Chapter 4

^{18}F-FDG PET/CT for detecting bone and bone marrow involvement in sarcoidosis patients

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Abstract

Background

The prevalence of bone involvement in sarcoidosis has been estimated to be 3-5%, mostly affecting the phalanges. The aim of this study was to assess the prevalence and distribution pattern of bone and bone marrow involvement as detected by fluorine18-fluorodeoxyglucose positron emission tomography/ computed tomography (PET/CT) in sarcoidosis patients.

Methods

Between June 2006 and September 2010, 122 patients suffering from severe sarcoidosis that underwent a PET/CT and met the inclusion criteria were studied. In 94 (77%) patients, the PET/CT demonstrated positive findings associated with sarcoidosis. The 94 PET/CTs were screened to localize any bone/bone marrow lesions. Additionally, low-dose CT scans were screened for other causes of increased bone uptake. Relevant clinical data were gathered retrospectively.

Results

Evidence for bone/bone marrow involvement was found in 34% of the 94 patients with PET/CT-positive findings. Of these patients, 60% showed obvious focal bone lesions at various locations: axial skeleton (47%), pelvis (40%), extremities (34%), and skull (2%). In 40% diffuse increased uptake in both axial and peripheral bone marrow, without focal lesions, were found. Both diffuse and focal uptake was seen in 34%, whereas in 25% only focal lesions. In all but two (6%) patients no bone-abnormalities on low-dose CT were found.

Conclusions

More than one-third of PET/CT-positive sarcoidosis patients had osseous abnormalities on PET/CT. The majority of these lesions (94%) could not be detected on low-dose CT. No single preferred location was found. These preliminary results stress the value of PET/CT imaging in the assessment of bone/bone marrow involvement in sarcoidosis patients.

Introduction

Sarcoidosis is a multisystemic disease characterized by activity of cellular immunity with formation of noncaseating granuloma in various organ systems.[1] The first case of sarcoidosis involving bone was described by Besnier in 1898.[2] After that case-report, more publications followed, and several retrospective series reported a prevalence of bone involvement in sarcoidosis patients of 3-5%.[3,4] However, the reported prevalence varies widely depending on the studied population and the used diagnostic techniques. In most studies, conventional radiography was performed for detection of bone involvement. A study on bone scintigraphy conducted in a population of 63 sarcoidosis patients showed bone abnormalities, defined as enlarged osteoclast activity, in 38.1% of the patients.[5] Until today, the exact prevalence of bone involvement in sarcoidosis is unknown, due to these different results and because many lesions are asymptomatic.

Osseous sarcoidosis is more common in blacks and females and is associated with a chronic and severe course of the disease as well as multisystemic involvement.[3,6] A frequent association between skeletal sarcoidosis and both lupus pernio and ocular involvement has been reported.[3] Both are associated with a worse prognosis. In contrast, erythema nodosum is rare in patients with osseous sarcoidosis but often present in Löfgren's syndrome, which is an acute presentation of sarcoidosis with, in general, a favorable outcome. This implicates that assessment of bone involvement is relevant in the clinical management of sarcoidosis patients.

Bone and bone marrow involvement detected by fluorine18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET) in sarcoidosis patients has been reported by several groups.[7-12] However, these reports mainly concerned case-reports and a case series of three sarcoidosis patients. Until now, the usefulness of ^{18}F-FDG PET/CT (PET/CT) in detection of osseous involvement has not been evaluated in a large patient population. The aim of this study was to determine the prevalence and distribution pattern of bone and bone marrow involvement as detected by PET/CT in 122 sarcoidosis patients.

Materials and methods

Study population

Between June 2005 and September 2010 a PET/CT scan was performed in 134 sarcoidosis patients referred to the interstitial lung disease service (ild care team) of the department of Respiratory Medicine at the Maastricht University Medical Centre (Maastricht, The Netherlands), a tertiary referral center. The indication for performing PET/CT was the presence of unexplained disease related disabling symptoms that persisted for at least one year. Persistent disabling symptoms were defined as the

presence of more than one symptom that had substantial influence on quality of life, and that could not be explained with the results of routine investigations including lung function tests or chest X-rays (CXR).

Laboratory testing, lung function testing and a CXR were performed within an interval of less than two weeks of the PET/CT scanning. Blood samples were simultaneously obtained. Sarcoidosis was proven by the presence of noncaseating granulomas on biopsy according with a compatible clinical picture. Moreover, other causes of granulomatous disease were excluded, in accordance with the consensus statement on sarcoidosis of the American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and Other Granulomatous Disorders.[1] Patients with other conditions associated with PET-positive findings were excluded. Therefore, five patients with common variable immunodeficiency, six patients with malignancy and one patient with both rheumatoid arthritis and amyloidosis were excluded. After exclusion for these criteria, 122 patients (median age 46 years; range 24-76; 72 males) were selected. The median time since diagnosis was two years (range 1-53 years). In all, 112 patients were Caucasian, seven of African origin and three of Asian origin. The most frequently recalled symptoms were fatigue (91%), symptoms compatible with small fiber neuropathy (70%), arthralgia and/or muscle/skeletal pain (45%), dyspnea (45%), and coughing (21%). At the time of performance of the PET, a total of 27 patients (22%) were treated for their sarcoidosis. This treatment consisted of prednisone alone (median dose 10 mg daily [range 7.5-40 mg] in 15 patients (12%), methotrexate (MTX) alone (median dose 10 mg a week [range 5-12.5 mg]) in three patients (2%), prednisone combined with MTX (all patients 10 mg prednisone daily and median dose MTX 11.25 mg a week [range 10-12.5 mg]) in seven patients (6%), infliximab alone (400 mg intravenous [IV] every four weeks) in one patient (1%) and infliximab (400 mg IV every four weeks) combined with MTX (both patients 7.5 mg a week) in one patient (1%).

A summary of the demographic and clinical characteristics of the patients is shown in Table 4.1, organized first by PET/CT-negative and -positive patients (n=94), and accordingly, the PET/CT-positive patients were divided in those patients without PET/CT bone lesions and those with PET/CT-positive bone lesions (n=32).

Relevant clinical data were gathered retrospectively. All patients signed an informed consent to allow using their data for study purposes.

Laboratory tests

Laboratory tests were performed on the Synchron LX20 Pro Clinical System (Beckman Coulter B.V., Woerden, The Netherlands) according to the manufacturers' instructions.

Serum angiotensin-converting enzyme (ACE) was measured by colorimetric method (cat. no. FU 116; Fujirebio Inc.), serum levels of soluble interleukin-2 receptor (sIL-2R) were analyzed in commercially available Diaclone ELISA kits (Sanquin, Amsterdam,

The Netherlands) and serum levels of neopterin were evaluated by the principle of a competitive ELISA, using a kit produced by IBL (Hamburg, Germany).

Table 4.1   Summary of relevant clinical characteristics of the studied sarcoidosis patients (n=122) organised first by PET/CT-negative and -positive patients (n=94), respectively.

	PET - patients (n=28)	PET + patients (n=94)	p-value[a]	PET +/bone − patients (n=62)	PET +/bone + patients (n=32)	p-value[b]
Age (y)	49 (24-73)	46 (24-76)	NS	49 (24-76)	42 (26-65)	0.01
Sex (male)	18 (64%)	54 (57%)	NS	43 (69%)	11 (34%)	0.001
Time since diagnosis (yrs)	2 (1-27)	2 (1-27)	NS	2 (1-26)	2 (1-27)	NS
Caucasian/Black/Asian	26/1/1	86/6/2	NS	56/4/2	30/2/0	NS
Chest X-ray stage 0/I/II/III/IV	20/3/3/2/0	16/23/19/9/27	<0.001	10/14/14/8/16	6/9/5/1/11	NS
Therapy total/1/2/3/4	5/2/0/3/0	22/13/3/4/2	NS	16/9/3/2/2	6/4/0/2/0	NS
FVC (% pred)	101±19	91±26	NS	90±27	92±24	NS
DLCO (% pred)	81±18	73±20	0.046	71±22	76±14	NS
Calcium (2.10-2.60 mmol/l)	2.31±0.11	2.33±0.09	NS	2.31±0.07	2.31±0.07	NS
Alkaline phosphatase (45-140 U/l)	79±24	97±45	NS	97±51	95±27	NS
Lactate dehydrogenase (0-480 U/l)	382±195	353±107	NS	347±112	383±95	NS
Hemoglobin (8.2-11.0 mmol/l)	9.3 (7.3-10.6)	8.9 (6.8-10.7)	NS	9.2 (8.1-10.7)	8.7 (6.8-10.2)	NS
Leucocytes (3.5-11.0 10^9/l)	7.9 (4.0-14.1)	8.1 (3.2-17)	NS	7.3 (4.0-17.0)	7.2 (3.2-15.7)	NS
Trombocytes (130-350 10^9/l)	234 (129-369)	302 (144-1033)	NS	266 (144-1033)	282 (173-448)	NS
ACE (9-25 U/l)	17±15	21±18	NS	25±22	18±6	NS
sIL-2R (240-3154 pg/ml)	1656±751	4459±2783	<0.001	3481±2722	4813±2922	NS
Neopterin (<2.5 ng/ml)	1.8±0.4	3.9±3.6	0.009	3.9±4.0	3.9±2.1	NS
CRP (2-9 µg/ml)	5±5	12±17	NS	12±17	12±17	NS

Accordingly, the PET/CT positive patients were divided in those patients without PET/CT bone lesions and those with PET/CT positive bone lesions (n=32). Data are presented as median with range in parentheses; mean±SD; absolute numbers or percentages if appropriate. [a]: p-value for PET-negative versus PET-positive patients. [b]: p-value for bone-negative versus bone-positive patients. p<0.05 was considered to be significant. PET indicates positron emission tomography; -: negative; +: positive; n:number; yrs: years; NS: not significant; therapy total: total number of patients treated at time of PET scanning; 1: prednisone monotherapy; 2: methotrexate (MTX) monotherapy; 3: prednisone and MTX combination therapy; 4: MTX and infliximab combination therapy; FVC: forced vital capacity; % pred: percentage of predicted values; DLCO: diffusion capacity for carbon monoxide; ACE: serum angiotensin-converting enzyme; sIL-2R: soluble interleukin-2 Receptor; CRP: C-reactive protein.

Chest X-ray

According to the Scadding radiographic staging system, five stages of radiographic abnormality were recognized: stage 0 (normal CXR), stage I (bilateral hilar lymphadenopathy [BHL]), stage II (BHL and parenchymal abnormalities), stage III (parenchymal abnormalities without BHL) and stage IV (end-stage lung fibrosis).

Lung function test

Forced vital capacity (FVC) was measured with a pneumotachograph (Masterlab, Jaeger, Würzburg, Germany). The diffusing capacity for carbon monoxide (DLCO) was measured by the single-breath method (Masterlab, Jaeger). Values were expressed as a percentage of predicted values.[13]

^{18}F-FDG PET/CT

A ^{18}F-FDG PET/CT scan was performed. Patients were scanned using a Gemini® PET-CT (Philips Medical Systems) scanner with time-of-flight (TOF) capability and a 64-slice Brilliance CT scanner. The PET scanner has a transverse and axial field of view of 57.6 and 18 cm, respectively. The transverse spatial resolution is around 5 mm.

Patients were fasting for at least six hours before the examination. In all patients, blood glucose was measured to ensure that the blood glucose was <10 mmol/l. ^{18}F-FDG (GE Health, Eindhoven, The Netherlands) was injected intravenously and flushed with physiologic saline (10 ml). The injected total activity of FDG depended on the weight of the patient. Mean injected dose was 200 MBq. After a resting period of 45 minutes (time needed for uptake of FDG), PET and CT images were acquired from the head to the feet. A low-dose CT-scan was used for attenuation correction of the PET images, with 5 mm slice thickness without intravenous contrast. Typical values were 120 kVp; 30 mAs; volume computed dose index, 1.8 mGy and dose-length product 143 mGy. The PET images were acquired in 5-minute bed positions. The complete PET data set was reconstructed iteratively, with a reconstruction increment of 5 mm to provide isotropic voxel.

All PET/CT were interpreted by two experienced nuclear medicine physicians (M.v.K., L.P.). If bone lesions were present, all low-dose CT scans were again examined by an experienced musculoskeletal radiologist (R.W.) to exclude other causes of increased bone uptake. PET/CT findings regarding bone or bone marrow involvement were scored as either positive or negative. PET/CT findings were described as positive if increased FDG-uptake was seen in the skeleton. PET/CT-positive findings in the skeleton were subdivided by locations in the skull, upper extremity, lower extremity, axial skeleton, pelvis and the bone part of the rib. Diffuse and focal uptakes were scored separately. The available follow-up PET/CT scans were evaluated as well.

Statistical procedure

Statistical analyses were performed using SPSS, version 15.0 for Windows. Differences between groups in demographic and clinical characteristics (such as, duration of disease and pulmonary function tests) were tested for statistical significance using the Student t-test for independent samples in case of continuous variables or chi-square test in case of categorical variables. $p < 0.05$ (two sided) was considered to indicate statistical significance.

Results

Of the 122 included patients, 94 (77%) patients had PET/CT-positive findings associated with sarcoidosis. In 32 (34%) of these 94 patients, PET/CT-positive bone or bone marrow lesions were present. Sixty percent (19/32) of the patients with bone/bone marrow lesions on PET/CT, showed obvious focal bone lesions at various locations: axial skeleton (47%), pelvis (40%), extremities (34%), bone part of the rib (18%) and skull (2%). In 41% of the patients (n=13/32), diffuse enlarged uptake in both the axial and peripheral bone marrow, without focal lesions, was found. Both diffuse and focal uptake was seen in 34% (11/32), whereas only focal lesions were seen in 25% (8/32). A rather interesting finding is that corresponding CT lesions were identified in only 2 (6%) of the patients with PET-detected bone abnormalities.

In the total population, PET/CT-positive patients had significantly lower DLCO, sIL-2R and neopterin levels and higher CXR stages when compared with the PET/CT-negative patients. In the PET/CT-positive population, female sex and younger age were significantly more common in patients with bone/bone marrow involvement (Table 4.1). Mean ACE levels were calculated after exclusion of ACE values <9 U/l (n=10), because these values were under the lower limit of the reference value and due to the use of ACE-inhibitors.

Signs of decreased hematopoiesis were present in only one patient of the total population. This female patient had a slight anemia (hemoglobin, 6.8 mmol/l; lower reference value for the female population 7.3 mmol/l) and a minor leucopenia (leucocytes, $3.2 \cdot 10^9$/l; lower reference value, $3.5 \cdot 10^9$/l). PET/CT showed diffuse uptake in the pelvis and proximal femora, consistent with bone marrow activity in this patient.

Histological evidence of osseous sarcoidosis was available in two patients. PET/CT was repeated after a change in therapy in three patients with bone involvement. The reason for therapy change was not the bone involvement itself, but was based on the general presentation (e.g. pulmonary function decline, hypercalciuria). This therapy change consisted of starting prednisone in one patient and adding MTX to prednisone therapy in two patients. Follow-up PET/CT after a median time interval of 7 months (range 3-20 months) showed a decrease in the mean total number of bone lesions from 13.7±14.8 to 3.3±5.8 and the maximum standardized uptake value (SUVmax) decreased from 9.8±3.5 to 3.1±4.3. Testing for statistical significance on these results was not considered to be relevant due to the low number of involved patients.

An example of a patient with diffuse bone lesions and other sarcoidosis-related lesions visible on the pretreatment PET/CT and with obvious improvement after therapy is shown in Figure 4.1.
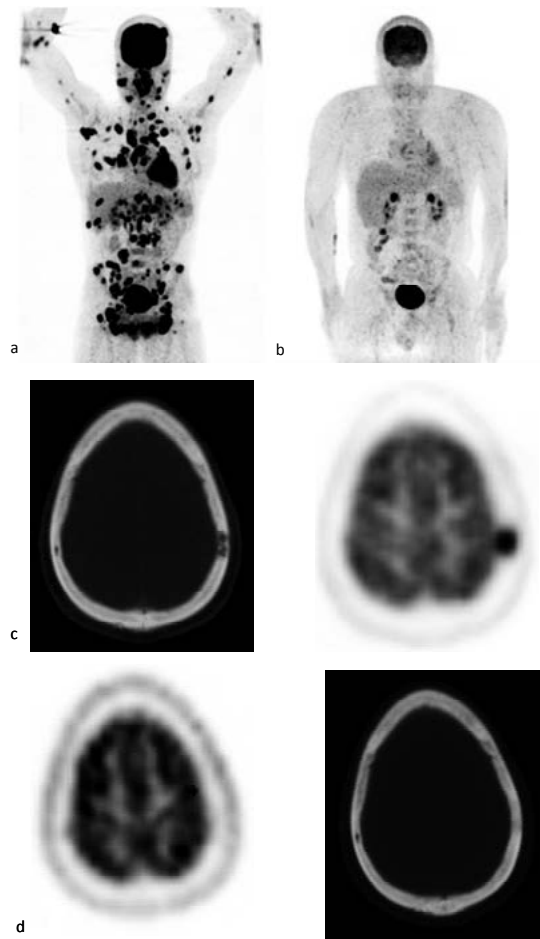
Figure 4.1   Example of a 40-year-old PET-positive sarcoidosis patient with focal PET-positive lesions at multiple locations. **a.** Overview projection of the pretreatment ^{18}F-FDG PET scan showing diffusely increased focal ^{18}F-FDG uptake in multiple bone locations and multiple locations in mediastinal and peripheral lymph nodes, muscles, spleen and parotid glands. **b.** Overview projection of the ^{18}F-FDG PET scan after 18 months of treatment with prednisone and methotrexate showing obvious decrease of the ^{18}F-FDG uptake with only mild residual uptake in mediastinal, hilar and inguinal lymph nodes. **c.** Corresponding transversal CT and PET images at a cranial level showing a focal lytic bone lesion and increased ^{18}F-FDG uptake pretreatment in the left parietal bone. The right parietal bone shows a lucency in the diploe as part of the normal venous structures. **d.** Corresponding transversal CT and PET images at the same level as in c. after 18 months of treatment with prednisone and methotrexate. The lesion in the left parietal bone resolved as indicated by the normalization of the bone mineralization on the CT image and of the ^{18}F-FDG uptake on the PET image.

Discussion

To the best of our knowledge, this was the first study investigating the prevalence of bone/bone marrow involvement assessed by PET/CT in a large population of sarcoidosis patients with persistent symptoms. In more than one-third (32/94) of the patients PET/CT-positive findings compatible with bone/bone marrow involvement were present. This was much higher than expected according to most previously published studies. Moreover, it showed that PET/CT may be an excellent modality to detect bone/bone marrow involvement compared with more conventional modalities.[3,4]

Previous studies suggest that sarcoidosis most commonly affects the phalanges.[3,14] No single preferred location was found in our study. Both the axial and peripheral skeleton was affected. However, it should be noted that evaluation of the phalanges was not possible in all patients since the hands and most of the arm and lower extremities were outside the field of view. Of great interest is the low rate of abnormalities on low-dose CT. Clear bone lesions on CT were identified in only two of the 32 patients with PET detected bone abnormalities. This finding suggests that physiological changes precede morphological changes, which is a concept known from PET/CT in oncology.[15] One of the limitations of our study is that only low-dose CT was available for evaluation of anatomical abnormalities. Although high-dose CT could have improved detection of abnormalities on CT, we observed a clear difference between the rate of physiological abnormalities and morphological abnormalities. This finding is in line with the report of Milman et al.[5], showing a similar low rate of anatomical abnormalities when comparing bone scintigraphy to conventional radiography. However, it should be realized that bone scintigraphy is not able to visualize bone marrow activity directly. Concerning PET/CT, differentiation between increased FDG uptake in bone and bone marrow is difficult, but we assumed diffuse uptake in the femora and/or pelvis without focal lesions to be more likely bone marrow involvement.

Magnetic resonance imaging (MRI) could also be an interesting tool for evaluation of bone or bone marrow involvement in sarcoidosis, but only case reports and one series of 13 patients have been published so far.[14,16-18]

In our population, bone/bone marrow involvement was more common in female patients, which is in accordance with data from previous studies.[3,6]

Bone marrow involvement in sarcoidosis may cause a decreased hematopoiesis (anemia, leucopenia or thrombocytopenia).[8,19] Thrombocytopenia in sarcoidosis patients could, apart from bone marrow involvement, also be due to autoimmune thrombocytopenic purpura, a shortened lifespan of the platelets or hyper-splenism.[20,21] Signs of decreased hematopoiesis were present in only one patient of our study population. This patient had a slight anemia and leucopenia. In this patient, the anemia could be due to inflammatory bone marrow activity associated with sarcoidosis. However, it could not be excluded that the bone marrow activity was

associated with anemia, secondary to another cause than sarcoidosis. To date, no other cause of anemia was established.

No patients had trombocytopenia or splenomegaly at the time of PET/CT scanning (data concerning splenomegaly is not shown).

Two of the patients with bone/bone marrow lesions on PET/CT used MTX, a drug that might affect the bone marrow metabolism. In only one of these patients, diffuse enlarged uptake in both the axial and peripheral bone marrow was demonstrated. The dose of MTX was 7.5mg once a week in this patient, which is rather low. None of the studied patients used other drugs that might affect the bone marrow metabolism.

No data exist on the prognostic significance of PET/CT-positive osseous findings in sarcoidosis patients or on whether there is an increased risk of fracture at these sites. However, sarcoidal bone involvement has been associated with a chronic course of the disease and therefore, establishing its presence is valuable in the clinical assessment of sarcoidosis patients.[6] Because follow-up PET/CT after therapy showed improvement of the osseous involvement, PET/CT may play a role in monitoring osseous involvement in sarcoidosis. Another limitation to our study is that histological evidence of osseous sarcoidosis was only available in few patients. Nevertheless, the diagnosis of sarcoidosis was already confirmed in all the studied cases, and other causes of bone lesions were excluded as far as possible by examining all lesions on the concurrent low-dose CT scans. During the follow-up period, no other pathology was found. Moreover, our centre is a referral centre for sarcoidosis, and therefore, the refractory character may be more severe than in a general sarcoidosis population. Besides, PET/CT was not performed in every referred patient.

In conclusion, PET/CT findings consistent with bone or bone marrow involvement were present in more than one-third of the patients with positive PET scans. This is far more than in most studies described previously. The rate of anatomical abnormalities on low-dose CT was low compared to the physiological abnormalities detected by PET. This may suggest that physiological changes may precede anatomical abnormalities and stresses the strength of functional PET imaging as a potentially sensitive tool to investigate bone involvement in sarcoidosis. The detection of sarcoidal bone or bone marrow involvement can change the clinical assessment of severity of disease and, therefore, may influence the management and follow-up. Further studies are needed to evaluate the exact clinical relevance and prognostic value of these bone lesions.

References

1. Costabel U, Hunninghake GW. ATS/ERS/WASOG statement on sarcoidosis. Sarcoidosis Statement Committee. American Thoracic Society. European Respiratory Society. World Association for Sarcoidosis and Other Granulomatous Disorders. *Eur Respir J* 1999;14:735-7.
2. Besnier E. Lupus pernio de la face. *Ann Dermatol Syph (Paris)* 1898; 10: 333.
3. Neville E, Carstairs LS, James DG. Sarcoidosis of bone. *Q J Med* 1977;46:215-27.
4. James DG, Neville E, Siltzbach LE. A worldwide review of sarcoidosis. *Ann N Y Acad Sci* 1976;278: 321-34.
5. Milman N, Lund JO, Graudal N, Enevoldsen H, Evald T, Nørgård P. Diagnostic value of routine radioisotope bone scanning in a series of 63 patients with pulmonary sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis* 2000;17:67-70.
6. Zisman DA, Shorr AF, Lynch JP, 3rd. Sarcoidosis involving the musculoskeletal system. *Semin Respir Crit Care Med* 2002;23:555-70.
7. Baldini S, Pupi A, Di Lollo S, Marchionni N, Shraim R, Bosi A. PET positivity with bone marrow biopsy revealing sarcoidosis in a patient in whom bone marrow metastases had been suspected. *Br J Haematol* 2008;143:306.
8. de Prost N KK, Sibony M, Talbot J-N, Wislez M, Cadranel J. Fluorine-18 Fluorodeoxyglucose with Positron Emission Tomography Revealed Bone Marrow Involvement in Sarcoidosis Patients with Anaemia. *Respiration* 2010;79:25-31.
9. Aberg C, Ponzo F, Raphael B, Amorosi E, Moran V, Kramer E. FDG positron emission tomography of bone involvement in sarcoidosis. *AJR Am J Roentgenol* 2004;182:975-7.
10. Clarençon F, Silbermann-Hoffman O, Lebreton C, Fernandez P, Kerrou K, Marchand-Adam S, Hourseau M, Schouman-Claeys E, Feydy A. Diffuse spine involvement in sarcoidosis with sternal lytic lesions: two case reports. *Spine (Phila Pa 1976)* 2007;32:E594-7.
11. Kaira K, Oriuchi N, Otani Y, Yanagitani N, Sunaga N, Hisada T, Ishizuka T, Endo K, Mori M. Diagnostic usefulness of fluorine-18-alpha-methyltyrosine positron emission tomography in combination with 18F-fluorodeoxyglucose in sarcoidosis patients. *Chest* 2007;131:1019-27.
12. Ludwig V, Fordice S, Lamar R, Martin WH, Delbeke D. Unsuspected skeletal sarcoidosis mimicking metastatic disease on FDG positron emission tomography and bone scintigraphy. *Clin Nucl Med* 2003; 28:176-9.
13. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J Suppl* 1993;16: 5-40.
14. Moore SL, Teirstein AE. Musculoskeletal sarcoidosis: spectrum of appearances at MR imaging. *Radiographics* 2003;23:1389-99.
15. Tutt AN, Plunkett TA, Barrington SF, Leslie MD. The role of positron emission tomography in the management of colorectal cancer. *Colorectal Dis* 2004;6:2-9.
16. Valencia MP, Deaver PM, Mammarappallil MC. Sarcoidosis of the thoracic and lumbar vertebrae, mimicking metastasis or multifocal osteomyelitis by MRI: case report. *Clin Imaging* 2009;33:478-81.
17. Fisher AJ, Gilula LA, Kyriakos M, Holzaepfel CD. MR imaging changes of lumbar vertebral sarcoidosis. *AJR Am J Roentgenol* 1999;173:354-6.
18. Poyanli A, Poyanli O, Sencer S, Akan K, Sayrak H, Acunaş B. Vertebral sarcoidosis: imaging findings. *Eur Radiol* 2000;10:92-4.
19. Lower EE, Smith JT, Martelo OJ, Baughman RP. The anemia of sarcoidosis. *Sarcoidosis* 1988;5:51-5.
20. Mahevas M, Le Page L, Salle V, *et al.* Thrombocytopenia in sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis* 2006;23:229-35.
21. Dickerman JD, Holbrook PR, Zinkham WH. Etiology and therapy of thrombocytopenia associated with sarcoidosis. *J Pediatr* 1972;81:758-64.