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Case Report

North American Erionite-Associated Mesothelioma with Pleural Plaques and Pulmonary Fibrosis: A Case Report

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Abstract: Erionite, a fibrous zeolite mineral, has been categorized as a class I carcinogenic agent for its causative role in mesothelioma. In select villages in Turkey, erionite is the cause of more than 50% of mesotheliomas. In contrast, in the United States mesotheliomas are frequently associated with asbestos exposure. We describe the first reported case of a patient with erionite-associated pleural mesothelioma with classic pathologic changes typical of asbestos-related pulmonary and pleural pathology. This case report indicates that in addition to Turkey, erionite-associated disease can occur in North America and that subjects with erionite exposure are not only at risk of developing mesothelioma, but may develop interstitial fibrosis and additional pulmonary pathology impacting lung function and patient survival.
Keywords: Mesothelioma, pulmonary fibrosis, zeolite, erionite, ferruginous bodies

Introduction

Malignant mesothelioma, a cancer arising from the mesothelial cells of the pleural and peritoneal surfaces, is rare in the United States with an incidence of 3,000 new cases per year [1]. Diagnosis is often late and patients have a dismal prognosis with a medium survival of approximately 7 months. In the United States, mesothelioma is frequently associated with asbestos exposure. In contrast, in selected villages in Turkey, more than 50% of mesotheliomas are secondary to erionite exposure [2]. This high incidence of endemic erionite-induced mesothelioma in these villages in Turkey may in part be due to a genetic predisposition for mesothelioma in this population [2]. To our knowledge, there are no reported cases of mesothelioma secondary to erionite exposure in North America.

Erionite is a fibrous zeolite mineral and has been categorized as a class I carcinogenic agent by the International Agency for Research on Cancer [3]. Erionite-associated disease has a latency period of 20-25 years before symptom manifestation. Chemical properties of erionite fibers include Si/Al ratios greater than 2.5 and have been further characterized to include cationic elements: calcium, sodium, potassium or iron [4].

In the United States, there have been no proven human cases of mesothelioma due to erionite exposure to date [4]. Here we report an extremely rare U.S. case with a diagnosis of malignant mesothelioma with confirmed erionite exposure, and characteristic asbestos-related pathology.

Case Report

This case was a 47-year-old male with a diagnosis of right pleural mesothelioma with metastasis to the lymph nodes. His social history includes 20-25 years living in Mexico after which time he resided in the United States. His reported work history indicated a possible exposure to asbestos-containing floor tiles for 2 years, between 1988 and 1990, when he worked in janitorial and maintenance services for a supermarket.

Dr. Tim Qury serves as an expert medico-legal consultant for asbestos-associated mesothelioma cases.

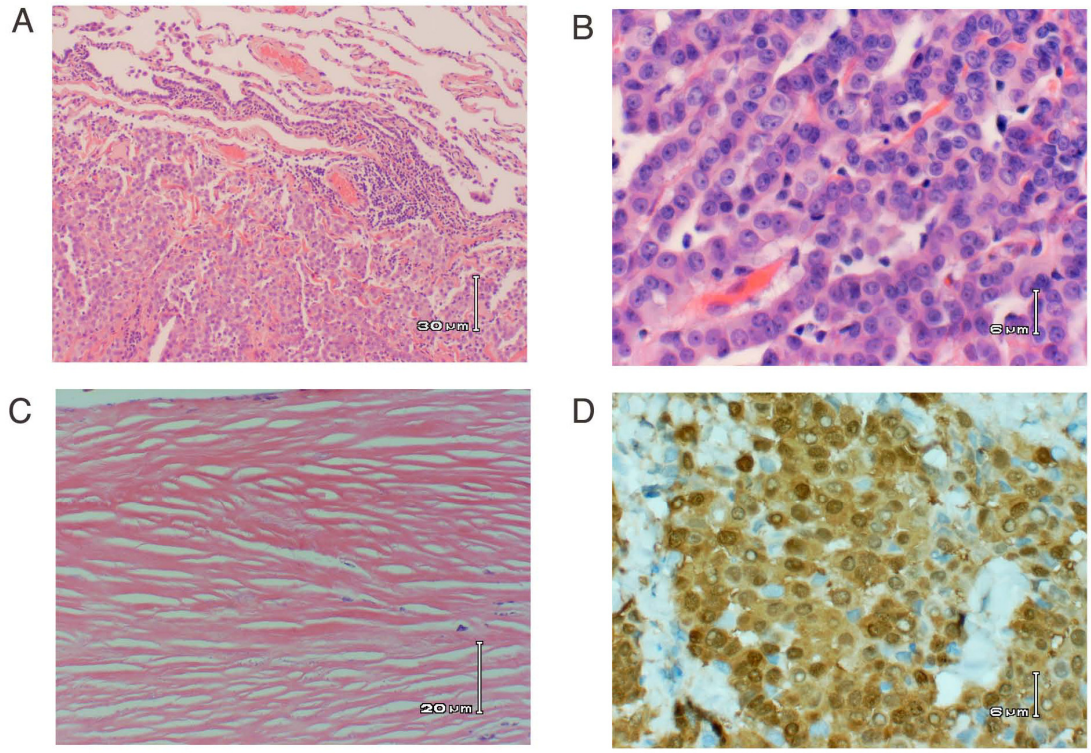

Figure 1 H&E staining shows an epithelial tumor of the visceral pleura (**A**, 10 x magnification) with a tubulopapillary growth pattern of the tumor cells (**B**, 40 x magnification) as well as acellular hyalinized collagen of a parietal pleural plaque (**C**, 20x magnification). Immunohistochemical staining shows the tumor cells are positive for calretinin (**D**, 40 x magnification).

A right radical extrapleural pneumonectomy was performed to remove the malignant tumor. On gross examination, the right lung pleura had a nodular appearance with 60% encasement of the lung by the mesothelioma and invasion into adjacent skeletal muscle. There was adherence of the parietal pleura to the visceral surface.

Microscopic examination revealed an epithelial tumor of the visceral and parietal pleura (**Figure 1A**). The tumor displays large sheets of pleomorphic cells with vesicular nuclei, prominent nucleoli and moderately abundant eosinophilic cytoplasm in a tubulopapillary pattern (**Figure 1B**). The malignant cells invade the adipose tissue, skeletal muscle and the diaphragm. Areas of parietal pleura were also found to contain parietal pleural plaques with acellular, hyalinized collagen in a "basket-weave" pattern (**Figure 1C**). Immunochemical stains of the tumor sections were positive for pan-cytokeratin and calretinin (**Figure 1D**, cytoplasmic and nuclear staining) and negative for CD15 and CEA. Ferruginous bodies were abundant throughout lung tissue that was not involved by tumor (**Figure 2A**). These ferruginous bodies were also present in areas with interstitial fibrosis (**Figure 2B**).

A lung digest was completed on 0.32 grams of the tissue from paraffin-embedded lung. The sample was digested using a sodium hypochlorite technique, as previously described [5], and collected on a 0.45 micron pore size Millipore filter. One-half of the filter was mounted on a glass slide for ferruginous body quantification by light microscopy. This analysis revealed that there were 1,097 ferruginous bodies per gram of wet lung. The other one-half filter was mounted on a carbon disc, sputter coated with colloidal graphite and evaluated by scanning electron microscopy (SEM) and energy dispersive x-ray analysis (EDXA). Calculations based on the number of fibers greater than 5 microns in length indicated that there were 124,000 uncoated fibers per gram of wet tissue. EDXA was performed on thirty uncoated fibers for the identification of the fiber mineral content. 24

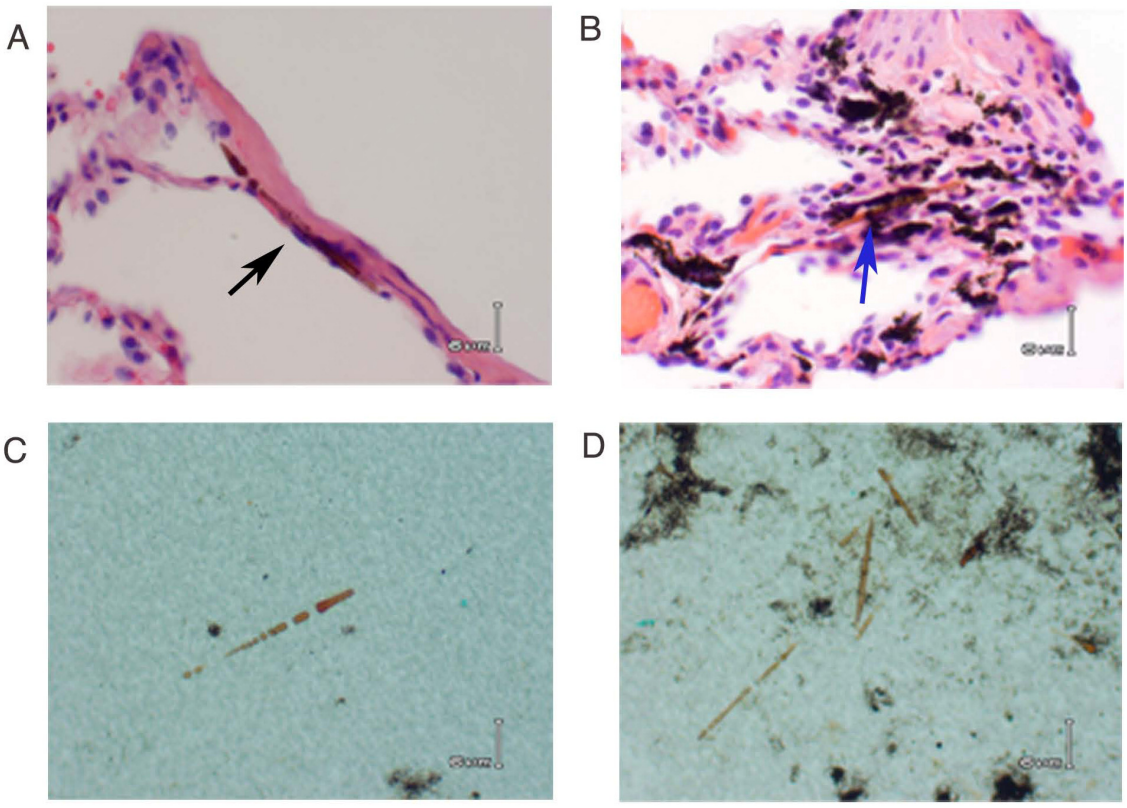

Figure 2 H&E sections show ferruginous body formation (**A**, black arrow) within the lung tissue and interstitial fibrosis surrounding a ferruginous body (**B**, blue arrow). After lung digestion, a significant amount of ferruginous bodies was detected on the filter (**C** and **D**).

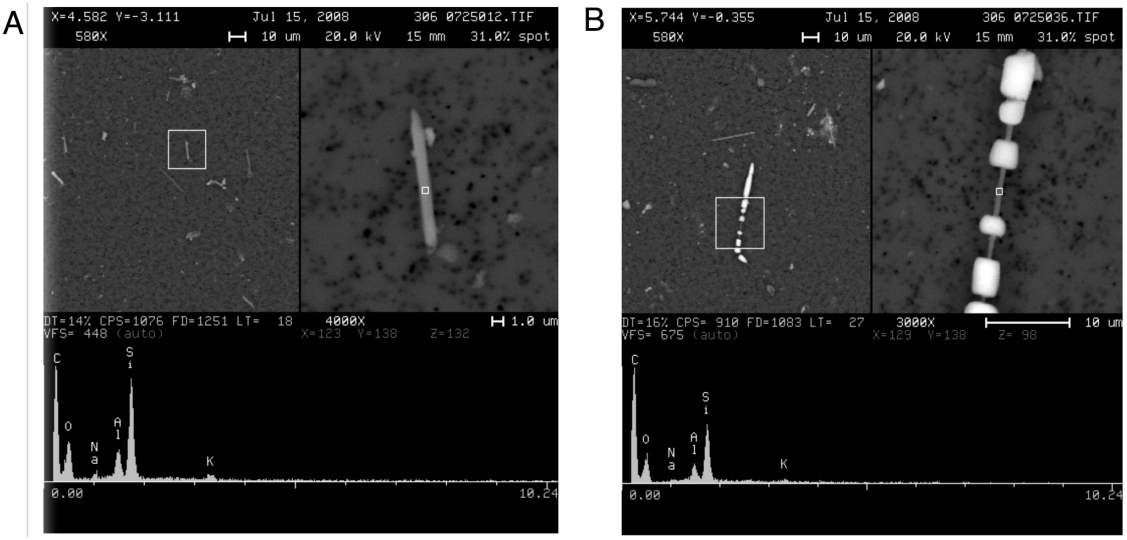

Figure 3 After lung digestions, the digest filter was evaluated by scanning electron microscopy (SEM) and energy dispersive x-ray analysis (EDXA). The analysis revealed erionite fibers (greater than 5 microns in length) and erionite ferruginous bodies. An uncoated fiber containing Na, Al, Si, and K in a proportion indicative of erionite (**A**) and a ferruginous body with a fiber that contains Na, Al, Si, and K in a proportion indicative of erionite (**B**).

of these fibers contained various combinations of Al, Si, K, Na, and Ca in ratios indicative of erionite (**Figure 3A**). Six fibers contained only Al and Si in a proportion similar to the erionite fibers. There was no spectral evidence found for commercial amosite, crocidolite, or crysotile asbestos, nor non-commercial amphiboles.

By SEM, there were 2 ferruginous bodies identified during the quantitative analysis which indicated a burden of 2,480 ferruginous bodies per gram of wet tissue. These ferruginous bodies were analyzed by EDXA, as were an additional eight ferruginous bodies identified in a non-quantitative scan of the filter. Of the ten ferruginous bodies analyzed, eight contained various combinations of Al, Si, K, and Na in proportions indicative of erionite (**Figure 3B**). The other two ferruginous bodies contained only Al and Si, but in a proportion similar to the erionite fibers above. These studies indicate that there were 124,000 uncoated erionite fibers per gram of wet lung tissue and 2,480 erionite ferruginous bodies per gram of wet lung tissue.

Discussion

In this case report, we describe the first reported case of erionite-associated right pleural mesothelioma in North America. Notably, in addition to lung tissue with mesothelioma, this patient also had classic pathological changes typical of asbestos-related diseases, including ferruginous body formation, interstitial fibrosis, and pleural plaque development. These pathogenic findings are prototypical of asbestos related disease development with pleural plaques being the most common manifestation. In the present case, there is strong evidence of elevated erionite fiber burden and the presence of ferruginous bodies in the lung; however, there is no evidence of asbestos exposure. This supports previous animal studies that indicate that erionite fibers can contribute to the pathogenesis of mesothelioma and fibrosis [5] and human computed tomographic (CT) findings related to asbestos and erionite exposure [6]. This is the first report in humans indicating that erionite can result in all 4 classical pathological findings of asbestos-related pulmonary disease. In animal studies comparing the carcinogenic levels of asbestos and erionite exposure, erionite was much more potent in causing mesothelioma than asbestos fibers [5, 7]. The potential for erionite to cause other pulmonary pathologies and its associated potency has not been studied.

Fibrous and non-fibrous zeolites, such as erionite, are common in the western United States [4]. There are also reports of zeolite deposits in Mexico [8]. Subjects with a genetic predisposition to erionite-associated disease [2] and erionite exposure are not only at risk of developing mesothelioma, but may potentially develop interstitial fibrosis and additional pulmonary pathology impacting lung function and survival.

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