Case Report

Pulmonary sarcoid-like reaction in metastatic synovial sarcoma

Sameh A. Hashem a,*, Iyad Sultan b, Maysa Al-Hussaini c, Feras Hawari c, Sameer Yaserc

a Department of Radiation Oncology, King Hussein Cancer Center, Queen Rania Al-Abdullah Street, P.O. Box 1269 Al-Jubeiha, Amman 11941, Jordan
b Department of Medical Oncology, King Hussein Cancer Center, Queen Rania Al-Abdullah Street, P.O. Box 1269 Al-Jubeiha, Amman 11941, Jordan
c Department of Pathology, King Hussein Cancer Center, Queen Rania Al-Abdullah Street, P.O. Box 1269 Al-Jubeiha, Amman 11941, Jordan

Article info

Article history:
Received 26 December 2009
Accepted 18 January 2010

Abstract

A 22-year-old female patient, with synovial sarcoma of the left thigh, was treated with marginal resection and adjuvant chemoradiotherapy. Two years later, she developed sub-pleural metastatic nodules that were resected. Follow-up chest CT-scans revealed small yet new left lower lobe sub-pleural nodules, which were observed closely. These lesions progressed over time and, 20 months later, the patient underwent pulmonary metastasectomy. Histopathology examination of the lung tissue showed changes consistent with a sarcoid-like reaction. There were no systemic manifestations of sarcoidosis. To date, there have been no reported cases of sarcoid-like reaction associated with synovial sarcoma. Reporting this case, therefore, may help to improve our overall understanding of the relationship between malignancy and sarcoid-like reactions in the lungs.

1. Introduction

Sarcoidosis is a multisystem granulomatous disorder of unknown etiology that affects individuals worldwide and is characterized pathologically by the presence of noncaseating granulomas in involved organs. It typically affects young adults, and initially presents with one or more of the following abnormalities: bilateral hilar adenopathy, pulmonary reticular opacities, and skin, joint, and/or eye lesions. Sarcoidosis can mimic cancer and conversely local sarcoid granulomatous reactions can be observed in cancer disorders with or without systemic manifestations of sarcoidosis.1–5

Multiple descriptive terms have been used in the literature since this entity was first described by Nickerson in 1937. Such descriptive terms are: sarcoid-like reaction, sarcoid-like lesion, epitheloid granulomas, tuberculoid granulomas, and pseudotuberculous reaction. The most commonly used and preferred terminology is "sarcoid-like reaction".

Numerous case reports of patients with concurrent local sarcoid granulomatous reaction and cancer have been published and it typically occurs with or after other malignant disorders. Most of the patients had sarcoid-like reaction associated with either lung cancer or lymphomas,5–8 and in most cases the occurrence of sarcoid-like reactions precedes the diagnosis of lymphoma, but in general, the association between sarcoid-like reaction and malignancy is unclear.

The true incidence of such a disorder in malignancy is difficult to determine, because the majority of published literature are case reports, which usually can help in generating hypotheses rather than establishing evidence-based facts. Historically, the frequencies of sarcoid-like reactions adjacent to solid tumors and/or in regional lymph nodes and associated with lymphomas are 4.4% and 13.8%, respectively.9

According to literature review, association of sarcoid-like reaction and neoplasm has been described in gastric cancer,9 breast cancer,10 lung cancer,11 testicular cancer,12 renal cell cancer,13 and leiomyosarcoma.14 There were no reports describing the association with synovial sarcoma, but it was found that our present case is one of the few cases reported in literature that showed an association between sarcoid-like reaction and metastatic disease to the lungs. This makes it unusual, as most sarcoid-like reactions are usually found either adjacent to the primary solid tumors or in draining lymph nodes. As such, this case can be considered as the first case in which a pulmonary sarcoid-like reaction is associated with metastatic synovial sarcoma.

Reporting this case may, therefore, help improve our overall perception of the relationship between a malignant neoplasm and sarcoid-like reaction in the lungs.

2. Case report

Our patient is a 22-year-old woman with synovial sarcoma of the left thigh. She was treated with wide local excision of her primary tumor. However, in spite of the wide local approach, the margins were positive. Therefore, she was treated with adjuvant...
Radiation therapy, 66 Gy, followed by 4 cycles of Ifosfamide and Adriamycin.

Twenty two months after the patient completed her therapy, she developed sub-pleural nodules in the left lower lobe of the lung. A tru-cut biopsy from those nodules revealed the presence of metastatic synovial sarcoma (Fig. 1A), with proliferation of malignant spindle cells, which stained positive for cytokeratin (Fig. 1B). Metastasectomy was performed, but the resection margins were positive. As such, the patient was kept under close follow-up with regular clinical visits and imaging studies.

Follow-up CT-scans showed stable post-surgical changes at the site of metastasectomy, and new, less than 1 cm non-significant nodules with low suspicion for malignancy were noted in the right middle and left lower lobes (Fig. 2).

During observation there was no reported history of systemic symptoms indicative of systemic sarcoidosis like fatigue, malaise, fever, and weight loss. On physical examination there was neither lymphadenopathy nor hepatosplenomegaly elicited, and both dermatologic and ophthalmologic examinations were unremarkable.

Twenty months into follow-up, a chest CT-scan revealed an increase in the number and size of the pulmonary nodules (Fig. 3). Therefore, another metastasectomy was performed, due to the assumption that the progressive lung nodules were a manifestation of an active metastatic disease, especially since there was a previously established diagnosis of lung metastases.

The histopathologic examination of the resected specimen showed several scattered small epithelioid granulomas, some containing multinucleated giant cells, within the lung interstitium (Fig. 4A and B). Special stains for acid-fast bacilli and fungi were negative. There was no evidence of eosinophils, necrosis or malignancy. The features were consistent with a sarcoid-like reaction. Five months after the last surgery, a repeat CT-scan of the chest revealed spontaneous resolution of all previously noted lung nodules.

3. Discussion

The patient was diagnosed to have malignancy associated with sarcoid-like reaction. It is clear that she had undergone an unnecessary, highly morbid, operative procedure. This intervention could have been avoided if a simple CT-guided percutaneous biopsy or even a transbronchial biopsy was performed prior to the metastasectomy. However, the likelihood of developing recurrent lung metastases was high and carried a definite concern, especially since there was a positive resection margin following the first metastasectomy, and because of the high tendency of synovial sarcoma metastasize to the lung.

The absence of clinical findings indicative of systemic sarcoidosis played a misleading role, but the absence of the clinical criteria of sarcoidosis does not necessarily exclude an existing sarcoid-like granulomatous reaction secondary to malignancy. In general, sarcoid-like reactions can occur in a number of several conditions other than malignancies, for example, tuberculosis, and fungal infections. The histology of the lung specimen was negative for mycobacterial and fungal stains.

The histologic findings of a sarcoid-like reaction could be attributed to a local immune response, reaction to tumor products or metabolites, a degenerative substance from an adjacent metastatic malignancy, or a reaction to host resistance to the tumor.

Previous reports indicate that sarcoid-like reactions may develop after curative resection of cancer, and their presence does...
not necessarily denote neoplastic recurrence. In 2004, Parra et al. described two patients with resected lung and gastric cancers who later developed pulmonary interstitial infiltrates. An open lung biopsy revealed that the pulmonary infiltrates were actually benign granulomatous reactions interpreted as sarcoidosis. Thus, they encourage performing lung biopsy in relapse-free patients with pulmonary infiltrates to confirm a sarcoid-like reaction, thereby avoiding unnecessary chemotherapy for presumed tumor recurrence.

What is also worth considering is the relationship of sarcoid-like reactions and immunodeficiency; a recent report from the ophthalmology service, Hospital of Avicenne in France, described two cases with malignancy, in which a sarcoid-like reaction in the lung appeared a few months to few years after diagnosis with immunodeficiency. In our case no immunologic tests were done to suggest an altered immunologic status of the patient.

In oncology patients, there are few studied therapeutic agents which were found to induce a sarcoid-like reaction in the lungs, e.g. Methotrexate and BCG therapy. Our patient did not have a history of exposure to any of those therapeutic agents, but she did receive Adriamycin as part of her chemotherapeutic treatment for synovial sarcoma. Reviewing the literature for an association between Adriamycin and sarcoid-like reactions, we found six reports of sarcoid-like reactions following chemotherapy for Hodgkin’s disease in which Adriamycin was used as a part of the Hodgkin’s disease treatment protocol (ABVD regimen).

It was proposed that the immunosuppressive effect of chemotherapy, and the influence of a specific chemotherapy agent, such as Bleomycin, might contribute to the development of sarcoidosis, since Bleomycin is known to have relatively higher lymph node and lung tissue concentrations than other agents included in the ABVD regimen. This hypothesis may give us an idea as to why Bleomycin was selected as a causative agent, but it certainly cannot exclude the effect of other immunosuppressive agents, such as Adriamycin. Based on the fact that Adriamycin was used in our case and in all reported cases, we may suggest an association which needs to be evaluated further. However, since most reported cases were associated with lymphomas, one can attribute the occurrence of the sarcoid-like reaction to the presence of the lymphoma itself rather than the exposure to an immunosuppressive agent and the assumption that this sarcoid-like reaction is induced by chemotherapy remains hypothetical.

In conclusion, our patient has clinical findings that haven’t been reported before: an uncommon association of sarcoid-like reaction with metastatic synovial sarcoma. The development of sarcoid-like reaction might be attributed to a number of causative conditions and agents. Because of the potential for confusion, clinicians need to keep in mind that sarcoidosis can mimic cancer, particularly in patients with an established diagnosis of a malignant neoplasm. In the case of absent clinical evidence of generalized sarcoidosis, one should consider sarcoid-like reaction in the differential diagnosis, particularly in relapse-free patients with pulmonary infiltrates that appear in the first few months following curative resection. Therefore, lung biopsy is recommended to avoid unnecessary action for assumed tumor progression.

Conflict of interest
No conflicts of interest.

Financial support
The authors declare that all authors have no proprietary, financial, professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in, or the review of, the manuscript entitled, “Pulmonary sarcoid-like reaction in metastatic synovial sarcoma”.

References


