

Case Report

Mesothelioma: a misdiagnosed entity in Pakistan

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Abstract:

The incidence of malignant pleural mesothelioma is rising in many nations worldwide, owing to the late banning of asbestos use and the latency between exposure and disease development. However it remains difficult to detect early and treat effectively. A case report of a young woman from northern Pakistan is reported here in whom the diagnosis was confirmed histologically after three inconclusive biopsies. It is emphasised that this diagnosis should be kept in mind when dealing with recurrent pleural effusion, pleural thickening with pain, and there should be a close liaison with histopathologist.

Key Words: Asbestos, mesothelioma, exudative pleural effusion, histology, immunohistochemistry.

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Introduction:

Malignant pleural mesothelioma is an aggressive and universally fatal neoplasm. Asbestos is implicated as the causative agent in most cases and there is usually a long latency between exposure and presentation. We dealt with a young woman whose diagnosis was only possible after repeated histologies and opinions due to a high index of suspicion.

Case Report:

IB, a 26 yrs old woman from Swat in northern Pakistan presented to us in August 2007 with an 18 month history of worsening right sided non pleuritic chest pain, exertional dyspnoea, dry cough and intermittent low grade fever. She was anorexic, and had lost 6 kg weight in the last year. She was a housewife who had never worked outdoors, had no addictions and all family members were healthy. Examination revealed a frail young woman with pallor and clubbing. The right hemithorax appeared depressed with decreased respiratory movements, a dull percussion note and diminished breath sounds in the mid and lower zones. Her abdomen felt firm with hepatomegaly.

She had been admitted with pleural effusion in Swat hospital in June 2006 where straw coloured pleural fluid was aspirated twice, including tube thoracostomy. The pleural fluid D/R is as under:

Protein 3gm/dl; Glucose 60 mg/dl; White cell count total 310/ cmm, 99% lymphocytes; RBC: WBC 20:1; and no malignant cells or Acid Fast Bacilli (AFB) seen. Her sputum for AFB was negative.

On basis of pleural fluid report, she was given standard anti-tuberculosis treatment (ATT) which she completed in eight months. She continued to be unwell with persistent chest pain.

Our investigations showed a microcytic hypochromic anemia, thrombocytosis and an Erythrocyte Sedimentation Rate of 115. Liver function tests and renal biochemistry were within normal range. Several chest radiographs (fig 1) showed right sided pleural shadow with volume loss of right lung. A CT scan of chest (fig 2) revealed diffuse irregularity and thickening of parietal and visceral pleura completely surrounding the right lung resulting in compression atelectasis and volume loss, shift of mediastinum towards right, hyper inflation of left lung and thick walled lenticular shaped collection in right pleural space. Ultrasound chest showed extensively septated thick pleural collection on right side. Abdominal sonography additionally showed hepato splenomegaly and no ascites or lymphadenopathy.

In December 2007, a pleural biopsy with Abrams needle yielded firm gritty tissue, but histologists reported no pleural tissue and only fibrinous clots, skeletal muscle fibers and inflammatory cells. In January 2008, patient was referred to thoracic department of a tertiary care hospital in Karachi for advice where an open pleural biopsy was done. Its histology reported chronic inflammatory cells, occasional epithelial histiocytes but no definite granulomas. Immunohistochemistry of the biopsy specimen showed positive Calretinin and CD 68, and negative Ber-EP4. The patient was suggested retreatment of ATT, which we did not agree to and stopped it.

In March 2008, a second thoracic surgeon was consulted elsewhere who did a pleurectomy (decortication). Its histology reported acute on chronic inflammation only. Due to lack of improvement in patient's condition, residual pleural thickening on post thoracotomy CT scan and suspicion of malignancy, second opinion was taken on this histology. It reported nests of poorly differentiated tumour highly suggestive of mesothelioma.

For personal reasons the patient went back to her native town and took further treatment by an oncologist in Peshawar who gave her 8 cycles of chemotherapy comprising of Cisplatin and Adriamycin. Repeat CT scan did not show resolution in pleural thickening, although patient reported slight improvement in pain.

She is alive and mobile after 12 months of original diagnosis, maintained on pain relief medicines and nutritional supplements.

Discussion

Mesothelioma is a disease rarely diagnosed in Pakistan. The commonest presentation is with dyspnoea due to pleural effusion; most of such cases are expected to be treated as Tuberculosis as the biochemistry mimics that of TB (exudative with lymphocytic predominant leucocytosis) and cytology is positive in only a minority of cases¹. Most of the cases have been reported from Northern Pakistan where this disease is common and thought to occur as environmental exposure². Our patient also belonged to Swat, Northern Pakistan and was initially treated with Anti-TB treatment after a pleural effusion was detected.

Most cases of mesothelioma occur in men in their 60s with prior exposure to asbestos in 60 to 80% of cases. Ninety six percent of patients have a latency of more than 20 years between exposure and subsequent tumour development. In patients with minimal or apparently inconsequential asbestos exposure, genetic predisposition or exposure to tumorigenic SV40 is thought to play a role in tumour development³. Tissue diagnosis is not straight forward and definitive diagnosis often relies on immunohistochemistry. The prognosis remains poor with a median survival of approximately 9 months. The Cancer and Leukemia Group B prognostic index identified poor performance status, age (>75 yrs), chest pain, non epithelioid histology, elevated serum LDH and elevated platelet counts as adverse prognostic indicators. There is no known cure although newer chemotherapeutic agents hold promise in improving survival.

This was an unusual case being a young woman with no known asbestos exposure. However keeping in view her native area's preponderance of mesothelioma in the mentioned report² and the evidences that the disease can occur as a result of non occupational 'environmental' exposure and even spontaneously^{4,5}, occurrence of this disease in this woman is still understandable.

The suspicion in this case that lead to further investigations was the presence of thoracic pain, an unusual feature of post TB pleural thickening, and the circumferential pleural thickening virtually encasing the right lung. The latter along with other CT features of nodular pleural thickening and mediastinal pleural involvement is described as characteristic feature of malignant pleural disease⁶. Blind pleural biopsy with Abram's needle did not confirm the diagnosis hence open thoracoscopic biopsy was performed. Although initially there were no malignant cells

reported, the immuno histochemical stains confirmed positive staining with calretinin and CD68 and negative Ber-EP4, features that distinguish mesothelioma with adenocarcinoma with which it is commonly confused with⁷. A subsequent histology sent at pleurectomy two months later initially was reported as inflammatory. Reanalysis at another center was requested, due to suspicion of malignancy, where malignant mesothelioma was finally confirmed. In all these three histologic attempts, we were constantly reminded of the fact that in areas where mesothelioma is not common, the unwary pathologist may miss the diagnosis and it is up to the suspicion of the clinician to pursue it further.

The optimal treatment of mesothelioma is uncertain and is mostly disappointing. Very few cases are subject to surgical resection, radiotherapy carries no cure and most cases are treated with palliation. Chemotherapy with cisplatin and adriamycin and lately with pemetrexed have shown some promise but survival remain poor, median being between 8 and 14 months from diagnosis^{8,9}

The patient is alive 12 months after the diagnosis was confirmed having had a pleurectomy , followed at another center, by eight cycles of chemotherapy with cisplatina and adriamycin. She still has residual disease as evidenced by post chemotherapy CT scan and is managed palliatively mostly with pain relief medicines.

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Fig 1: Chest X ray at presentation in August 2007



Fig 2: CT scan chest



