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Postradiation-associated sclerosing mediastinitis diagnosed in fine needle aspiration specimen: A cytological–pathological correlation

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ABSTRACT

Sclerosing mediastinitis (SM) is an aggressive fibroproliferative process in the mediastinum that may lead to encasement of mediastinal structures within a dense fibrotic mass. This disease may cause significant clinical complications, morbidity, and even mortality. The etiology and pathogenesis of SM is unclear and in more than one third of cases remains idiopathic. Among the known causes of SM, granulomatous infection is the commonest. Association of SM with radiation therapy has been rarely reported. Herein, we are reporting a case of postradiation sclerosing mediastinitis diagnosed in fine needle aspiration (FNA) specimen. To our knowledge, this is the first reported case of postradiation sclerosing mediastinitis with unusual striking intracytoplasmic glycogen accumulation. Having high index of suspicion and awareness of the fact that this entity may be also associated with radiation therapy, will be helpful in avoiding diagnostic pitfalls in FNA specimens and guiding proper clinical management.

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1. Introduction

A 56-year-old male with history of esophageal carcinoma, status post esophagectomy with gastric pull-through and neoadjuvant chemoradiation therapy eight years prior, presented on follow-up examination with shortness of breath, cough and wheezing. A Computed Tomography (CT) scan performed at outside institution demonstrated a left-sided pleural effusion and a large mass infiltrating the posterior mediastinum. The mass was seen just below the carina and was extending into the inferior posterior medial hemithorax slightly displacing the gastric pull-through. Positron Emission Tomography (PET) scan showed a pleural effusion Standardized Uptake Value (SUV) 5.2, and posterior mediastinal hypermetabolic mass with SUV 9.0. These radiological findings deemed to be consistent with "recurrent tumor within the posterior mediastinum" and left pleural effusion "consistent with recurrent esophageal carcinoma".

2. Materials and methods

CT-guided fine needle aspiration (FNA) of the mediastinum was performed to rule out metastatic/recurrent carcinoma (Fig. 1). Both air-dried and alcohol-fixed smears were prepared from two passes, and the remaining material was rinsed into CytoRich Red fixative for cell block preparation. On-site evaluation of the air-dried Diff-Quik-stained (DQ) smears performed by the pathologist confirmed the adequacy of the samples. The alcohol-fixed smears were stained with Papanicolaou stain (PAP) in the laboratory. The material for cell block preparation was routinely processed, and the slides were stained with hematoxylin and eosin (H&E). Immunohistochemical (IHC) stains were performed on the cell block preparation slides in an automated immunostainer in the presence of appropriate positive and negative controls. Table 1 shows the information regarding the source and dilution of the antibodies used in the case.

3. Results

The aspirate smears and cell block preparations showed numerous fibrous tissue fragments, intimately associated with cells exhibiting abundant finely vacuolated cytoplasm, low nuclear to cytoplasmic ratio, and mild nuclear pleomorphism (Figs. 2–5). In the majority of these cells these vacuoles occupied the entire cytoplasm; however, some cells with similar nuclear morphology contained the vacuoles only at the endo-ectoplasmic border. The fibrous tissue

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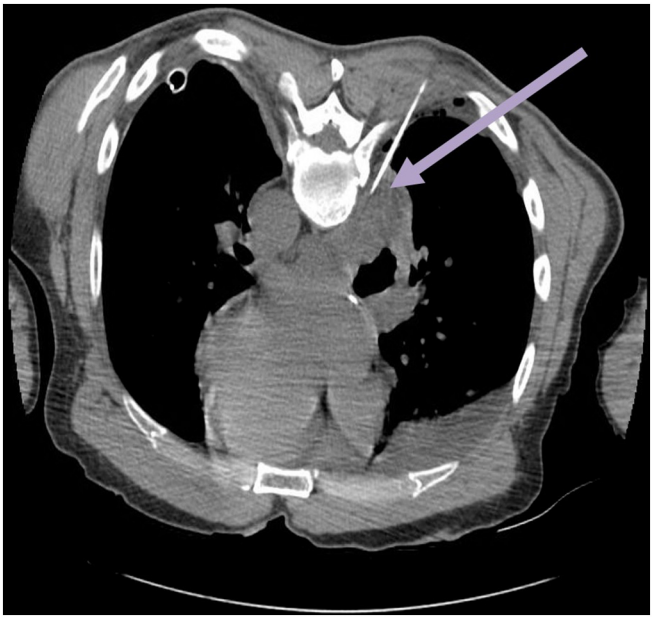

Fig. 1. CT scan of the chest showing the mediastinal mass with FNA needle within mass (arrow).

Table 1
Information regarding the source and dilution of the antibodies used in the case.

Antibody	Company	Dilutions
CK ae1/ae3	Leica	RTU
CK5/6	Dako	[1:75]
D2–40	Signet	[1:50]
Calretinin	Invitrogen	[1:80]
EMA	Dako	[1:100]
BerEP4	Dako	[1:50]
B72.3	Biogenex	[1:200]
S-100	Leica	RTU
p63	Biocare Medical	RTU
CD68	Dako	[1:4000]
IgG4	Cell Marque	RTU
IgG	Dako	[1:10,000]

fragments demonstrated mixed inflammatory infiltrate composed predominantly of lymphocytes, plasma cells, and macrophages. Immunostains showed the lesional cells to be positive for cytokeratins (CK) AE1/AE3, and CK5/6, D2–40, Calretinin, and Electron Membrane Antigen (EMA), consistent with their mesothelial origin (Fig. 6). IHC stains for BerEP4, B72.3, S-100, p63, and AR were negative in the lesional cells, while CD68 immunostain highlighted macrophages. As determined with IHC stains, the ratio of IgG4/IgG-positive plasma cells was not increased. Striking accumulation of intracytoplasmic vacuoles imparted histiocytoid and sebaceous-cell-like appearance to the mesothelial cells. However, periodic acid –Schiff (PAS) and PAS with diastase (DPAS) special stains confirmed accumulation of glycogen within these cells, most likely reflecting degenerative changes (Fig. 7). Special stains for microorganisms (GMS and AFB) were negative. Overall, the cytomorphologic findings of the aspirate were consistent with postradiation sclerosing mediastinitis with reactive mesothelial proliferation. There was no evidence of malignancy. Left pleural fluid cytology specimen also was negative for malignant cells showing reactive mesothelium and macrophages.

Concurrent biopsy demonstrated portions of pleural tissue with marked fibrosis, reactive mesothelium and extensive acute and chronic inflammation. Histiocytic aggregates were also noted, focally suggestive of a possible granulomatous process (Fig. 8). Special stains (AFB and GMS) were negative for microorganisms.

4. Discussion

Sclerosing (fibrosing) mediastinitis (SM) is a rare pathological condition that clinically and radiologically can mimic malignancy. SM is an aggressive fibroproliferative process in the mediastinum that leads to encasement of mediastinal structures within a dense fibrotic mass [1]. The clinical presentation of this disease depends on the structures of mediastinum that are compressed, entrapped or invaded. The patient may present with shortness of breath, hemoptysis, dysphagia, hoarseness, pleuritic chest pain. Presentations with aortic compression, superior vena cava obstruction, pulmonary artery obstruction with core pulmonale, stenosis of the pulmonary veins, pericarditis with pericardial effusion, tracheal or bronchial

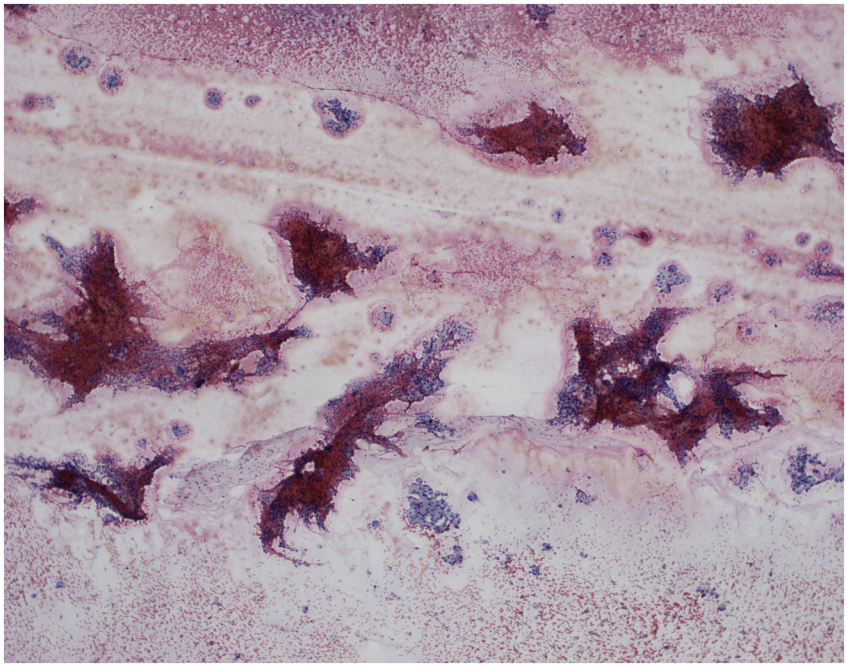

Fig. 2. FNA showing numerous fibrous tissue fragments, and groups of cells with abundant cytoplasm. PAP stain, ×40.

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