Is there a role of immunosenescence in the pathogenesis of malignant mesothelioma? A case study

Sir,

Malignant pleural mesothelioma is the most common cause of primary pleural malignancy. Approximately, 35% of effusions associated with it are described to be inflammatory/reactive/lymphocytic in nature.[1] The latency period, defined as the time between the first exposure to asbestos and the development of mesothelioma, has been reported to be 40 years on an average. However, latency periods as long as 72 years have been documented.[2]

Here, we present an interesting case of malignant mesothelioma in a 90-year-old female with a remote and minimal history of exposure to asbestos. The case is quite interesting because this is one of the longest latency periods ever reported.

A 90-year-old female with a history of bronchiectasis and chronic pseudomonas infection, prior *Mycobacterium avium intracellulare* infection, pulmonary arterial hypertension, and atrial fibrillation was seen in the clinic for increasing shortness of breath over a period of 5 days. A chest X-ray revealed a large left-sided pleural effusion that was considerably larger in size compared to 8 months back. A thoracentesis was performed after admission which revealed yellow colored hazy fluid. A total of 1200 cc of pleural fluid was aspirated from the left pleural space under ultrasound guidance. The fluid analysis revealed a lymphocyte predominant exudative fluid [Table 1]. The differential diagnosis for the lymphocyte predominant fluid is narrow and includes the following-Tuberculosis, sarcoidosis, lymphoma, yellow nail syndrome, chylothorax, and rheumatoid pleurisy. Flow cytometry was performed which excluded lymphoma and demonstrated a CD4 to CD8 ratio of 12:1. The clinical picture and result of the fluid analysis excluded chylothorax, yellow nail syndrome, and rheumatoid arthritis as possible causes. Further immune-histochemical evaluation of the pleural fluid revealed cells that were positive for Calretinin and CD68, and negative for Ber-EP4, supporting a reactive process. Malignant cells were not encountered. Post-procedure computed tomography scans revealed a small hydropneumothorax, and to our surprise, multiple left-sided pleural-based soft tissue masses [Figures 1 and 2]. A single chest wall implant was also noted. A transthoracic needle biopsy from the mass was performed, followed by a small-bore indwelling pleural catheter catheter placement. It demonstrated large epithelioid tumor cells in cords, nests and tubular glandular structures [Figure 3]. These tumor cells were immunoreactive for cytokeratin AE1/AE3, calretinin, cytokeratin 5/6, WT1, D2-40 [Figure 4] and negative for thyroid transcription factor-1, and Napsin A. This immunoreactive pattern was consistent with mesothelioma. A nonaggressive course of treatment, focusing on comfort care was preferred by the patient. A more detailed history, obtained after this rather unexpected diagnosis, revealed that the patient was employed as a messenger at naval yard in 1940s about 74 years back. Any further exposure to asbestos was ruled

Table 1: Results of pleural fluid analysis

Pleural fluid	Value
WBC	4800/cmm
Differential count	1% N, 85% L, 14% mesothelial
Pleural protein/serum protein	4.5/6.2
Pleural glucose	107 mg %
Pleural chylomicron	Negative
Pleural fluid LDH/serum LDH	473/252
Pleural fluid pH	7.41
Pleural fluid culture	Negative
Pleural fluid RBC	9900/cmm

WBC: White blood cell, RBC: Red blood cell, LDH: Lactate dehydrogenase

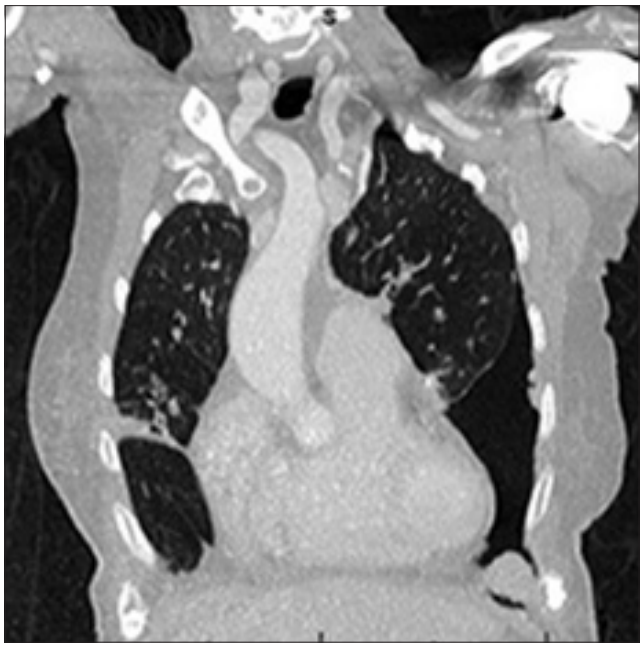

Figure 1: Coronal view demonstrating left pleural based multiple masses. A large left pneumothorax is seen

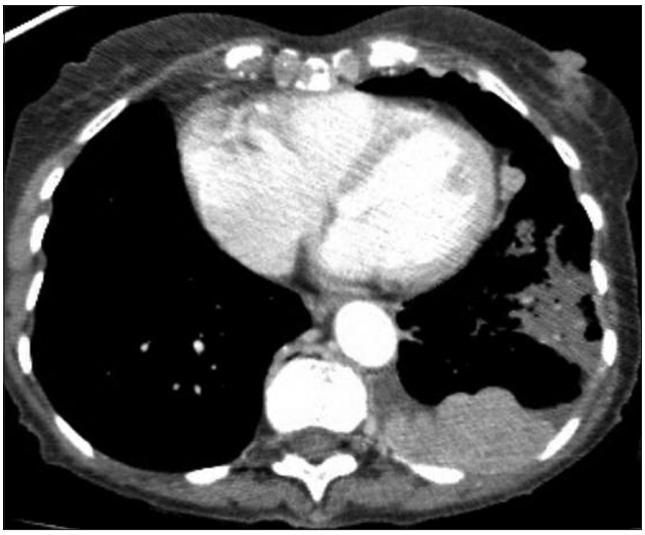

Figure 2: Mediastinal window demonstrating a posterior lobulated mass along with pleural effusion that tracks along the fissure. A small juxta-pericardial pleural based mass is also noted on this view

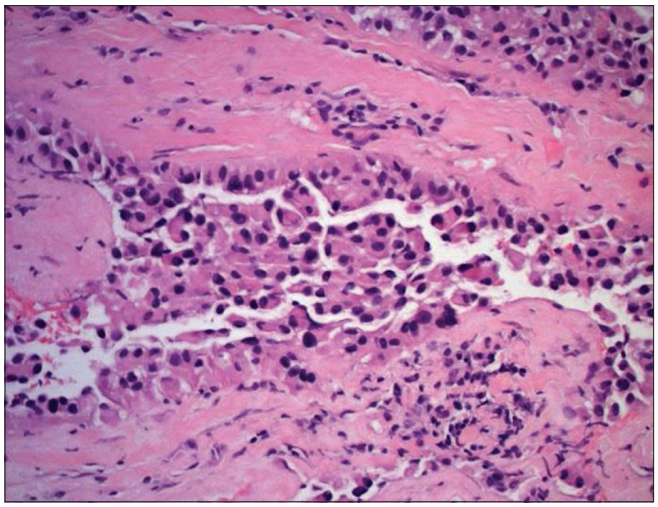

Figure 3: This microscopic image (×200) shows sheets of epithelioid cells in an infiltrating pattern typical of epithelioid mesothelioma

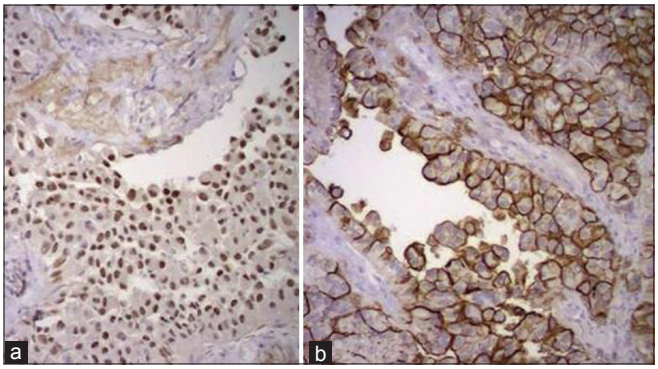

Figure 4: Immunohistochemistry is positive for WT 1 (a) (×200) and D2-40 (b) (×400) stains. Greater than 90% of mesotheliomas stain positive for both these markers which are negative in other lung cancers thus helping to distinguish between them

out. Based on this history of rather indirect exposure to asbestos, and that too with a long latent period of >70 years, we felt that it would be worthwhile to review the cause-and-effect relationship between asbestos and mesothelioma.

One explanation for such a long latency period could be that minimal exposure to asbestos resulting in delayed development of cancer. It is also interesting to note that mesothelioma can occur among immunocompromised people even without any history of exposure to asbestos.

We feel that age-related frailty of the immune system might explain the development of mesothelioma in her case. Lending support to this hypothesis would be the absence of pleural plaques/calcifications.

We reviewed some of the principal concepts of tumorigenesis associated with asbestos exposure. Even though the available data is unclear, the intensity of exposure and latency periods are commonly assumed to be inversely related in those who develop cancer.[3,4] The risk of cancer development is related to the intensity of exposure. The duration of exposure, even though considered to be less important, is also related to the risk of cancer.[5] Thus, chronic low-level exposure can account for the development of cancer. It is postulated that cancer will develop when the exposure to asbestos has reached a certain degree, which varies between individuals.[3] It is also thought that the failure of the body's immunological surveillance system to detect and kill cancer cells results in the development of cancer.[6] The reports of mesothelioma being related to HIV/AIDS, simian virus 40 infection, organ transplant, or advanced age lends credence to the theory.[5]

Cancer is the result of the interplay of multiple factors: Exposure to asbestos as well as the way the immune system responds to it. Considering the low-degree of exposure and development of cancer after such a long period, this case provides support for the role of immunosenescence in the development of mesothelioma.

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Conflicts of interest
There are no conflicts of interest.

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REFERENCES

1. Segal A, Sterrett GF, Frost FA, Shilkin KB, Olsen NJ, Musk AW, *et al*. A diagnosis of malignant pleural mesothelioma can be made by effusion cytology: Results of a 20 year audit. Pathology 2013;45:44-8.
2. Hilliard AK, Lovett JK, McGavin CR. The rise and fall in incidence of malignant mesothelioma from a British Naval Dockyard, 1979-1999. Occup Med (Lond) 2003;53:209-12.
3. Bianchi C, Giarelli L, Grandi G, Brollo A, Ramani L, Zuch C. Latency periods in asbestos-related mesothelioma of the pleura. Eur J Cancer Prev 1997;6:162-6.
4. Bianchi C, Bianchi T. Malignant mesothelioma: Global incidence and relationship with asbestos. Ind Health 2007;45:379-87.
5. Behling CA, Wolf PL, Haghighi P. AIDS and malignant mesothelioma – Is there a connection? Chest 1993;103:1268-9.
6. James CO, Woods AW, Arya P, Abuelgasim KA, Heath LT, Sitapati A. Mesothelioma in an HIV/AIDS patient without history of asbestos exposure: Possible role for immunosuppression in mesothelioma: A case report. Cases J 2009;2:7498.

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