Case Report

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Sclerosing Mediastinitis Presenting as Complete Heart Block

Pathology Section

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ABSTRACT

Sclerosing Mediastinitis (SM) is a rare condition which is characterized by the presence of dense fibrosis which infiltrates and encroaches upon various structures in the mediastinal cavity. Depending on the extent and the predominant organ of involvement, the patient presents with symptomatology of dysphagia, superior vena cava compression syndrome or dyspnoea. However, the involvement of the heart is rarely seen. Aetiologies of SM are several, with infections being the most common. We discuss a case of SM involving the oesophagus, descending aorta, hilum of lungs and the heart secondary to mucormycosis in an immunocompetent male.

Keywords: Immunocompetent, Mediastinal cavity, Mucormycosis

CASE REPORT

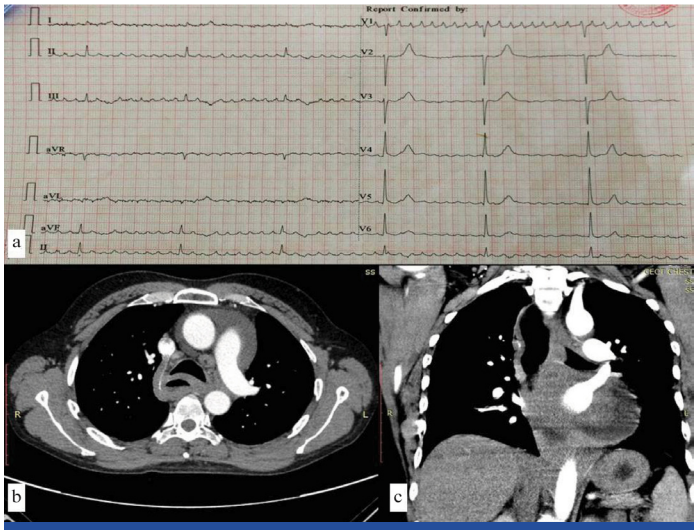
A 39-year-old male, cook by profession presented to the medical out-patient department with chief complaints of weakness and tremulousness. Initial examination revealed a pulse rate of 39 beats per minute. Cardiovascular examination revealed normal heart sounds with absence of murmur. An electrocardiogram done to investigate the cause of bradycardia showed presence of complete heart block [Table/Fig-1a]. The patient was taken up for placement of a pacemaker. However, an attempt at cardioversion was unsuccessful and the pacemaker was left in-situ. On further evaluation, the patient gave history of progressive dysphagia from last three months; for solids more than liquids. An endoscopic examination was done, which showed a normal oesophageal mucosa with few antral erosions.

A biopsy tissue was taken from the lower end of oesophagus which revealed normal histomorphology. A CECT was done which showed a mass encircling the lower part of oesophagus and descending aorta encroaching the right lung hilum and right diaphragmatic crura [Table/Fig-1b,c]. To assess the mediastinal lesion, a Positron Emission Tomography (PET) was done, which showed the lesion to be metabolically active. Also, noted were similar metabolically active lesions in the myocardium involving the both atria and ventricles.

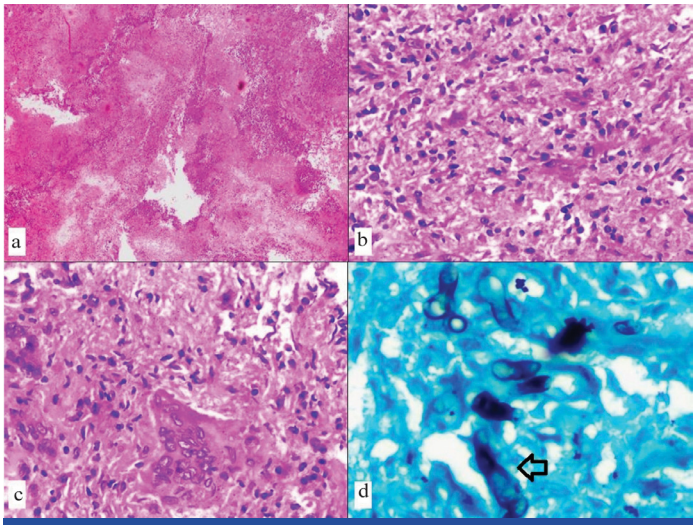
With a high suspicion of a malignancy, the patient underwent CT-guided FNAC of the para oesophageal lesion. However, the aspirate smears were grossly haemodiluted and remained inconclusive. In view of the extensive myocardial involvement seen on PET scan, an endomyocardial biopsy was attempted. The biopsy showed normal cardiac muscle fibers with a focus of perivascular accentuation of fibrosis and no neoplasia.

Due to absence of a conclusive diagnosis, the patient was taken up for a thoracotomy. Intraoperatively a whitish lesion was seen plastering the posterior wall of the heart infiltrating and impinging the hilum of right lung. Biopsies were sent for frozen section evaluation. The pericardium was thickened which on histology showed thick fibro collagenous stroma with scattered lymphoplasmacytic cell infiltrate. The hilar lymph node showed a preserved nodal architecture with prominent histiocytes. Multiple biopsies from the whitish lesion show necroinflammatory tissue composed of scattered epithelioid cell granulomas, multinucleated giant cells and fibrotic areas [Table/Fig-2a-c]. An opinion of inflammatory tissue with no evidence of neoplastic pathology was offered at frozen section.

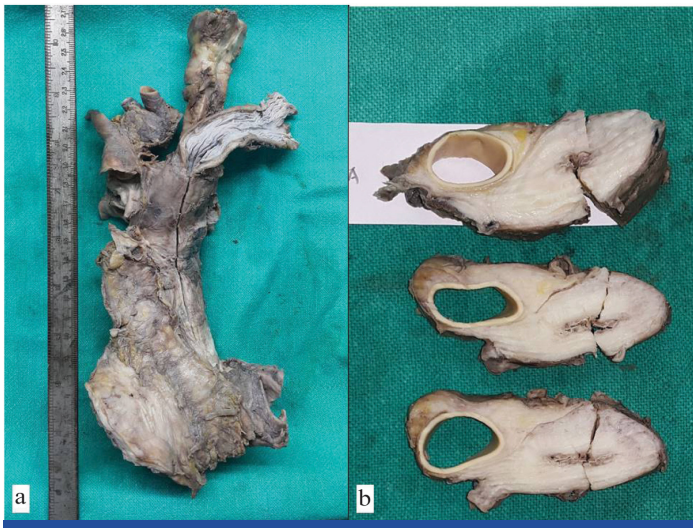
The specimens were further submitted for processing. The sections confirmed the presence of epithelioid granulomas and multinucleated giant cells. Large areas of hyalinised fibrosis were seen. Foci of dense lymphoplasmacytic cell infiltrate were seen with accompanying obliterative phlebitis. Grocott silver impregnation stain on the necrotic areas showed presence of broad, ribbon-like non-septate hyphae of mucormycosis [Table/Fig-2d]. An extensive immunohistochemistry panel of CK, EMA, CK7, CK20, Calretinin, LCA, CD3, CD20, CD19, CD79a, CD15, CD30 and Pax5 was done to rule out a possibility of a concurrent Hodgkin's lymphoma, sclerotic Non-Hodgkin's lymphoma and carcinomas. A diagnosis of SM secondary to mucormycosis was offered. Tests for HIV I & II were negative. A CD4 count done was within normal range. The patient



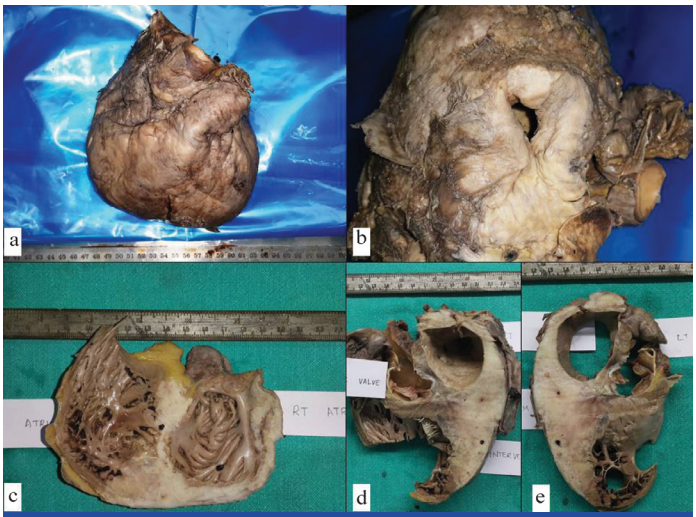
[Table/Fig-1]: (a) Electrocardiogram showing evidence of complete heart block; (b) Transverse CECT showing a mass encasing the descending aorta and oesophagus; (c) Sagittal CECT showing an enlarged heart.



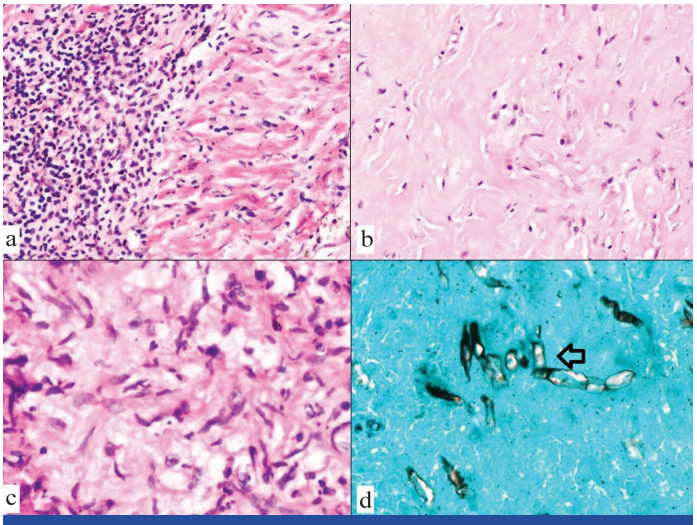
[Table/Fig-2]: (a) Biopsy specimen composed of abundant necroinflammatory tissue (H&E 10X); (b) Ill-defined epithelioid cell granulomas which were seen to be scattered in a few foci (H&E 40X); (c) One of the few multinucleated giant cell seen in the sections from the biopsy specimen (H&E 40X); (d) Broad aseptate fungal hyphal structures (arrow) in the necrotic areas (Grocott stain 40X).



[Table/Fig-3]: (a) Photograph shows the gross specimen of the descending aorta and oesophagus with a lesion which is seen to encase the two tubular structures; (b) Photograph shows the transverse sections of the oesophagus and descending aorta being surrounded by the whitish lesion.



[Table/Fig-4]: (a) Heart which appears enlarged; (b) Superior aspect of the heart shows a whitish infiltrative lesion surrounding the opening of the superior vena cava; (c) Cut surface of the heart with the right atrium, left atrium and interatrial septum which is seen to be infiltrated by a similar whitish lesion; (d) Plane of cut surface with the interventricular septum which appears to be widened and replaced by the whitish lesion. The infiltrative whitish lesion is also seen to surround the aortic annulus; (e) Plane of the heart with the right and left atrium and the interatrial septum. The whitish lesion is seen to infiltrate and replace the atrial and right ventricular wall.



[Table/Fig-5]: (a) Dense mononuclear inflammatory cells seen infiltrating and destroying the cardiac muscle fibers (H&E 10X); (b) Myocardium replaced by areas of dense hyalinised fibrosis (H&E 10X); (c) Epithelioid cell granulomas in the form of collections of cells having slipper shaped nuclei (Epithelioid cells) surrounded by lymphomononuclear inflammatory cells (H&E 40X); (d) Area of necrosis shows presence of aggregates of broad aseptate fungal hyphal forms (arrow) similar to those seen in the initial biopsy (Grocott stain 40X).

was put on steroids and liposomal amphotericin. However, the patient developed features of aortic regurgitation and subsequently succumbed to left heart failure.

A clinical autopsy was done and it revealed the infiltrating lesion to surround the lower third of oesophagus and descending aorta [Table/Fig-3a,b]. The lesion was seen to plaster the posterior surface of the heart and impinge on the right lung hilum. On grossing the enlarged heart, the lesion was seen to infiltrate and involve all the layers, replacing the most of the myocardium and the conducting system [Table/Fig-4a-c]. The lesion was seen to involve the annulus of aortic valve which resulted in the regurgitation [Table/Fig-4d,e]. Histopathology from the whitish infiltrative lesion showed the myocardium being destroyed and replaced by a fibro-inflammatory lesion with epithelioid cells granulomas and multinucleated giant cells [Table/Fig-5a-c]. Necrotic areas showed similar broad, ribbon like non-septate hyphae of mucormycosis, confirming the ante mortem findings of SM secondary to mucormycosis [Table/Fig-5d]. Examination of other organs showed presence of chronic venous congestion of liver and acute tubular necrosis of kidney. An immunohistochemistry done on sections with dense lymphoplasmacytic cell infiltrate showed an increased number of IgG4 positive cells correlating the ante mortem increased serum IgG4 levels of 900 mg/dl. Presence of obliterative phlebitis and foci of cellular fibrotic areas were also noted. A final cause of death was given as cardiac failure as a result of mucormycosis induced SM.

DISCUSSION

SM as an entity was initially reported in 1855 by Oulmount [1]. The pathogenesis stems from an idiosyncratic immunologic response [2]. The disease affects young males in the age group of 30-45 years [2]. The aetiological associations include infections, among which fungi are commonest followed by tuberculosis [3]. Histoplasmosis has been reported as the most frequently associated fungi in the Western literature [3]. However, Indian literature shows a higher incidence of association with mucor mycosis, aspergillosis and *Mycobacterium tuberculosis* among the infective causes [4]. Mucormycoses are a group of fungi from the class of zygomycetes. The common species of zygomycetes include *Rhizopus, Absidia,* and *Mucor*. These fungi are known to be vasotropic and disseminate from the initial site of cutaneous or sinonasal entry [4]. The non-infectious causes include autoimmune diseases, sarcoidosis, Hodgkin's lymphoma, radiation and drugs like methysergide [5]. Few cases are related to the emerging entity of IgG4 related diseases [6].

The symptomatology depends on the organ involved by the lesion; dysphagia, superior vena cava obstruction syndrome, chest tightness, cough and systemic features such as fever [7]. Involvement of the myocardium is extremely rare, with involvement of superior vena cava being more common [8]. A tissue diagnosis is mandatory as imaging including CT and PET scans are more indicative of a neoplastic aetiology [9,10]. However, there exists no pathognomonic feature or consensus histopathological criteria for diagnosis of SM and is considered to be a diagnosis of exclusion [7]. In view of the features of dense fibrosis, obliterative phlebitis and dense lymphoplasmacytic infiltrate with a predominant IgG4 cell population (40%) a possibility of a concomitant role of IgG4 related disease becomes evident [11]. The role played by the infection can be the inciting event in triggering the proliferation of the IgG4 secreting plasma cells. This can be explained by the absence of the angioinvasive nature of the fungi in our case and restriction of the fungi to few sites [6]. Amongst the various components of the mediastinum, involvement of the heart and in particular the myocardium is a rarity [8]. SM can present as a mass lesion when it needs to be differentiated from other mass forming sclerosing lesions such as Nodular Sclerosis Hodgkin's lymphoma, sclerotic mesothelioma and desmoplastic carcinomas [7]. Hence, the importance of an early biopsy is of paramount importance to arrive at the diagnosis and to identify the aetiology of the sclerosis; so as to institute appropriate therapy. Management of such cases should be directed to achieve an early tissue diagnosis as steroids and other immunomodulators can alter the course only in the early stages of fibrosis [5]. The cases with infective aetiologies need to appropriately cover by antifungals or antibiotics. Role of surgery is in debulking the mass lesions and addressing the obstructive aliments [10].

CONCLUSION

SM is a manifestation of an altered immunological reaction which results in diffuse dense fibrosis which infiltrates and encroaches upon the mediastinal structures. The index case has shown the possible role of mucormycosis in tandem with IgG4 plasma cells in causation of SM with an exceptionally rare involvement of the myocardium. This case highlights possibility of rare presentations of rare diseases in rare sites which need to be approached with high index of suspicion in an endeavor to achieve an early tissue diagnosis for effective management and favourable outcome.

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