Systemic Sarcoidosis Associated with Double Cancers of the Esophagus and Stomach

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Abstract

To discriminate between sarcoidosis and sarcoïd reaction in the lymphadenopathy of malignancy is sometimes clinically important. We describe a case of sarcoidosis associated with double cancers of the esophagus and stomach. A patient who six months previously was found to have early gastric cancer, was then found to have esophageal cancer. The chest radiography demonstrated bilateral hilar lymphadenopathy. Pathological analysis of the lymph nodes and lungs showed non-caseating epithelioid cell granuloma, revealing the existence of sarcoidosis. The findings suggest that the possibility of systemic sarcoidosis should be considered in cases with established malignancy and newly disclosed radiographic findings.

Key words: sarcoid reaction, lymphadenopathy, granuloma

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Introduction

Systemic sarcoidosis is characterized by systemic inflammatory and non-caseating epithelioid cell granulomas of involved organs, frequently hilar lymph nodes and lung, of unknown origin. Sarcoïd reaction is also observed as epithelioid cell granulomas of lymph nodes from malignancy. Although systemic sarcoidosis and sarcoïd reaction may occasionally emerge with malignant tumors, there is no report concerning sarcoïdosis occurring with double cancers. Here, we describe a case that developed alimentary double cancers with non-caseating epithelioid cell granulomas of bilateral hilar lymphadenopathy, which required careful narrowing of the differential diagnosis.

Case Report

A 60-year-old Japanese man without any symptoms was found to have early gastric cancer by endoscopic biopsy during a regular medical checkup. The cancer was located on the posterior wall of the distal antrum and the clinical stage was T1N0M0 Stage IA (UICC TNM classification). We found no abnormality in the esophagus at that time. Endoscopic mucosal resection (EMR) was performed, and pathological analysis of the specimen revealed well-differentiated tubular adenocarcinoma in adenoma. Chest radiography showed no lymphadenopathy. His tuberculin skin test was positive (19×12 mm) as are those of most Japanese people because of the bacillus Calmette-Guérin (BCG) vaccine. Six months later, he was found to have esophageal cancer in a follow-up endoscopic study. The esophageal cancer was located on the right wall of the middle thoracic esophagus and the clinical stage was T1bN0M0 Stage I (UICC TNM classification). Local recurrence of gastric tumor was not seen. In addition, the chest radiography demonstrated bilateral hilar lymphadenopathy (Fig. 1A). EMR for esophageal cancer was performed again. As the pathological analysis of the EMR specimen revealed submucosal layer invasion, thoracoscopic esophagectomy with lymph node dissection was performed. While pathological analysis demonstrated squamous cell carcinoma with a tumor-free margin, sections of the lymph nodes showed well-formed epithelioid cell granuloma. Infiltration of inflammatory cells was not found and atypical cells were absent. These suggested sarcoïdosis or sarcoïd reaction to the esophageal cancer (Fig. 1B). At this time, his tuberculin skin test had turned to negative (9×7 mm). Ocular manifestations such as...
Figure 1. Chest radiograph showing bilateral hilar lymphadenopathy (A). Light microscopic pictures of a hilar lymph node (B) and lung (C) biopsy specimen. Non-caseating epithelioid cell granulomas can be seen in both specimens (small magnification ×20, large magnification ×400, Hematoxylin and Eosin staining).

Figure 2. Whole-body gallium-67 scintigram revealed increased uptake in the bilateral hilar and mediastinal regions. In addition, uptake was also seen in the left thigh and in both lower legs.

uveitis and conjunctival were not observed. Cardiac ultrasonography was within the normal range and no abnormal cardiac rhythm was found. Urinalysis results were normal and renal involvement of sarcoidosis was not found. His serum angiotensin-converting enzyme (ACE) level increased (29.9 U/l; normal range, 7 to 25 U/l). His serum soluble interleukin-2 receptor (sIL-2R) level, which is known to be increased in the serum of patients with sarcoidosis, was also increased from 472 U/ml to 807 U/ml (normal range, 145 to 519 U/ml) over the six months. A constant enhanced computed tomography scan of the chest revealed paratracheal and hilar lymphadenopathy, which had become enlarged after the resection of the esophageal cancer. A transbronchial lung biopsy specimen demonstrated non-caseating epithelioid cell granuloma (Fig. 1C). Whole-body gallium-67 scintigram showed increased uptake in the bilateral hilar and mediastinal regions. In addition, uptake was also seen in the left thigh and both lower legs (Fig. 2). In a further systemic investigation, slightly higher signal intensity on magnetic resonance (MR) T1-weighted images and high signal intensity on MR T2-weighted images were detected in the right anterior tibial and bilateral soleus muscles, suggesting muscle sarcoidosis (1) (Fig. 3).

Discussion

It is known that sarcoidosis or sarcoid reaction can occur in association with malignancy (2). In the present case, it was necessary to discriminate between sarcoidosis and sarcoid reaction because the hilar lymph nodes are sometimes involved with metastasis of esophagus cancer. Our patient showed the following findings: [1] increased serum ACE
Figure 3. Magnetic resonance (MR) T2-weighted image showing high signal intensity in the right soleus muscle (arrow).

References


...has long been considered. The differentiation of sarcoid reaction and systemic sarcoidosis has also been discussed (7, 8). Because these two could not be distinguished histopathologically when diagnostic radiology was still primitive (9), attempts were made based on the sum of the clinical data (10). Sarcoid reaction is caused by various malignant tumors (11). Brincker found that 4.4% of malignant tumor patients had sarcoid reactions (2). The incidence of mediastinal sarcoid reaction is relatively high in breast cancer and lymphoma. The lymphadenopathy is sometimes taken as proof of metastatic tumor before surgery (12), which interpretation can result in an inappropriate treatment of the malignancy. At the same time, we have to pay attention to the possibility of under-diagnosis because of cases with coexisting splenic metastasis of gastric cancer and sarcoid reaction in the regional lymph nodes (13) as well as those with coexisting hilar lymph node metastasis of lung cancer and sarcoid reaction in mediastinal lymph nodes (14).

As far as alimentary malignancy and sarcoid reaction are concerned, cases including rhabdomyosarcoma of the esophagus or early gastric cancer have been reported (15, 16). Maekawa and Nogami described a case of the sarcoid reaction from esophagus adenocarcinoma and progressive systemic sclerosis, although the time course was not clear (17). The association of sarcoidosis with some types of cancer, including lung cancer, lymphoma, and uterine cancer, has been noted (2). To our knowledge, however, this is the first case of systemic sarcoidosis, which emerged with alimentary double cancers of the esophagus and stomach. A causal linkage between double cancers and systemic sarcoidosis cannot be confirmed. Battesti et al stated that the relationship between systemic sarcoidosis and the development of a malignant tumor is purely a matter of chance (18). On the other hand, one linkage analysis provided evidence that sarcoidosis and malignancy were epidemiologically related in at least one-fourth of all cases (19).

The present findings suggest that the possibility of systemic sarcoidosis should be considered in cases with established alimentary double malignancy and regional lymphadenopathy based on newly disclosed radiographic findings. Not only biochemical data but also histopathological findings with transbronchial lung biopsy are required to avoid confusion between systemic sarcoidosis and sarcoid reaction of the regional lymph nodes.


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