Characteristics of Sarcoidosis in Patients with Previous Malignancy: Causality or Coincidence?

Nissim Arish^a Rottem Kuint^a Eli Sapir^b Liran Levy^a Avraham Abutbul^a
Zvi Fridlender^a Uri Laxer^a Neville Berkman^a

^aInstitute of Pulmonary Medicine and ^bDepartment of Oncology, Hadassah – Hebrew University Medical Center, Jerusalem, Israel

For editorial comment see p. 234

Keywords

Sarcoidosis · Malignancy · Lymphoma · Breast cancer

Abstract

Background: The association between sarcoidosis and malignancy is poorly defined. Sarcoidosis can precede, be diagnosed concurrently with, or follow malignancy. **Objectives:** We describe the clinical and radiological features of patients with sarcoidosis following malignancy to determine whether this association is causal or coincidental. **Methods:** We performed a search for all patients with confirmed sarcoidosis following malignancy in our institution during 2001–2015. Clinical and radiological features, bronchoscopic findings, bronchoalveolar lavage cell counts, and pulmonary function tests (PFTs) were reviewed to evaluate patterns of disease involvement. Details of the histological type of cancer, staging, treatment, and follow-up were reviewed. **Results:** Twenty-nine patients were identified. The most prevalent malignancies were breast cancer and lymphoma (24% each). Based on the incidence of these malignancies, we estimated the incidence of sarcoidosis was 175 times higher after lymphoma and 38 times higher after breast cancer as compared to the general population. Most patients had early stage cancer (stage I, II) (75%), and only 2 patients (7%) had

recurrence of their malignancy after diagnosis of sarcoidosis. Sarcoidosis was diagnosed within 5 years of malignancy in over half the patients, 76% were asymptomatic and 69% had normal PFTs. Mediastinal lymphadenopathy was present in 81% of cases, hilar lymphadenopathy in 67%, and pulmonary parenchymal involvement in 41%. Fifty percent of patients had received Adriamycin, 38% cyclophosphamide, and 33% vincristine. **Conclusions:** Sarcoidosis following malignancy is indistinguishable from “idiopathic” sarcoidosis, although it is frequently asymptomatic. The high frequency of sarcoidosis after specific cancers but not others, suggests a causative association between malignancy and development of sarcoidosis.

© 2017 S. Karger AG, Basel

Background

Sarcoidosis is a systemic inflammatory disease that is characterized by the presence of noncaseating granulomas in affected tissues [1]. The disease has multiple clinical manifestations, ranging from single organ involvement to multisystem disease [2]. The most frequent pattern of sarcoidosis is intrathoracic lymphadenopathy, usually mediastinal and hilar, with or without pulmonary

parenchymal disease. Diagnosis is based on the presence of a compatible clinical-radiological pattern, together with histological evidence of granulomas, and in the absence of an alternative granulomatous disease.

The etiology of sarcoidosis remains elusive, and is likely due to an aberrant “Th1-type” immune response to extrinsic antigen, in a susceptible host. Several candidate antigens have been identified, including infectious and environmental agents, along with several genetic predisposing factors [3].

The association between sarcoidosis and malignancy has been a subject of controversy since the 1950s when it was first reported [4], but there is evidence to suggest that such an association exists [5–7].

Sarcoidosis may predispose to or be a harbinger of malignancy. Patients with sarcoidosis have a more than 5-fold increased incidence of hematological malignancies such as lymphoma. This condition has been termed the “sarcoidosis-lymphoma syndrome” [8, 9]. Patients with established sarcoidosis may also have an increased incidence of solid cancer, and in a large cohort study including 5,738 sarcoidosis patients, there was an increased risk of some neoplasms. The risks of rectal cancer (relative risk 2.12), colon cancer (relative risk 1.55), and kidney cancer (relative risk 1.84) were increased in sarcoidosis patients when compared with other Veterans hospital patients, whereas the risk of lung cancer was decreased (relative risk 0.60). The overall risk for cancer in this series was however not increased (relative risk 0.99) [10]. In addition, a recent meta-analysis by Bonifazi et al. [11], reviewing 16 studies with over 25,000 patients, showed moderately increased risk for several solid tumors, hematological malignancies and skin cancer in patients with sarcoidosis, in the 10 years following their diagnosis, with an RR of 1.19 (95% CI, 1.07–1.32).

The presence of noncaseating granulomas in local lymph nodes or organs in patients with active malignancy is well described. [12]. This local reaction, termed “sarcoid-like reaction,” is particularly prevalent in testicular cancer and lymphoma [13], but has been reported in a wide variety of neoplasms. The term “sarcoid-like reaction” is also used to describe cases with radiological and histological features similar to classic thoracic sarcoidosis (i.e., mediastinal and symmetrical hilar lymphadenopathy) developing in the setting of extrathoracic malignancy, without clinical manifestations [14–17].

There is also some evidence to suggest that either malignancy itself [18–23] or specific chemotherapy agents, such as alpha interferon, may be predisposing factors for the development of sarcoidosis [24–27] and there is on-

going debate as to whether the finding of noncaseating granulomatous disease after malignancy is analogous to idiopathic sarcoidosis [28]. Routine use of computed tomography (CT) and positron emission tomography (PET) in the follow-up of patients with previous malignancy has led to the identification of patients with intrathoracic lymphadenopathy [14–17], in whom biopsies are suggestive of sarcoidosis. In these cases, it remains unclear whether sarcoidosis is merely a coincidental finding or if there is a true association between previous malignancy and this disorder [22].

In this study, we describe the clinical and radiological features of a cohort of 29 patients with previous malignancy, in whom noncaseating granulomas were identified during follow-up. We attempt to clarify 2 questions: First, does sarcoidosis after malignancy differ from “idiopathic” sarcoidosis, and second, can any inferences be made as to whether sarcoidosis is a consequence of the malignancy rather than simply coincidence?

Methods

Local ethics research board approval was obtained for this study (Hadassah – Hebrew University Medical Center), waving the need for informed consent. We performed a retrospective and prospective analysis of all patients seen in the Institute of Pulmonary Medicine at the Hadassah-Hebrew University Medical Center during the years 2001–2015 in whom the diagnosis of sarcoidosis was made. In addition, we reviewed all the hospital pathology reports for the years 2001–2015 using a search tool for cross-queries with the phrases “cancer” or “carcinoma” and “granuloma” or “sarcoid.” We excluded patients in whom the diagnosis of sarcoidosis predated the diagnosis of malignancy and cases in which there was concomitant histological evidence of active cancer together with granulomas (either locally or elsewhere). All identified cases were reviewed in detail to verify the histological, clinical, and radiological features of sarcoidosis. Chest X-rays, CT scans, and PET scans (when available) were reviewed to evaluate patterns of disease involvement, as were bronchoscopy findings, bronchoalveolar lavage (BAL) cell counts, and pulmonary function tests (PFTs).

In patients considered suitable for inclusion in this study, details of the histological type of cancer, staging at diagnosis, and treatment of their malignancy were reviewed.

Results

Epidemiology

We identified 29 patients with previous malignancy and a subsequent histological documentation of sarcoid-like granulomas. There were 19 female and 10 male patients, aged 27–81 years (at the time of the diagnosis of

sarcoidosis) with a mean age of 53 years. The frequency of different malignancies is listed in Table 1. Hematological malignancies and breast cancer were the most common tumors identified (28 and 24%, respectively), followed by gastrointestinal tumors.

The median time interval between the diagnoses of cancer and a diagnosis of sarcoidosis was 49 months (range 7–248 months), with 57% of patients being diagnosed with sarcoidosis within 5 years following diagnosis of malignancy (Table 2).

Clinical Presentation and Diagnosis of Sarcoidosis

Clinical Features

Most patients (76%) were asymptomatic. The remainder presented with either cough (4 patients), dyspnea (2 patients), or weakness (1 patient). Extrapulmonary manifestations were present in 7 patients, half of whom had extrathoracic lymphadenopathy. PFTs were available for 14 patients and were normal in 9 (69%). In those with impaired function, the abnormalities (either obstructive or a reduced DLCO) were mild.

Radiological Presentation

Chest CT was available in 27 patients. Twenty-three patients (85%) had evidence of mediastinal or hilar lymphadenopathy (Table 3). Radiological evidence of pulmonary parenchymal involvement was present in 11 patients (41%). In all but 2 of these cases, mediastinal lymphadenopathy was also present.

PET-CT Findings

In 17 patients, PET-CT studies were available from the time of diagnosis of sarcoidosis, all of which showed positive intrathoracic findings. Ten of these patients also had previous PET-CT scans performed at the time when the malignancy was diagnosed, and in all these cases, the positive findings were not apparent on these previous scans.

Diagnosis

Sarcoidosis was diagnosed by bronchoscopy in 23 of the 29 patients (79%). Two additional patients required mediastinoscopy following a nondiagnostic bronchoscopy, and in the remaining 4 patients the diagnosis was made by biopsies of extrathoracic sites (cervical lymph node biopsies in 3, and a liver biopsy in 1). Using bronchoscopy, either endobronchial or transbronchial biopsies were sufficient to make the diagnosis in 61% (14) patients. The remaining 9 patients required transbronchial needle aspiration to demonstrate noncaseating granulomas in lymph nodes. In 19 patients, BAL analysis was per-

Table 1. Frequency of different malignancies in sarcoidosis patients

Tumor	n (%)
Hematologic malignancy	8 (28)
HL	3 (10)
NHL	4 (14)
AML	1 (3)
Breast	7 (24)
GI	3 (10)
Thyroid	2 (7)
Uterine	2 (7)
RCC	2 (7)
Cervix	2 (7)
Other ^a	3 (10)

HL, Hodgkin lymphoma; NHL, non-Hodgkin lymphoma; AML, acute myeloid pneumonia; GI, gastrointestinal; RCC, renal cell carcinoma. ^a Ewing sarcoma, seminoma, melanoma.

Table 2. Time interval between diagnosis of cancer and diagnosis of sarcoidosis

Years	n (%)
<1	4 (14)
2–1	6 (21)
3–2	3 (11)
3–5	3 (11)
>5	12 (43)

Table 3. Radiological features

Finding	n (%)
Mediastinal lymphadenopathy	22 (81)
Subcarinal	13 (48)
Right paratracheal	11 (41)
Aortopulmonary	8 (30)
Hilar lymphadenopathy	18 (67)
Symmetrical	15 (55)
Asymmetrical	3 (11)
Parenchymal findings	11 (41)
Both parenchymal findings and lymphadenopathy	9 (33)

formed. In 58% (11/19 patients), BAL showed the presence of alveolitis, defined as more than 10% lymphocytes in the BAL fluid.

Treatment and Staging

Of 29 patients with sarcoidosis, 21 (72%) had a solid (nonhematological) tumor in their past medical history.

Table 4. Common chemotherapy agents used prior to diagnosis of sarcoidosis

Agent	n (%)
Adriamycin	12 (50)
Cyclophosphamide	9 (38)
Vincristine	8 (33)
Bleomycin	5 (21)
Etoposide	5 (21)
Rituximab	4 (17)
5FU	3 (13)
No chemotherapy	7 (29)

We acquired staging data for 16 of those 21 patients. Five patients (31%) had limited disease without evidence of metastatic or lymph node involvement, while an additional 7 patients (44%), had local lymph node involvement (stage 2 disease). Four patients (25%) showed evidence of distant involvement (stages 3–4).

Treatment

Cancer treatment details were available for 24 of our patients, 17 of which received some kind of antineoplastic medication. In these 17 patients, the most commonly used drug was Adriamycin (50%) followed by cyclophosphamide (38%) and vincristine (33%). The most common agents used are listed in Table 4. Three patients had undergone autologous bone marrow transplantation, and 9 patients were treated with radiation therapy. Two patients received treatment with radioactive iodine I-131 for thyroid cancer.

Follow-Up

The median time of follow-up was 10 years. Of note, only 2 patients (7%) had recurrence of their malignancy after the diagnosis of sarcoidosis was made. One with gastric cancer had local recurrence with ascites and subsequently died, the other with breast cancer had local recurrence and required mastectomy.

Lymphoma and Breast Cancer

In order to further evaluate a possible causative association between prior diagnosis of lymphoma or breast cancer and subsequent diagnosis of sarcoidosis, we acquired annual incidence data of these malignancies in our institution. There were 133 new cases of lymphoma (106 non-Hodgkin lymphoma [NHL], 27 cases of Hodgkin lymphoma [HL]) and 600 new cases per year of breast cancer. Using these data, we estimated the incidence of

postmalignancy sarcoidosis associated with these malignancies. Sarcoidosis was estimated to be 1:285 for lymphomas (1:407 for NHL, 1:135 cases of HL), 1:1,304 cases of breast cancer. This translated to 175 times and 38 times higher, respectively, than the estimated incidence of 1:50,000 for sarcoidosis in the general population in Israel, suggesting a true association. In a subgroup analysis of these 14 patients (7 with prior lymphoma and 7 with prior breast cancer), the median time interval between the diagnoses of malignancy and sarcoidosis was 40 months (54 and 27 in the breast cancer and lymphoma groups, respectively). In 6 of these 14 patients (4 in the lymphoma group and 2 in the breast cancer group) with positive findings on PET-CT when sarcoidosis was diagnosed, a PET scan that showed no evidence of sarcoidosis was available from the time of initial diagnosis of cancer.

Discussion

We describe the clinical and radiological features in 29 patients who developed sarcoidosis following malignancy. The most common tumors were breast cancer and lymphoma. The radiological features observed in these patients are similar to those in “idiopathic” sarcoidosis. The sarcoidosis tends to be mild, and is probably diagnosed early, mostly due to the use of routine CT or PET-CT as part of the patients’ oncological follow-up. Most patients had relatively early stage cancer with a favorable long-term outcome.

Our findings strongly suggest that sarcoidosis following malignancy is no different from the “idiopathic” form of the disease. Patterns of lung parenchymal disease and particularly of lymph node involvement in our cohort, with predominantly subcarinal, paratracheal, and bilateral hilar lymphadenopathy, were similar to the radiological features and pattern of lymphadenopathy described previously in a cohort of sarcoidosis patients referred for biopsy [29], as well as to a previous report of CT findings in Israeli sarcoidosis patients [30]. We also found that many of our patients had evidence of BAL lymphocytosis, or of granulomas in the bronchial mucosa or lung parenchyma, as seen on endobronchial and transbronchial biopsies. This further strengthens the claim that sarcoidosis after malignancy is not a granulomatous reaction limited to regional lymph nodes but is similar to “idiopathic” disease. Nevertheless, the routine use of CT and PET-CT in the follow-up of oncology patients may result in an earlier diagnosis of subclinical disease. Our patients were indeed usually asymptomatic,

with normal PFTs, again suggesting early diagnosis of relatively mild disease.

The second issue we attempt to address is whether malignancy or treatment thereof may cause or predispose to the development of sarcoidosis. Several previous studies have tried to evaluate whether sarcoidosis is more frequent in patients with previous malignancy. In a recent retrospective study of 565 consecutive mediastinoscopies, 41 cases of sarcoidosis were identified, of which 21 (53%) had a previous diagnosis of cancer. The most prevalent malignancy was breast cancer (48%) [31]. In another retrospective study, the authors collected data from 2,048 consecutive PET-CT studies performed in cancer patients undergoing staging or restaging of solid-organ malignancy. A “sarcoid-like” pattern of lymph node involvement (i.e., mediastinal and hilar lymphadenopathy, mostly symmetrical with or without parenchymal disease), was initially suspected in 23 of the 2,048 PET-CT examinations (1.1%), with the diagnosis confirmed histologically or by clinicoradiological follow-up in 13 of the 23 cases (57%). Symmetric hilar uptake was demonstrated in 11 of the 13 (85%), and all 13 had additional mediastinal nodal uptake. Pulmonary uptake was seen in 7 of the 13 cases (54%). Extrathoracic involvement was present in 8 of the 13 (61.5%), including nodal, splenic, and hepatic lesions [14].

In our series, the most prevalent malignancies that preceded the diagnosis of sarcoidosis were breast cancer and lymphoma. Breast cancer is the most prevalent malignancy in the population, and it may reflect a coexistence of 2 prevalent diseases; however, other prevalent neoplasms, such as lung, prostate and colon, were infrequent in our cohort, suggesting a true association. Although lung cancer may be underrepresented due to its poor prognosis and short life expectancy, the same cannot be said for prostate and colon cancer. Breast cancer and lymphoma are more likely to involve or drain to intrathoracic lymph nodes, and we can speculate that somehow they may therefore be more likely to trigger sarcoidosis than would extrathoracic tumors. These malignancies were also previously described in association with future development of sarcoidosis [21, 22].

In order to further evaluate whether sarcoidosis may be caused by malignancy rather than coincidental, we evaluated the incidence of sarcoidosis in the 2 larger patient subgroups (lymphoma and breast cancer), and found the incidence to be far higher than in the general population. There is obviously a bias in that these patients undergo routine radiological evaluation but this is unlikely to explain all of the discrepancy in disease frequen-

cy. For several of our patients, there is documented evidence with sequential CT-PET scans, that sarcoidosis developed after malignancy, again suggesting subsequent and causative association with malignancy.

There are several reports trying to connect anticancer therapy with the development of sarcoidosis [24, 25, 32, 33], with the most common postulated causative agent being the biological modifier alpha interferon [26, 27, 34]. We, however, did not identify a clear correlation between a specific agent and the subsequent appearance of sarcoidosis (with alpha interferon only seldom used), and a larger cohort would be required to address this issue. In patients with breast cancer, 62% were treated with chest radiotherapy as a neoadjuvant treatment. However, such a treatment is common among patients with breast cancer, especially with known lymph node involvement, and so causality or a true association cannot be confirmed.

Our data suggest that the presence of sarcoidosis may be associated with a good prognosis. For nonhematological tumors, most of our patients had relatively limited disease, and only 25% had stage 3–4 disease. Only 7% of our patients had recurrence of their malignancy after a diagnosis of sarcoidosis was made. There is a bias in that only patients who do not die of their malignancy can develop sarcoidosis, but in almost half of our patients (44%), sarcoidosis developed within 3 years of the diagnosis of malignancy, and if diagnosed it seems to predict a good outcome. Steinfort et al. [35] have previously suggested that in patients undergoing definitive surgical resection of early-stage non-small cell lung cancer, the presence of “sarcoid-like” reactions in regional lymph nodes may be associated with a reduced rate of disease recurrence, compared with those without this pathological finding. Other reports have noted improved prognosis in patients with “sarcoid-like” reactions in HL [12, 13]. Hunsaker et al. [16] also reported fewer relapses and longer survival rates in HL patients with sarcoidosis, raising the possibility of the potential protective effects of sarcoidosis on malignancy relapse.

The interpretation of the results is limited by the small number of patients studied and the partly retrospective design of the study. Therefore, the conclusions drawn from the analysis must be interpreted with caution and have to be confirmed by larger prospective cohorts.

In conclusion, sarcoidosis following malignancy seems clinically and radiologically indistinguishable from idiopathic sarcoidosis, although it is frequently asymptomatic. The high frequency of sarcoidosis after specific cancers (lymphoma, breast cancer) but not others, suggests a causative association between malignancy or the treatment thereof, and development of sarcoidosis.

Financial Disclosure and Conflicts of Interest

All authors declare no conflict of interest regarding this article.

Author Contributions

Conception and design: N.A., R.K., N.B. Patient selection and data collection: N.A., R.K., E.S., Z.G.F., L.L., A.A., U.L. Data analysis: N.A., R.K., N.B. Drafting of manuscript: N.A., R.K., Z.G.F., N.B.

References

- 1 Costabel U, Hunninghake GW: ATS/ERS/WASOG statement on sarcoidosis. *Eur Respir J* 1999;14:735–737.
- 2 Iannuzzi MC, Rybicki BA, Teirstein AS: Sarcoidosis. *N Engl J Med* 2007;357:2153–2165.
- 3 Morgenthau AS, Iannuzzi MC: Recent advances in sarcoidosis. *Chest* 2011;139:174–182.
- 4 Gorton G, Linell F: Malignant tumours and sarcoid reactions in regional lymph nodes. *Acta Radiol* 1957;47:381–392.
- 5 Brincker H: Sarcoid reactions and sarcoidosis in Hodgkin's disease and other malignant lymphomata. *Br J Cancer* 1972;26:120–123.
- 6 Caras WE, Dillard T, Baker T, et al: Coexistence of sarcoidosis and malignancy, *South Med J* 2003;96:918–922.
- 7 Reich JM, Mullooly JP, Johnson RE: Linkage analysis of malignancy-associated sarcoidosis. *Chest* 1995;107:605–613.
- 8 Brincker H: The sarcoidosis-lymphoma syndrome. *Br J Cancer* 1986;54:467–473.
- 9 Papanikolaou IC, Sharma OP: The relationship between sarcoidosis and lymphoma. *Eur Respir J* 2010;36:1207–1209.
- 10 Boffetta P, Rabkin CS, Gridley G: A cohort study of cancer among sarcoidosis patients. *Int J Cancer* 2009;124:2697–2700.
- 11 Bonifazi M, Bravi F, Gasparini S, et al: Sarcoidosis and cancer risk. Systematic review and meta-analysis of observational studies. *Chest* 2015;147:778–791.
- 12 Brincker H: Sarcoid reactions in malignant tumours. *Cancer Treat Rev* 1986;13:147–156.
- 13 Sacks EL, Donaldson SS, Gordon J, et al: Epithelioid granulomas associated with Hodgkin's disease: clinical correlations in 55 previously untreated patients. *Cancer* 1978;41:562–567.
- 14 Chowdhury FU, Sheerin F, Bradley K, et al: Sarcoid-like reaction to malignancy on whole-body integrated F18-FDG PET/CT: prevalence and disease pattern. *Clin Radiol* 2009;64:675–681.
- 15 Craun JB, Banks KP, Clemenshaw MN, et al: Sarcoidlike reaction of neoplasia causing hypermetabolic thoracic adenopathy in setting of extrathoracic malignancy: report of two cases and a review of the differential diagnostic considerations. *J Nucl Med Technol* 2012;40:231–235.
- 16 Hunsaker AR, Munden RF, Pugatch RD, et al: Sarcoid-like reaction in patients with malignancy. *Radiology* 1996;200:255–261.
- 17 Lau RK, Takasugi JE, Godwin JD, et al: Sarcoid-like reaction – computed tomography features in 12 patients. *J Comput Assist Tomogr* 2015;39:143–148.
- 18 Tjan-Heijnen VC, Vlasveld LT, Pernet FP, et al: Coincidence of seminoma and sarcoidosis: a myth or fact? *Ann Oncol* 1998;9:321–325.
- 19 Paparel P, Devonec M, Perrin P, et al: Association between sarcoidosis and testicular carcinoma: a diagnostic pitfall. *Sarcoidosis Vasc Diffuse Lung Dis* 2007;24:95–101.
- 20 Suen JS, Forse MS, et al: The malignancy-sarcoidosis syndrome. *Chest* 1990;98:1300–1302.
- 21 London J, Grados A, Fermé C, et al: Sarcoidosis occurring after lymphoma. Report of 14 patients and review of the literature. *Medicine (Baltimore)* 2014;93:e121.
- 22 Shigemitsu H: Is Sarcoidosis frequent in patients with cancer? *Curr Opin Pulm Med* 2008;14:478–480.
- 23 Reich JM: Neoplasia in the etiology of sarcoidosis. *Eur J Intern Med* 2006;17:81–87.
- 24 Murphy KP, Kennedy MP, Barry JE, et al: New-onset mediastinal and central nervous system sarcoidosis in a patient with metastatic melanoma undergoing CTLA4 monoclonal antibody treatment. *Oncol Res Treat* 2014;37:351–353.
- 25 Sybert A, Butler TP: Sarcoidosis following adjuvant high-dose methotrexate therapy for osteosarcoma. *Arch Intern Med* 1978;138:488–489.
- 26 Massaguer S, Sanchez M, Castel T: Mediastinal sarcoidosis induced by high-dose alpha-2-interferon therapy in a patient with malignant melanoma. *Eur Radiol* 2004;14:1716–1717.
- 27 Ravenel JG, McAdams HP, Plankeel JF, et al: Sarcoidosis induced by interferon therapy. Case report. *Am J Roentgenol* 2001;177:199–201.
- 28 Lequoy M, Coriat R, Rouquette A, et al: Sarcoidosis lung nodules in colorectal cancer follow-up: sarcoidosis or not? *Am J Med* 2013;126:642–645.
- 29 Trisolini R, Anevlaivis S, Tinelli C, et al: CT pattern of lymphadenopathy in untreated patients undergoing bronchoscopy for suspected sarcoidosis. *Respir Med* 2013;107:897–903.
- 30 Avital M, Hadas-Halpern I, Deeb M, et al: Radiological findings in sarcoidosis. *IMAJ* 2008;10:572–574.
- 31 Hunt BM, Vallières E, Buduhan G, et al: Sarcoidosis as a benign cause of lymphadenopathy in cancer patients. *Am J Surg* 2009;197:629–632.
- 32 Merchant TE, Filippa DA, Yahalom J: Sarcoidosis following chemotherapy for Hodgkin's disease. *Leuk Lymphoma* 1994;13:339–347.
- 33 Sawhney M, Sharma YK, Gera V, et al: Ichthyosiform sarcoidosis following chemotherapy of Hodgkin's disease. *Indian J Dermatol Venereol Leprol* 2003;69:220–222.
- 34 Hurst EA, Mauro T: Sarcoidosis associated with PEGylated interferon alfa and ribavirin treatment for chronic hepatitis C: a case report and review of the literature. *Arch Dermatol* 2005;141:865–868.
- 35 Steinfert DP, Tsui A, Grieve J, et al: Sarcoid reactions in regional lymph nodes of patients with early stage non-small cell lung cancer predict improved disease-free survival: a pilot case-control study. *Hum Pathol* 2012;43:333–338.