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CASE REPORT

FDG-PET to monitor early response to infliximab in refractory systemic sarcoidosis

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Fluorine 18-fluoro-deoxyglucose positron emission tomography

Summary
Background: Systemic sarcoidosis can result in dramatic manifestations despite therapeutic escalation. Tumor necrosis factor (TNFα) has a key role in this disease and antagonists of TNFα have been successfully used as an alternative to conventional therapy. We report a case of refractory sarcoidosis with mediastinal, bone and ear, nose, throat (ENT) lesions.
Methods: In this patient we monitored response to treatment by infusions of the anti-TNFα antibody, infliximab, with fluorine 18-fluorodeoxyglucose positron emission tomography (FDG-PET).
Results: Early and spectacular response to infliximab was demonstrated by FDG-PET, which evidenced complete response to treatment.
Conclusion: This case supports use of FDG-PET to evaluate the extent of active disease in refractory sarcoidosis and above all, FDG-PET could be an imaging method of choice showing response to infliximab in refractory sarcoidosis earlier than other imaging techniques.

Introduction

Systemic sarcoidosis is a chronic disease with unknown etiology. Its hallmark is noncaseating granuloma consisting

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of epithelioid cells derived from macrophages.[1] TNFα seems to have a key role in the inflammatory process. The use of TNFα antagonists has been reported to be effective in systemic sarcoidosis.[2] We report a case of refractory sarcoidosis with successful response to infliximab which was detected early by fluorine 18-fluorodeoxyglucose positron emission tomography (FDG-PET).

Case report

A 41 years old woman was referred in 2003, for right ankle pain. She complained of fever, orbital pain, nasal obstruction and dyspnea with normal chest auscultation. X-ray examinations, CT scan and MRI showed bone lytic lesions of right calcaneum and cuboide with soft tissue infiltration. Chest X-ray found bilateral mediastinal lymph nodes; sinus X-ray showed right maxillary sinusitis. Laboratory values revealed increased CRP = 16.9 g/l and ESR = 25 mm (first hour). Angiotensin-converting enzyme level was 28 U/l. Bone and maxillary sinus biopsies confirmed conglomerate masses of noncaseating epithelioid granulomas.

Systemic sarcoidosis with bone, mediastinal and ENT localisations was confirmed.

Intravenous pulses of methylprednisolone were followed by oral prednisone 30 mg daily in addition to methotrexate 7.5 mg per week.

In December 2004, despite escalation of steroids, symptoms worsened, with severe nasal obstruction and episodes of epistaxis. In 2006, facial and nasal wings infiltration appeared, consistent with lupus pernio (Figure 1). The patient suffered from ocular symptoms including diplopia and orbital pain. ESR was 100 mm (first hour), CRP <5 mg/l, angiotensin-converting enzyme level was 29.8 U/l. Whole body CT scan showed an inflammatory process of right frontal and ethmoidal cells with lytic lesions of bone palate and reactionnal osteitis (Figure 2(a)); it also found mediastinal adenopathies. FDG-PET performed on a Biograph® (Siemens) PET-CT imager found intense hypermetabolic lesions corresponding to active granuloma lesions (Figure 2(b)) in following sites: cervical, mediastinal and inguino-iliac lymph nodes, left lung, skeleton (spreading lesions), both tonsils and submandibular glands, nasal cavities.

Sarcoidosis was still active and progressive, refractory to corticoids and methotrexate. Thus a first intravenous infusion of infliximab 5 mg/kg daily (250 mg/day) was performed. After two infusions, clinical examination performed at day 45, demonstrated a spectacular improvement, with clinical recovery, and ankle pain together with facial infiltration had disappeared (Figure 1). The CT scan, performed before the fourth infliximab infusion, showed decreased infiltration of ethmoidal cells (Figure 2(a)) while mediastinal lymphadenopathies had almost disappeared. FDG-PET, performed at the same time showed complete disappearance of previously described abnormalities (Figure 2(b)).

Discussion

Published reports document infliximab, a chimeric TNFα antagonist, to be effective in systemic sarcoidosis.[2] ENT involvement is rare in systemic sarcoidosis, but it is a severity criterion.[3] Several case series report efficacy of infliximab for treatment of skin, eyes, central nervous system, gastro intestinal tract, liver, heart and lung involvement. This case is the second reported, at our knowledge, for which infliximab treatment was successful in ENT involvement.[2]

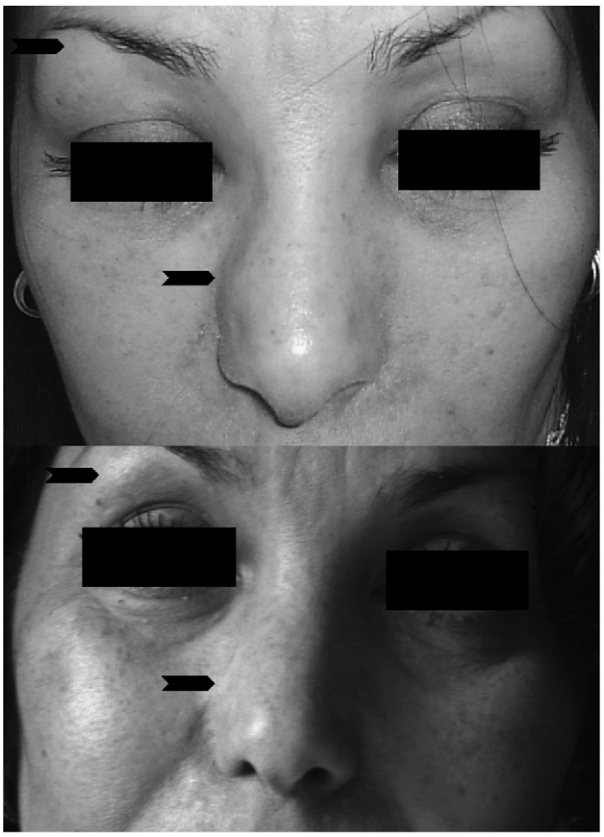

Figure 1 Facial skin and nasal wings infiltration before and after infliximab. First picture (above) was taken in March 2006 and the second in June 2006 after treatment (black arrows).

Because of high cost of such therapy and because of associated side effects, the treatment efficacy has to be evaluated, as early as possible. FDG-PET which was recently introduced in the management of malignant diseases, is based on the trapping of radiolabelled glucose inside the tumor cells; applications of FDG-PET are also developed in inflammatory diseases.[4] Several published case series report the ability of FDG-PET to identify sarcoidosis, but only in its cardiac localisation[5] and never in the multisystemic disease. Here FDG-PET, performed before treatment, depicted several sites of hypermetabolism to be considered in the context of the disease, of positive biopsy findings, and in the absence of any differential diagnosis, as sarcoidosis lesions. Based on this, and compared to CT scan, FDG-PET appeared to give a more complete assessment of the disease extent. The high contrast between lesions and healthy tissues in PET imaging, that confers a higher detectability, accounts probably for the higher sensitivity for FDG-PET compared to CT. After three infliximab infusions, FDG-PET was considered as normal, suggesting a complete response to therapy, in contrast to CT that still demonstrated

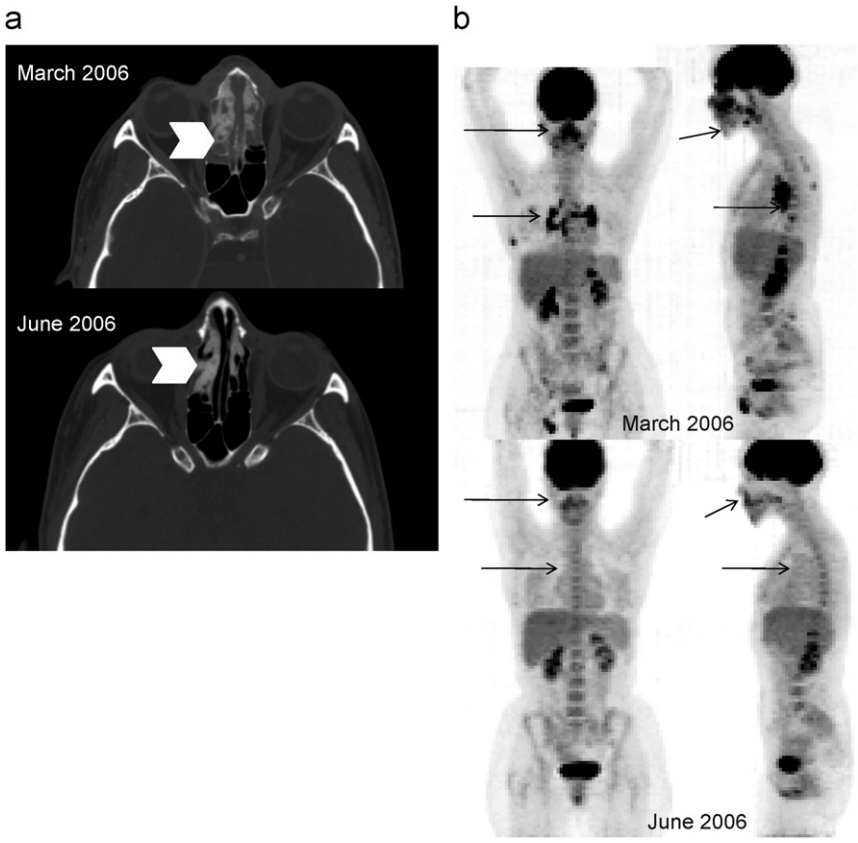

Figure 2 (a) Ethmoidal CT scanner: decrease of inflammatory process after infliximab (white arrows). (b) FDG-PET images: demonstration of response to infliximab with disappearance on FDG-PET performed after treatment of all lesions described on initial examination, especially ENT and mediastinal lesions (black arrows).

abnormalities in ethmoidal area. The negativity of FDG-PET together with the clinical improvement, suggested that CT showed persistent abnormalities corresponding to sequellae and not active lesions.

This case confirms the efficacy of infliximab in refractory multisystemic sarcoidosis especially in bone and ENT localizations. Above all, it suggests that FDG-PET could be more appropriate than CT scan in initial staging of the disease to localize and to determine sarcoidosis activity in soft and bone tissues and in evaluation of response to therapy. Further studies are needed to see if FDG-PET could become an imaging modality of choice for sarcoidosis management, as it is in some malignant diseases.

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Conflict of interest

None

Patient consent obtained

Abbreviations

ENT = ear, nose, throat

TNF = tumor necrosis factor.

FDG PET = fluorine 18-fluorodeoxyglucose positron emission tomography.

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