Localised Pleural Mesothelioma of Epithelial Type and Malignant Nature
Report of a Case

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Even though controversy exists,1 the primary nature of pleural mesotheliomas is at present generally accepted.2,3 These tumors are divided into two groups: (a) a diffuse malignant type, and (b) a localized (circumscribed) type which may be benign or, rarely, malignant.4 Clagett and co-workers5 have stressed the necessity for distinguishing these two types of tumors as pathologic and clinical entities.

Localized mesotheliomas, which may arise from any portion of the visceral or parietal pleura, are uncommon tumors. Among 31 cases of pleural mesothelioma traced by Lichtenstein7 in the medical literature up to 1931, only eight were classified as circumscribed type. In a thorough survey of the world literature, we have been able to gather at least 120 cases of localized pleural mesothelioma.

In contrast to the diffuse type which histologically consists of epithelial elements as a rule, the great majority of the reported localized mesotheliomas is of the fibrous type. It appeared, therefore, of interest to report the present case of localized mesothelioma which exhibited a predominantly epithelial structure and was malignant clinically, as well as histologically.

Case Report
A 60-year-old woman was referred to our department on January 10, 1961 because of an opacity at the apex of the right lung on the chest x-ray film. She complained of low back pain, headache and nonproductive cough, as well as chilly sensations and chills. The latter occurred a few times weekly and lasted one-half to one hour. She presumably had lost 20 kg. of weight during the past year. No history of chest pain, dyspnea or arthralgia in the extremities was elicited. The family and personal histories were non-contributory.

Physical examination on admission revealed a slightly obese patient in no acute distress. Her temperature and pulse were normal on admission. The blood pressure was 155/84 mm. Hg. She had no dyspnea or cyanosis. There was no true Horner's syndrome, but a slight ptosis of the right eyelid was noted which was said to be present for some 20 years. A moderate degree of clubbing of the fingers was apparent. In the upper part of the right side of the anterior chest and in the right arm, the venous pattern was distinctly increased. The physical examination of the lungs revealed only a dullness to percussion of the right apex. The rest of the examination of the systems was negative. Lymph nodes were not palpable.

Laboratory findings were as follows: erythrocyte count 4.300,000 and leukocyte count 5,200 per cmm., with normal differential count; sedimentation rate 50 mm. in one hour; Wassermann and Kahn serology tests, negative; urinalysis was normal, except for a few erythrocytes and leukocytes microscopically; no micro-hematuria was noted in subsequent repeated urinalyses.

A roentgenogram (Fig. 1) and planigrams of the chest showed on the right side an apple sized, circumscribed homogeneous opacity in the superior mediastinum. The size and shape of this

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Figure 1: Localized pleural mesothelioma in the upper part of the right hemithorax.
mass did not change during an observation period of two and one-half months on repeated roentgenograms. X-ray examination of the stomach and duodenum revealed only ptosis and hypotonia of the stomach. X-ray films of the lumbar spine and pelvis were negative except for sacralization of the fifth lumbar vertebra and hypertrophic changes of the lumbar spine. On excretory urograms the renal calyces were normal; the somewhat larger appearance of the right kidney as compared to the left one was compatible with an enlargement of the kidney projection due to a torsion associated with a ptosis of the kidney. A cholecystography showed a normally functioning gallbladder.

Intradermal tuberculin test was positive. Smears of sputum for acid-fast bacilli were negative and cultures did not show growth of tubercle bacilli. No parasites or ova were found in examination of feces. A benzidine test for occult blood in the stool was negative.

The bronchoscopic examination showed no anomalies. Histologic examination of a scalene fat-pad biopsy specimen revealed non-specific inflammatory lymph node tissue.

During the course of the disease, occasional low-grade fever up to 37.5°C (99.5°F.) was observed. General condition of health of the patient remained little reduced.

FIGURE 2A: Localized mesothelioma of the pleura. General view with epithelial structure on the surface and a stroma partly fibrous and partly cellular (H. and E. x200).

FIGURE 2B: Detail of the epithelial component; papillary structure and cleft-like cystic spaces lined by poorly defined epithelial cells (H. and E. x400).
At right thoracotomy† on March 27, 1961, it was noted that the tumor in the superior mediastinum, embedded within the arch of the first rib, extended from the sternum to the posterior arch of the first rib and had grown cranially towards the basis of the neck. The tumor arose from the parietal pleura, after the incision of which it was observed that the gray-brownish firm mass with little vascularization involved the subclavian artery and the brachiocephalic vein. Consequently, it was not possible to resect it. The tumor was biopsied.

Histologic examination of the excised specimen (Fig. 2) revealed tumor tissue which consisted of an epithelial component at the periphery and a fibrous one in the deeper parts. In the former area there were papillary excrescences which in some places formed clefts and irregular cystic spaces (Fig. 2B). In the deeper parts, clefts and cystic spaces were intermingled with cellular islets and trabecular structures. On examination with high power, the clefts, cysts, as well as papillary structures were noted to be lined by moderately large polyhedral cells having eosinophilic cytoplasm and large round or oval vesicular nuclei with prominent nucleoli. Mitotic figures were not seen, and cellular atypia was of slight degree. The cellular islets and trabeculae were formed of the same type of cells. The stroma was very cellular and consisted of capillaries surrounded by “epithelioid” cells which had a large eosinophilic cytoplasm and elongated nucleus (Fig. 2C). In some areas these cells appeared as modified, elongated epithelial cells such as seen at the periphery. In the deeper parts of the section, however, these particular stromal cells resembled fibroblasts. In these areas collagenous and precollagenous fibers were present. Some lymphocytic infiltration was observed in the periphery. Here, two dilated lymph vessels contained polyhedral tumor cells. No necrotic area was seen.††

Comment: The histologic appearance of the tumor is that of a mesothelioma of the mixed type in which epithelial features predominate. In regard to the pathogenesis of these mixed tumors, the following may be said: the presence of the particular stromal cells, which are indistinguishable from those of the epithelium on the one hand and from the fibroblasts on the other, is in agreement with the hypothesis that the mesothelioma has a potentiality to differentiate into epithelial and mesenchymal cells.

†Performed by T. Minkari, M.D.
††The patient died on October 12, 1961, elsewhere; unfortunately, a necropsy was not performed.

Comment

Clinically it is worthy to note that extra-thoracic symptoms predominated; chills were a prominent feature, and clubbing of the fingers was present. Clagett et al.10 have pointed out the frequent occurrence in cases of localized mesotheliomas of pulmonary osteoarthropathy and chills.

A true Horner’s syndrome was absent though the tumor was situated at the dome of the right hemithorax which would indicate that the stellate ganglion was not invaded. The tumor had, however, involved the brachiocephalic vein, the compression of which explained the increased venous pattern on the chest and on the right arm.

Although a necropsy has not been performed, the diagnosis in this case seems established on the basis of the histologic appearance of the excised tumor specimen obtained during thoracotomy. Such an appearance of a tumor from the parietal pleura can be considered to exclude a metastatic tumor.

Foster and Ackerman1 distinguish three histologic types of localized pleural mesothelioma: fibrous, epithelial, and mixed (fibrous and epithelial) tumors. These tumors are divided into a benign and a malignant form.11,12,13 The latter is occurring far more rarely. The prognosis of these tumors, even with a histologic malignant appearance, may be good, so long as no detectable local infiltration or spread is present.14,15 The histologic aspect of malignancy is, therefore, not always reliable.16,17 The malignancy of a mesothelioma depends on the presence of metastases in regional lymph nodes, the infiltration of the surrounding tissue or on the presence of distinct histologic signs of malignancy.18

In contrast to the pedunculated type of localized fibrous mesothelioma which is as a rule benign and encapsulated, and hence readily excisable, the encapsulation of histologically malignant localized fibrous mesotheliomas are poorly defined; and these tumors may occasionally invade neighboring organs, especially the ribs and superficial lung tissue.19,20 Their connection with
the pleura is broader; the masses may sometimes be embedded in the chest wall, lung or mediastinum. Though distant metastases are a rarity, this type of tumor may recur after surgery\(^4,13,14\) or even be inoperable.\(^4\)

The circumscribed mesothelioma in our patient, originating from the parietal pleura, had a broad base and histologically exhibited a predominantly epithelial structure. It could not be enucleated, nor could a more extensive resection be performed, since the neck vessels were involved in the invasive growth of the neoplasm. Cellular polymorphism, the absence of a capsule, the presence of tumor cells in lymph vessels, as well as scattered epithelial cells in the surrounding connective tissue, indicated distinct histologic malignancy. Based on these features and on the fatal course of the illness, this localized mesothelioma of the pleura is to be classified into the malignant and epithelial type.

Circumscribed mesotheliomas of an epithelial structure seem to be rare: only five of the thus far reported cases\(^4,13,15,16\) were of epithelial type. Eight further cases have been recorded in the literature\(^4,14,15\) in which the mesothelioma showed a predominantly fibrous structure, yet also displayed epithelial elements. The great majority of these tumors proved to be benign and resectable. In only one instance,\(^1\) the tumor was stated to be malignant like the present case.

The considerable variations regarding the histologic structure, operability and prognosis in localized pleural mesothelioma are pointed out with the present case. It also indicates that intermediary forms exist between the localized mesothelioma which is, in general, benign and of fibrous type, and the malignant, epithelial variety.

References


