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Mesothelioma - A rare cause of dysphagia

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CASE STUDY

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ABSTRACT

A 81-year-old elderly Caucasian male presented with progressive dysphagia and unintentional weight loss over four months. His history was significant for asbestos exposure; however there was no history of asbestos related lung disease. Barium swallow showed achalasia and a subsequent CT chest showed a posterior mediastinal mass 11.8×9.1×5.8cm, compressing the distal oesophagus. Laparoscopic biopsy of the mass showed an epitheloid mesothelioma. Mass was deemed unresectable and patient was started on chemotherapy with Cisplatin/Pemetrexed. Localised mesothelioma is extremely rare, and dysphagia can be uncommon presenting feature. 7.4 per cent of cases of Pseudoachalasia are attributed to mesothelioma.

Key Words
Posterior mediastinal mass, mesothelioma, dysphagia

Implications for Practice:

1. What is known about this subject?
Incidence of mesothelioma is around 2,500 people every year in the United States. Dysphagia can be a presenting feature in 1.4 per cent of the cases.

2. What new information is offered in this case study?
Mesothelioma can very rarely also present as localized form. Posterior mediastinal mesothelioma is a very uncommon presentation for malignant mesothelioma.

3. What are the implications for research, policy, or practice?
Unexplained dysphagia in a patient with remote history of asbestos exposure should raise the suspicion for isolated posterior mesothelioma with mechanical compression. There is a long latency period between asbestos exposure and asbestos related mesothelioma.

Background

Pesudoachalsia is a condition where patients present with clinical features of achalasia in which an occult tumour is the cause of dysphagia. Advanced age >50 years, weight loss, and short duration of symptoms <1 year suggests secondary over primary achalasia[1.] Posterior mediastinal mesothelioma is a rare cause of pseudoachalasia.

Case details

An 81-year-old Caucasian male presented with complaints of dysphagia for four months. Dysphagia started with solids and progressed to liquids. He also noted 40 pounds weight loss in one month. Past medical history was significant for hypertension, hyperlipidemia, and hypothyroidism. His occupational history was significant for exposure to organic metal fumes, since he was a welder for over 30 years. He also worked on the rail road 35 years ago. Family history was positive for his mother who died of Hodgkin's lymphoma. He had a 40 pack year history of smoking. Labs were normal except for anaemia; Haemoglobin was 11.2g/dL. Physical exam was normal. CXR showed left sided pleural effusion. He initially underwent a barium swallow to evaluate his dysphagia that showed achalasia without stricture. This is was followed with a PET CT Chest that showed a posterior mediastinal mass 11.8×9.1×5.8cm which was PET avid, compressing the distal oesophagus & extending into gastrohepatic ligament and down to celiac axis (Figures 1 and 2). There was no evidence of distant metastasis. He underwent Endoscopic ultrasound for the diagnosis initially. No evidence of tumour was noted in the

stomach. Biopsies results were indeterminate. Oesophageal stent was placed in the oesophagus to relieve the compression. Since the stent failed to relieve dysphagia, patient underwent another EGD few days later, for G tube placement combined with diagnostic abdominal laparoscopy. There was no evidence of metastatic disease or peritoneal studding. Frozen section of the mass was positive for malignancy. Final pathology came back as epithelioid malignant mesothelioma, with positive stains for calretinin, AE1/AE3, CAM 5.2, and CK5/6 (Figures 3–7). Given the rarity of this tumour in this location, second expert pathological opinion was obtained which concurred with diagnosis of epithelioid mesothelioma. The case was discussed in multidisciplinary thoracic oncology conference. Patient deemed not be a surgical candidate and started on Pemetrexed/Cisplatin.

Discussion

The incidence of mesothelioma is around 2,000–3,000 people in the United States every year.[2] Incidence of localized form as per one study conducted in Mayo clinic was 2.8 per 100,000 cases.[3]

Epidemiology

In a study on 23 cases of localized mesothelioma the incidence was higher in men (70 per cent) as compared to 30 per cent in women.[4] Women seem to have a favourable long term prognosis compared to men.[5] Average age of diagnosis was 62 years, and 91 per cent of the localized mesotheliomas were found to be pleural and only 9 per cent peritoneal.[4]

Asbestos has been implicated in the pathogenesis of mesothelioma. There is latency period of about 20–40 years after exposure.[6] However now we know of other factors known to affect pathogenesis including radiation, viral infections, other mineral fibres such as zeolites, chronic inflammation[7] and hereditary predisposition mutations in the BRCA 1 associated protein,[8] has been implicated. Indirect exposure from family members is associated with disease especially in women and children.[7] Mesothelioma can have three different histologies- Epithelioid, sarcomatoid sarcomatous, mixed biphasic types.[9] Survival rates are best for epitheloid type.[9] Presenting symptoms of mesothelioma include dyspnoea, chest pain, fever, malaise and symptoms due to local extension such as hemoptysis, dysphagia. Dysphagia as a presenting symptom was reported first in 1983.[10] It is reported to be a presenting symptom in 1.4 per cent of the patients with pleural mesothelioma.[11] 7.4 per cent of cases of pesudoachalsia are attributed to mesothelioma.[1] The pseudoachalasia seen is attributed to multiple factors including, the tumour infiltrating the myenteric plexus of the oesophagus, paraneoplastic effects and tumour extending into the smooth muscle at the GE junction, reducing compliance of the oesophagus.[1] Around ten such cases of mesothelioma causing dysphagia have been reported in the literature so far.[1]

Pathology

On gross examination localized mesotheliomas appear as solitary, circumscribed mass without any diffuse mass away from tumour. In contrast diffuse type, spread over the serosal surfaces and ultimately encase the tumour.[4] Ultrastrucurally and immunhistochemically they are both identical. They both stain positive for the mesothelial markers, and show same structural properties under electron microscope.[12]

Diagnosis-CXR, CT, PET scan can all aid in the diagnosis. Ultimately Video assisted thoracoscopic surgery is required for tissue biopsy and diagnosis. Staging is performed using the International mesothelioma interest group.[13] Recent studies have also shown benefit of testing levels of hyaluronic acid in the pleural effusion. Cytological testing of pleural fluid along-with HA levels (cut-off >30 mg/L) increase specificity and sensitivity of detection of Mesothelioma.[14]

Differential diagnoses include lung adenocarcinoma, metastatic disease to pleura from other organs. Cytokeratin5/6, WT-1, D2-40 are the positive mesothelial markers.[14] Organ specific markers can exclude metastatic disease. Examples- include TTF-1, Napsin A for lung adenocarcinoma; PAX-8 for renal and thyroid cancer.[15] Localized mesothelioma also needs to be differentiated from solitary fibrous tumour of pleura, which originate from submesothelial rather than mesothelial cells. They stain positive for vimentin, not cytokeratin.[15] Serum mesothelin related protein (SMRP) is elevated in 84% of the patient with malignant mesothelioma, and positive in only 2 per cent of patients with other pleural or pulmonary disease. This is can be another useful adjunct in diagnosis.[16] Electron microscopic features can be used to differentiate mesothelioma from other tumours- they usually have long slender microvilli, cytoplasmic fibrils and desmosomes.[11]

Treatment

Surgery if offered for stage 1 to 3.[17] It is mostly for cytoreduction. Chemotherapy is offered with or without surgery and is the only treatment for all stage 4 disease and sarcomatoid histology.[17] Combination of Pemetrexed with

Cisplatin or Carboplatin remains the treatment of choice. Pemetrexed is a potent dihydrofolate reductase inhibitor. Phase 3 trials have shown that the combination of Pemetrexed and Cisplatin increase the survival by 2.8 months compared to Cisplatin alone.[18]

Conclusion

Mesothelioma is a rare tumour that can have varied presentations; one such rare feature is dysphagia and pesudoachalsia. No screening guidelines exist for mesothelioma and in patients presenting unexplained dysphagia with asbestos exposure, this differential should be kept in mind.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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None.

PATIENT CONSENT

The authors, Swati V, Adebayo F, Farshaad B, Parth R, declare that:

1. They have obtained written, informed consent for the publication of the details relating to the patient(s) in this report.
2. All possible steps have been taken to safeguard the identity of the patient(s).
3. This submission is compliant with the requirements of local research ethics committees.

Figure 1: PET CT fused images of Sagittal and Coronal view respectively demonstrating the posterior mediastinal mass extending below the diaphragm

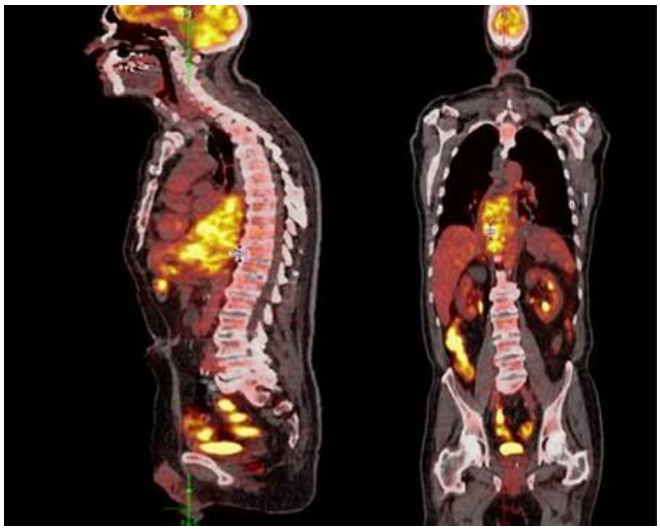

Figure 2: PET CT scan of the chest demonstrate a PET avid posterior distal mediastinal mass and bilateral pleural effusion

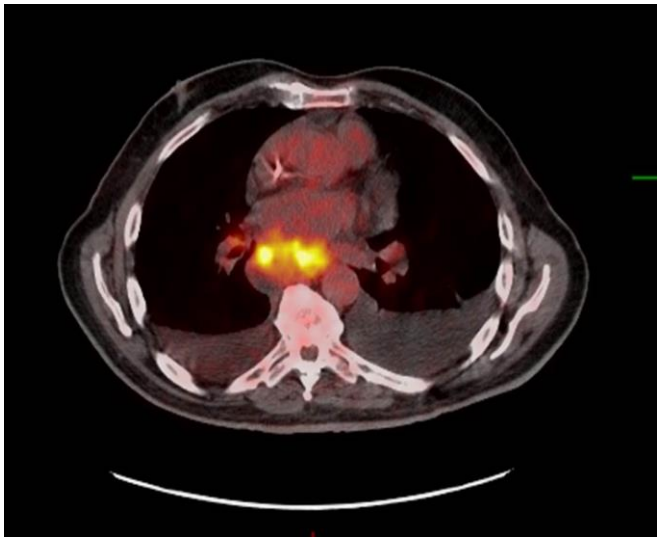

Figure 3: Positive stain for calretinin which is a marker for mesothelioma

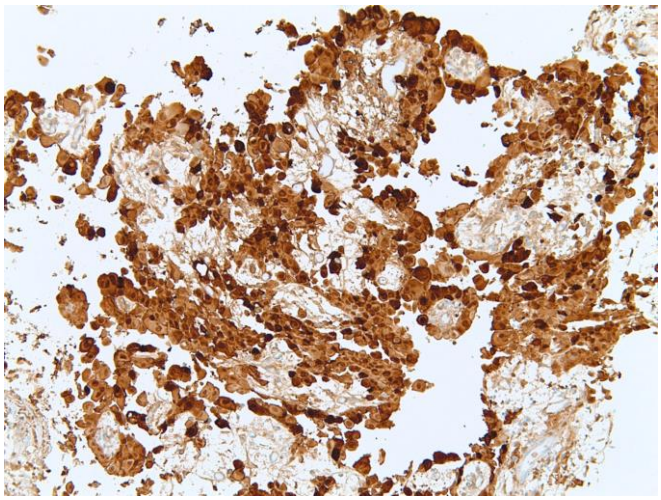

Figure 4: Positive stain for AE1/AE3, marker for mesothelioma

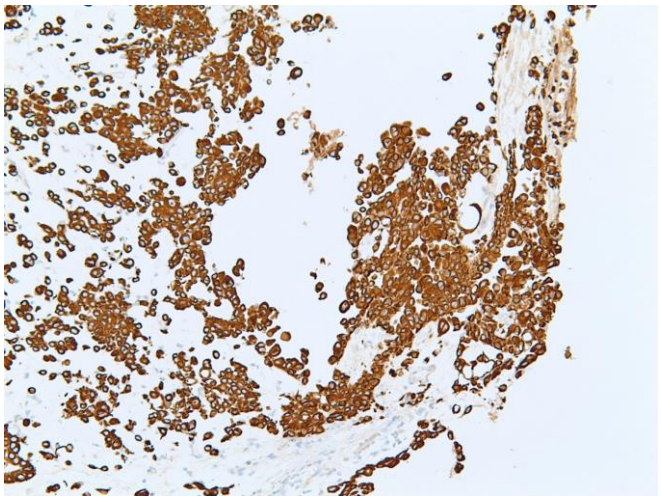

Figure 5: Positive stain for CAM 5.2, marker for mesothelioma

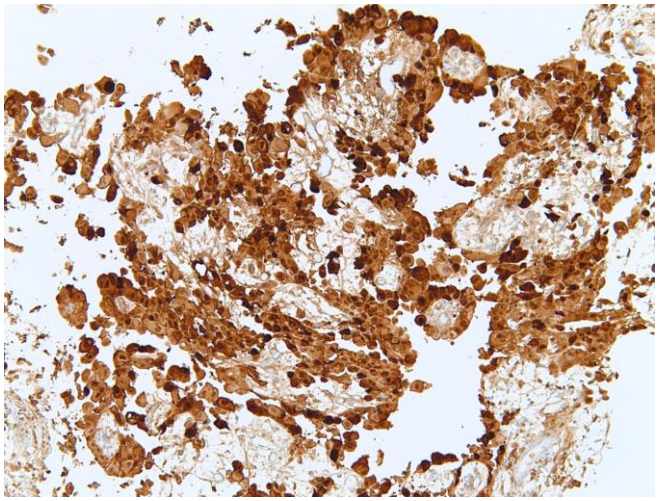

Figure 6: Positive stain for CK5/6 marker for mesothelioma

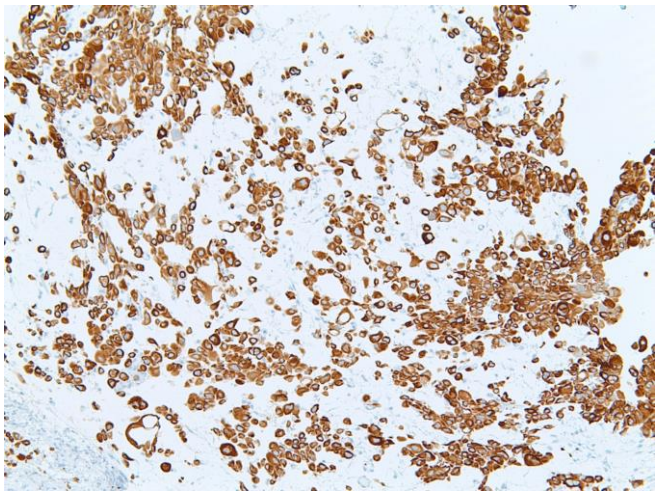

Figure 7: H/E stain of the mesothelioma showing atypical cells with round fuzzy cell membranes and frothy pink cytoplasm. The nuclei of these cells are also round with prominent nucleoli, open chromatin, and ranged from central to eccentric in their position in the cells. These combined cellular features give these cells the appearance of an epitheloid malignancy