagnostic and therapeutic challenge?

P. Mapelli a,∗, G. Mangili b, M. Picchio a,c, E. Rabaiotti b, L. Gianolli a, C. Messa c,d, M. Candiani b

a Department of Nuclear Medicine, San Raffaele Scientific Institute, Milan, Italy
b Department of Gynaecology and Obstetrics, San Raffaele Scientific Institute, Milan, Italy
c Institute for Bioimaging and Molecular Physiology, National Research Council, Milan, Italy
d Department of Nuclear Medicine, San Gerardo Hospital, Monza, Italy

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A B S T R A C T

Several case reports describing the coexistence of sarcoidosis and malignancy have been published. Therefore, sarcoidosis should always be considered as a differential diagnosis when a cancer patient develops lymphadenopathy. Positron-emission tomography (PET) 2-[18F]-fluoro-2-deoxy-D-glucose (FDG) combined with computed tomography (CT) is widely used for cancer staging and surveillance because it permits localization of metabolically active malignant tissue. PET/CT or CT findings in patients with suspected cancer recurrence can be used to guide early and aggressive therapy. However, benign hyper-metabolic lymphadenopathy can mimic malignant lymphadenopathy, both on a conventional CT scan and on PET/CT. Thus, it is important to obtain a histological diagnosis before initiating antineoplastic therapy based on imaging findings. Four cases of patients affected by gynaecological malignancies and coexisting sarcoidosis are reported in this study. Furthermore, the clinical relevance of making a differential diagnosis between gynaecological cancer recurrence and granulomatous disorder is given specific mention.

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Sarcoidosis imitando metástasis de cáncer ginecológico: ¿un reto diagnóstico y terapéutico?

R E S U M E N

Se han publicado casos clínicos que describen la asociación entre el cáncer y la sarcoidosis; por esta razón, la sarcoidosis siempre debe ser incluida en el diagnóstico diferencial cuando un paciente con cáncer presenta linfadenopatía. La tomografía de emisión de positrones (PET) con 2-[18F]-fluoro-2-desoxi-D-glucosa (FDG) combinada con la tomografía computarizada (TC) se utiliza ampliamente para la estadificación y la vigilancia del cáncer, ya que permite la localización de tejido maligno metabólicamente activo; los resultados de la PET/TC o TC en pacientes con sospecha de recurrencia de cáncer se pueden utilizar para guiar un tratamiento temprano y agresivo. Sin embargo, una adenopatía hiper-metabólica benigna puede ser similar a una adenopatía maligna tanto en la TC como en la PET/TC por lo que es importante disponer de un diagnóstico histológico antes de iniciar una terapia antineoplásica basada en las imágenes. En este estudio se presentan cuatro pacientes con tumores ginecológicos malignos y sarcoidosis y se menciona la importancia clínica del diagnóstico diferencial entre recidiva tumoral y enfermedad granulomatosa.

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Introduction

Sarcoidosis is a granulomatous disorder of unknown origin. The most common site is pulmonary, but involvement of the skin, eyes, lymphnodes, heart and liver has been reported. This disease has been described in association with a previous malignancy and such association does not seem to be causal.

Several case reports have been reported, covering a wide variety of tumours such as schwannoma and carcinoma of the lung, breast, thymus, liver, testis, digestive tract and gynaecological malignancies.1,2 2-[18F]-fluoro-2-deoxy-D-glucose (FDG) positron-emission tomography (PET) is widely used in the management of a variety of malignancies with excellent overall accuracy; however it has to be considered that PET/CT can lead to false-positive results in cases of infection and inflammation where glucose consumption can be found, particularly in the cellular component of the inflammatory lesion. Since sarcoid-like reaction may result in FDG uptake, this metabolic features needs to be differentiated from tumour recurrence.

In the present paper four cases of patients affected by gynaecological malignancies referred to our Institute for staging or restaging are reported. The aim of the present study is to underline...
the importance of recognizing the similar pattern of sarcoidosis and malignancies in order to avoid potential interpretative pitfalls which may lead to inappropriate management in these types of oncologic patients.

Clinical case

Patient 1 is a 41-year-old woman treated with hysterectomy, bilateral annectomy, pelvic lymphadenectomy, omentectomy for a poorly differentiated serous papillary ovarian adenocarcinoma (IIIIC, FIGO stage) in August 2006; after surgery there was no evidence of residual disease. The patient also received 6 cycles of adjuvant chemotherapy with taxol and carboplatin. During follow-up a CT scan was performed for persistent cough and it showed bilateral pulmonary micronodules (maximum diameter 7 mm), multiple mediastinal and bilateral pulmonary hilar adenopathies; with the suspicion of relapse of disease the patient underwent FDG-PET/CT. The scan revealed right paratracheal, bilateral hilar and parahilar pulmonary and subcarinal lymph nodal uptake; a tiny uptake in the right lung was also present (Fig. 1). The particular distribution of FDG uptakes gave rise to the possibility of inflammatory rather than metastatic findings. To confirm this suspicion, in May 2007, the patient underwent videomediastinoscopy with multiple paratracheal and subcarinal lymph nodes biopsies. Histopathological examination revealed the presence of giant cell epithelioid granulomatous necrotizing lymphadenitis compatible with sarcoidosis in paratracheal lymphnodes; subcarinal nodes were negative for metastasis and only inflammatory activated cells were present. The patient was treated for a stage II pulmonary sarcoidosis and during the last follow-up in June 2011 the patient had no evidence of disease.

Patient 2 is a 26-year-old woman affected by IB1 poorly differentiated adenosquamous carcinoma of the cervix with pelvic positive lymphnodes, treated with radical hysterectomy class C1 Morrow Querleu and lymphadenectomy in February 2010. The patient subsequently underwent concomitant chemoradiation therapy with cisplatinum. In September 2010, during follow-up, the patient presented multiple subcutaneous nodular lesions on both legs, suspected for erythema nodosum. A chest CT scan performed during follow-up on October 2010 revealed a pseudonodular finding (maximum diameter 11 mm) in the paramediastinic region of the left upper lobe, a smaller nodule (maximum diameter 5 mm) in the right upper lobe and multiple mediastiniec adenopathies suspected for metastases. 18F-FDG PET/CT was performed to obtain a metabolic characterization of CT findings and revealed bilateral tracer uptakes in the mediastinum extended to the peribronchial region, left supravacular and abdominal lymphnodal uptake. Splenic and multiple pulmonary uptakes were also present and suspected for neoplasia localization.

A fine needle aspiration biopsy (FNAB) was performed on the left supravacular adenopathy but the material was not adequate for cytological examination. The patient subsequently underwent mediastinoscopy to sample the paratracheal lymphnodes and the hystopathological examination revealed a chronic giant cell granulomatous necrotizing lymphadenitis compatible with sarcoidosis. The patient was treated for sarcoidosis with the resolution of lymph nodal involvement and disappearance of the subcutaneous legs nodule. At present the patient has no evidence of disease.

Patient 3 is a 63-year-old woman who was admitted for endometrioid endometrial cancer G1 grade, suspected for stage IV
disease for the presence of lung metastases on a chest X-ray performed for persistent cough. A whole-body CT scan was then performed and it showed a thickened endometrium, bilateral external iliac adenopathy, multiple bilateral lung nodules suspected for metastatic localization and multiple bilateral mediastinal adenopathies.

Before surgery a $^{18}$F-FDG PET/CT scan was performed showing high tracer uptake in the uterus and in multiple thoracic, abdominal and inguinal lymph nodal sites (Fig. 2). A bilateral hysteroanuexectomio with lymphoadenectomio was then performed. The hystopathological examination revealed the presence of endometrial cancer, endometrioid hystotipe, grade 1 stage I; the bilateral external iliac lymph nodes were not involved by tumour spreading, but a chronic giant cell granulomatous necrotizing lymphadenitis compatible with sarcoidosis was present in these sites.

The finding of chronic granulomatous involvement of iliac lymph node, gave rise to the suspicion that the pulmonary nodules, the mediastinal and pulmonary hilar lymph nodes were not metastatic sites of disease but sites of granulomatous disease as well.

A biopsy was then performed on the right paratracheal lymph node to confirm this hypothesis and hystopathological examination showed a giant cell epitelioid granulomatous necrotizing lymphadenitis compatible with sarcoidosis. The patient was treated for sarcoidosis and up to February 2011 the follow-up for endometrial cancer is negative.

Patient 4 is a 72-year-old woman who underwent bilateral hysteroanuexectomio and chemotheraphy for ovarian clear cell carcinoma (stage IC) in 1998. During follow-up, a CT scan performed in 2004 revealed mediastinal adenopathies and a lung nodule posterior to the left main bronchus. These findings were suspicious for metastatic localization of ovarian cancer. To better characterize CT findings, $^{18}$F-FDG PET/CT was performed showing subcarinal, bilateral hilar and aorto-pulmonary window lymph nodal uptakes; the initial stage of the disease together with the particular distribution of FDG uptakes, made inflammatory disease a more reliable diagnosis than metastases.

A biopsy of the mediastinal lymph nodes was then performed and confirmed the presence of chronic granulomatous lymphadenitis. The patient started a therapy for sarcoidosis and as far as we know, up to 2004 the patient had no evidence of disease.

**Discussion**

Several case reports and case series have been published describing the coexistence of sarcoidosis and malignancy. Although no definite causal relationship has been yet identified, sarcoidosis is to be considered in differential diagnosis, when a cancer patient develops diffuse lymph nodal involvement.\(^3\)

CT and $^{18}$F-FDG PET/CT are widely used for staging and surveillance of oncologic patients, because of their accuracy in detecting malignant tissues. Positive CT or PET/CT findings in patients with suspected cancer recurrence can be used to guide early, aggressive therapy. However it’s important to remind that benign hypermetabolic lymphadenopathy can mimic the appearance of malignant lymphadenopathy, both on a conventional CT scan and on $^{18}$F-FDG PET/CT, and the final diagnosis is based on histological evaluation. In the field of gynaecological malignancies, many isolated case reports and studies on small cohort of patients have been published on the association between sarcoidosis and gynaecological malignancies.\(^4-10\)

Sarcoidosis usually presents itself with pulmonary lesions that may mimic metastatic disease in oncologic patients. As the prognosis of sarcoidosis is favourable following glucocorticoid therapy and the possible symptoms often resolve spontaneously, it’s mandatory to further evaluate suspected pulmonary or lymph nodal lesions in oncologic patients when the clinical history, the tumour histology or the patient’s follow up are not so suggestive for metastatic disease.\(^9\)

In the reported cases, sarcoidosis was mainly suspected because the histology of the primary tumour was associated with a favourable prognosis and a lung and extensive lymph nodal metastatic involvement is unlikely. The differential diagnosis between sarcoidosis and metastatic neoplasia has been clinically relevant because it made possible to avoid further diagnostic procedure but, above all, to avoid excessive and useless treatment with aggressive chemotherapy.

In conclusion, when the clinical history of the patients suggests that metastatic disease is unlikely to be present, sarcoi1dsis should be taken into account as an alternative cause of suspicion CT and FDG PET/CT findings, to avoid further unnecessary diagnostic examination and potential toxic overtreatment.
References