Clinical note

Diagnosis of unknown sarcoidosis associated to erythema nodosum with $^{18}$F-FDG PET/CT

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**A B S T R A C T**

A 76-year-old woman was referred to our centre to perform $^{18}$F-FDG PET/CT with the clinical suspicion of vasculitis. Whole body PET was negative for vasculitis but it depicted moderate hypermetabolism in several lymph nodes of the mediastinum and intense uptake of the tracer in the parotid glands. Since the patient referred skin lesion on both legs a particular acquisition of the lower extremities was performed which showed diffuse uptake on the perimalleolar region of both legs. On the basis of the PET/CT findings that were suggestive for sarcoidosis the patient performed bronchoalveolar lavage (BAL) and biopsy of a mediastinal lymph node which confirmed the suspicion of sarcoidosis.

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**Diagnóstico de sarcoidosis desconocida asociada a eritema nodoso, mediante $^{18}$F-FDG PET/TAC**

**R E S U M E N**

Una mujer de 76 años fue remitida a nuestro Centro de Medicina Nuclear para someterse a $^{18}$F-FDG PET/TAC con sospecha clínica de vasculitis. La PET de cuerpo entero resultó negativa para vasculitis pero mostró hipermetabolismo moderado en varios ganglios linfáticos del mediastino y una captación intensa en las glándulas parótidas. Dado que la paciente refirió en anamnesis lesiones eritematosas de la piel en ambas piernas, realizamos una adquisición de PET de las extremidades inferiores que mostró una captación difusa en la región perimalleolar en ambas piernas. Sobre la base de los hallazgos de la PET/TAC que sugirieron sarcoidosis la paciente fue sometida a un lavado broncoalveolar (BAL) y a una biopsia de un ganglio linfático mediastínico que confirmó la sospecha de sarcoidosis.

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**Introduction**

$^{18}$F-FDG PET/CT has a well established role in the diagnosis, staging, restaging, follow-up and monitoring response to treatment for a variety of neoplastic conditions. $^{18}$F-FDG PET/CT is used also in the evaluation of several inflammatory diseases, such as sarcoidosis.

Sarcoidosis is a multisystemic disease of unknown etiology. Its characteristic hallmark is the formation of non-caseating granulomas. Most frequently it affects not only the lungs and hilar lymph nodes (<90%), but also the eyes (20%), liver (20%), skin (20%) and heart (5%). Skin manifestations range from the raised, tender, red nodules of erythema nodosum to remarkable array of skin lesions. Erythema nodosum, in particular, is associated to sarcoidosis in 11–25% of the cases and is typically correlated to bilateral hilar adenopathy.

We report here a case of unsuspected sarcoidosis diagnosed by $^{18}$F-FDG PET/CT performed for suspicion of vasculitis.

**Case report**

A 76-years-old woman was referred to our hospital on December 2011 presenting with malaise, persistent fever (37.5–38.1°C) in the past two weeks, with coughing in the last days associated to pharyngitis for which she was treated with steroid inhalation therapy. Biochemical exams have shown leukocytosis: 11,500/mm$^3$, erythrocyte sedimentation rate: 34 mm, C-reactive protein level: 37 mg/l. Of note the patient referred also arthralgia of the lower extremities associated to dolent reddish papules with symmetric distribution, localized in the inferior third of both legs.

In anamnesis the patient also referred arterial hypertension diagnosed 20 years ago (on treatment with angiotensin converting enzyme – ACE – inhibitors), venous insufficiency on both legs with varicose veins during the last 15 years and diffuse arthralgies in the last two years (occasionally self treated with anti-inflammatory drugs, with partial effect). In October of 2011 she performed thromboleoarterectomy of the left superficial femoral artery with percutaneous revascularization.

Due to the persistence of the above described signs and symptoms, the patient was referred to our nuclear medicine department for whole body $^{18}$F-FDG PET/CT with clinical suspicion of vasculitis.

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The whole body PET/CT scan was negative for vasculitis but revealed moderate uptake in various lymph nodes located in the mediastinum: right paratracheal, precardinal, hilar bilaterally and in the aortopulmonary window. Moreover intense symmetric uptake of the tracer was shown in the parotid glands (Fig. 1). The patient performed also an acquisition of the lower extremities, for the evaluation of the skin lesions that showed a moderate, diffuse FDG uptake with symmetrical distribution to the lower and middle third of both legs corresponding to the patient’s skin lesions (Fig. 2).

The $^{18}$F-FDG PET/CT scan suggested the presence of sarcoidosis associated to erythema nodosum on both lower extremities.

On the basis of the $^{18}$F-FDG PET/CT findings the patient was submitted to bronchoscopy with examination of bronchoalveolar lavage (BAL) fluid that demonstrated lymphocytosis (lymphocytes 42%), with elevate CD4:CD8 ratio and 55% of macrophages. The patient moreover underwent transbronchial biopsy of mediastinal lymph nodes that demonstrated the presence of non-caseating granuloma that confirmed the diagnosis of sarcoidosis, associated to erythema nodosum.

**Discussion**

Sarcoidosis with hilar adenopathy, polyarthritis and erythema nodosum is called Löfgren syndrome, occurs in 9–34% of patients, and is associated to good prognosis. The diagnosis of sarcoidosis is based on compatible clinical and imaging findings supported by histologic evidence of non-caseating epitheloid-cell granulomas. Moreover, imaging plays an important role in assessing the extent of the disease at both primary staging and patient follow-up and traditionally consists of chest radiography, computed tomography (CT) and $^{67}$Ga scintigraphy.

In the gallium scintigraphy the characteristic pattern is a “lambda” pattern of symmetrical and uniform intrathoracic lymph node $^{67}$Ga uptake frequently associated to a “panda pattern” of lacrimal and salivary gland $^{67}$Ga uptake, present only in patients affected by sarcoidosis. In 1990 Sulavik et al. first described the panda sign, i.e. normal accumulation of the radionuclide ($^{67}$Ga-citrate) in the nasopharynx combined with increased symmetric accumulation in the parotid and lacrimal glands, giving the impression of the mottled colouring of the giant panda. Intrathoracic lymphadenopathy typically manifests as bilateral hilar adenopathy with predominantly right paratracheal adenopathy, referred to as the lambda appearance.

In the last years hybrid PET/CT imaging has gained a major role in the management of several pathologies. The main radiotracers used in PET is the glucose analog $^{18}$F-FDG which is very sensitive in visualizing lesions that present high glucose metabolism but not specific for malignant tumours, since it is actively taken up also in inflammatory processes, such as the epitheloid granulomas of sarcoidosis. Thus, $^{18}$FDG PET/CT can be used for the evaluation of the extent of the disease in patients with known or suspected sarcoidosis and to target an optimal site for biopsy.

Moreover $^{18}$F-FDG PET/CT in comparison to the gallium scintigraphy is less time consuming, offers images with higher spatial resolution and presents a better sensitivity, associated to a better dosimetry for the patient.

In our case, $^{18}$F-FDG PET/CT revealed hypermetabolic intrathoracic lymphadenopathy involving right paratracheal, precarinal, aortopulmonary window lymph nodes of the mediastinum and of the parotid glands.

**References**

“panda” signs already described in the gallium scintigraphy and as proposed by other authors are present also in the FDG PET/CT scans as a characteristic distribution of sarcoidosis. The PET/CT findings were suggestive of sarcoidosis and bronchoscopic evaluation with examination of BAL fluid and biopsy was proposed on the PET findings. In bronchoalveolar lavage fluid, a lymphocytosis is quite sensitive but less specific, whereas an increased CD4:CD8 ratio increase is less sensitive but highly specific for sarcoidosis; in addition to lymphocytes, alveolar macrophages are activated in sarcoidosis. In our case the bronchoalveolar lavage showed lymphocytosis (lymphocytes 42%), with elevate CD4:CD8 ratio and 55% of macrophages. Histopathology of a transbronchial biopsy specimen confirmed the diagnosis of sarcoidosis.

The 18F-FDG PET/CT scan has shown absent uptake in the vessels thus excluding the clinical suspicion of vasculitis. On the other hand the uptake in the mediastinum lymph nodes associated to the intense uptake in the salivar glands and the uptake in the extremities, corresponding to the erythema nodosum lesions, has raised the clinical suspicion of sarcoidosis that was confirmed by biopsy.

References


Fig. 2. Maximum intensity projection (MIP) image of the low extremities which shows uptake of the tracer in the perimalleolar region.