

Diffuse Pleural Mesothelioma

Metastases to the Distant Visceral Organs and Thyroid Adenomas.

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INTRODUCTION

Diffuse pleural mesothelioma is a rare neoplasm, and is always regarded as malignant. The incidence of this tumor was about 0.05%, according to series of 22,976 autopsies in Japan, 1975¹.

In this paper, we report an unusual case of diffuse pleural mesothelioma with distant visceral involvement including metastases to giant- and micro-follicular adenoma of the thyroid gland.

CASE REPORT

A 68-year-old Japanese woman was admitted to a hospital in

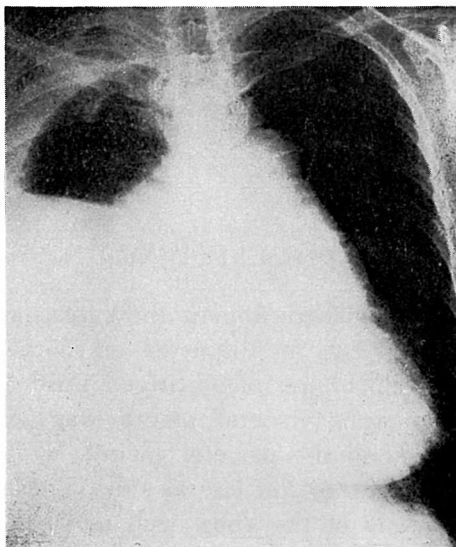


Fig. 1. Chest x-ray film shows pneumothorax and pleural effusion on the right.

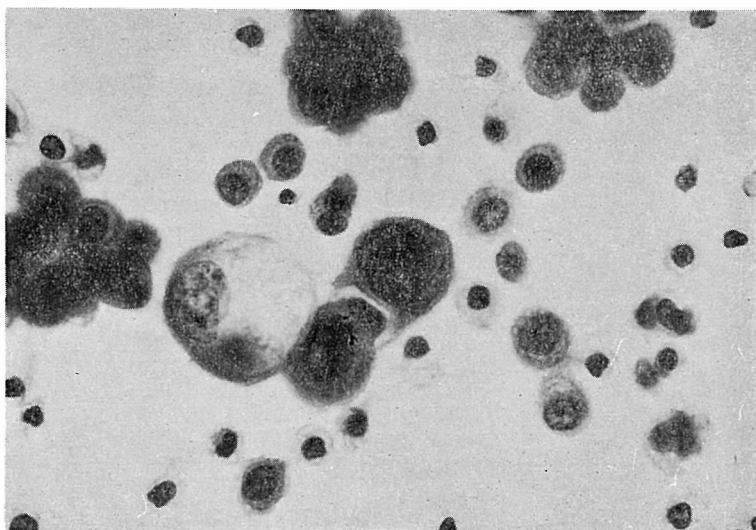


Fig. 2. Three atypical cells in the pleural fluid. Papanicolaou stain. $\times 400$.

December, 1975 because of pneumothorax and pleural effusion on the right (Fig. 1). Physical examination showed the decreased breath sound at the base of the right lung. Repeated thoracenteses yielded the blood-tinged pleural fluid and lactate dehydrogenase level of this fluid was markedly elevated (1,580 u/ml). Cytological examinations revealed numerous atypical cells (Fig. 2). In July 1976, several enlarged lymph nodes were palpable in both supraclavicular and right axillary regions. She received radiation therapy of 12,000 rads with ^{60}Co to the right chest and neck till December 1976. Laboratory examinations revealed slight anemia. In January 1977, chest x-ray film revealed the left pleural effusion, but plain film of the abdomen, complete examinations of gastrointestinal tract and cholecystography were reported as negative. She died on February 26, 1977.

GROSS FINDINGS

She was a poorly nourished woman and supraclavicular lymph nodes were enlarged up to 3 cm in diameter on both sides. The pleural cavity contained 1,500 ml of the blood-tinged fluid on the left and 1,500 ml on the right. The right visceral pleura was immensely thickened throughout and adherent to the parietal pleura by firm, yellowish, fist sized tumors from the apex to the lateral side. These tumors infiltrated to the subcutaneous tissue of the chest wall between the 1st and the 4th intercostal space. The diaphragm on the right was completely invaded

by the tumor which extruded into the peritoneal cavity but the left diaphragm and the liver were not involved. The right and anterior mediastinum was infiltrated by the elastic hard, grayish-white, multiple tumors ranging up to 3 cm in diameter. The pericardium was infiltrated by the firm, yellowish-white, bean-sized nodules on the right. The right lung was 850 g in weight and was mostly collapsed due to compression by tumors and pleural fluid and by the superficial invasion of neoplastic tissues. The bronchi and pulmonary parenchyma were carefully dissected but no primary lesion was detected. The left pleura was not adhered and the left lung, weighed 350 g, showed subpleural and parenchymal nodules measuring about 0.7 cm in diameter. The liver weighed 1,120 g and there were several yellowish-white nodules on the surface. The right kidney, weighed 200 g, had the several whitish nodules measuring 0.5 cm in diameter. In the gastrointestinal tract, numerous metastatic tumors up to 0.5 cm in diameter were scattered in the submucosal and subserosal layers.

Both lobes of thyroid gland contained adenomas about 1.3 cm in diameter with fibrous capsules. In these adenomas, grayish-white nodules without capsules were observed (Fig. 3). Retroperitoneal lymph nodes were markedly enlarged and completely adherent one another. These enlarged lymph nodes were composed of spongy yellowish-white tissue with many necrotic and cystic areas containing a honey-like fluid. The pancreas, especially the head, was embedded in adherent lymph nodes

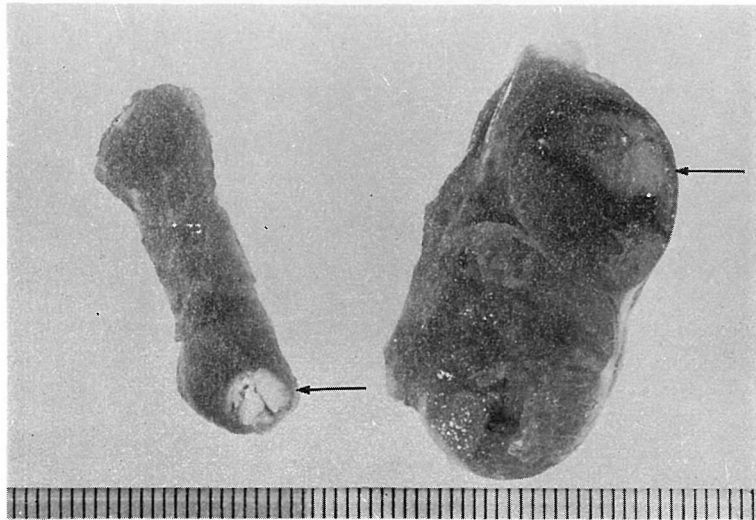


Fig. 3. Metastatic nodules (arrows) in the thyroid adenomas.

but the parenchyma was not infiltrated macroscopically. Abdominal aorta and inferior vena cava were also surrounded and compressed by these nodules.

MICROSCOPICAL FINDINGS

The tumor in most areas were consisted of cuboidal and polygonal cells with eosinophilic cytoplasm and round nuclei containing one or two conspicuous nucleoli. These tumor cells formed the tubular structures lined by a single layer of cuboidal cells or the solid, cellular areas consisted of cuboidal cells in which the peripheral cells were arranged like endothelial cells (Fig. 4). The tumor cells in some areas showed the papillary projections into the cystic lumina (Fig. 5). The sarcomatous patterns composed of spindle cells were occasionally observed in some areas mixed with epithelial structures (Fig. 6). Other sections disclosed many tumor cells with large clear vacuoles and nuclei depressed to the cell border. Although periodic acid-Schiff (PAS) reaction of these cells was nearly negative except for fine cytoplasmic granularity, acid mucopolysaccharide with colloidal iron and alcian blue stain was demonstrated. These material in extracellular, tubular or cystic spaces, and on the surface of individual tumor cells as well as in the surrounding loose connective tissue were removed by the prior testicular hyaluronidase digestion. A diagnosis of diffuse pleural mesothelioma was made from

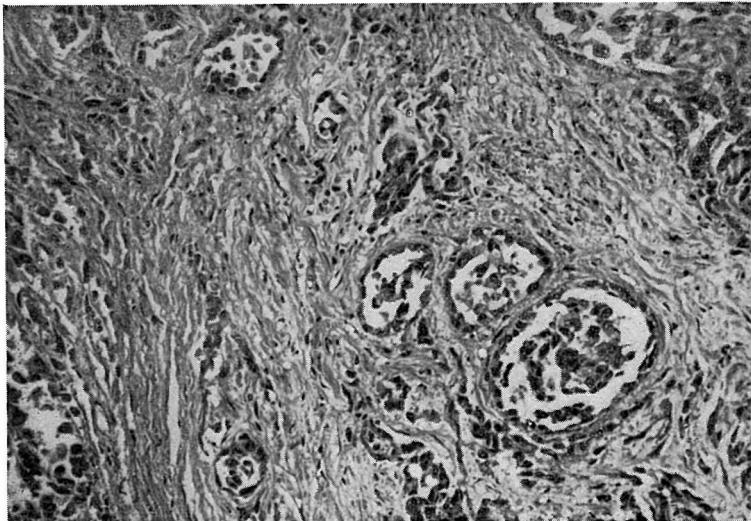


Fig. 4. Tumor cells in the right pleura are arranged like endothelial cells.
H.E. stain. $\times 100$.

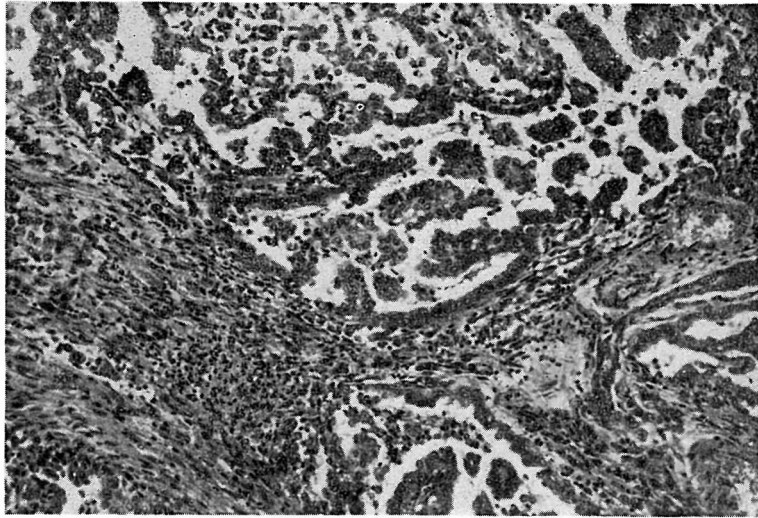


Fig. 5. Tumor cells in the right pleura show the papillary patterns in the cystic lumina. H.E. stain. $\times 100$.

these findings, which were regarded to be very helpful for the diagnosis of diffuse pleural mesothelioma²⁻⁴).

The right pleura was markedly thickened by the increase of hyalinized connective tissues and invasion of tumor cells, which infiltrated into the alveolar space. The tumor cells infiltrated to the subcutaneous tissue but the ribs were not involved. In the left lung, tumor cells were observed in the pleura and parenchyma. In both pleuras, small lymphatic vessels were invaded by the tumor cells. The nodular metastatic foci were found in the liver with tumor cell emboli in the portal vein. The surface of the pancreas was involved, and infiltration of tumor cells along lobular connective tissue, showing the sarcomatous pattern was present. In the right kidney, medullary fibroma and subcapsular papillary adenoma were noticed. Adjacent to the papillary adenoma, small metastatic nodules with papillary pattern were observed.

The giant- and micro-follicular adenomas with distinct capsules were observed in both lobes of the thyroid gland. Within the adenoma, metastatic nodules composed of tubulopapillary elements were identified. Although metastatic tumor cells resembled cytologically the tumor cells of micro-follicular adenoma (Fig. 7, 8), histochemical study could differentiate metastatic areas from the micro-follicular adenoma. The metastatic areas were stained for acid mucopolysaccharide with colloidal iron and alcian blue stain, which could be removed by the prior testicular hyalu-

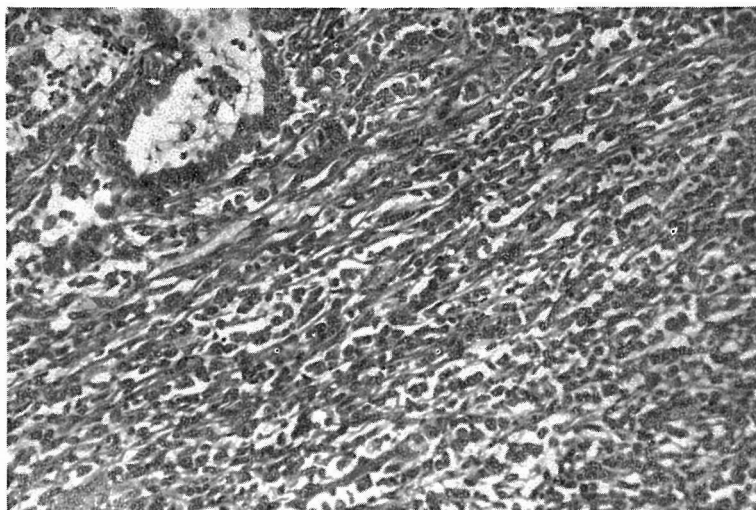


Fig. 6. Mixed area of epithelial and sarcomatous pattern in the right pleura. H. E. stain. $\times 100$.

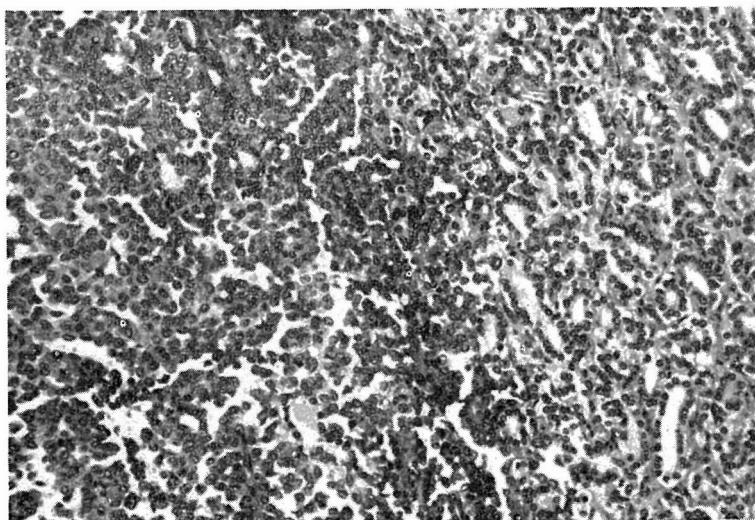


Fig. 7. Nest of metastatic mesothelioma (left) in the microfollicular adenoma (right). H.E. stain. $\times 100$.

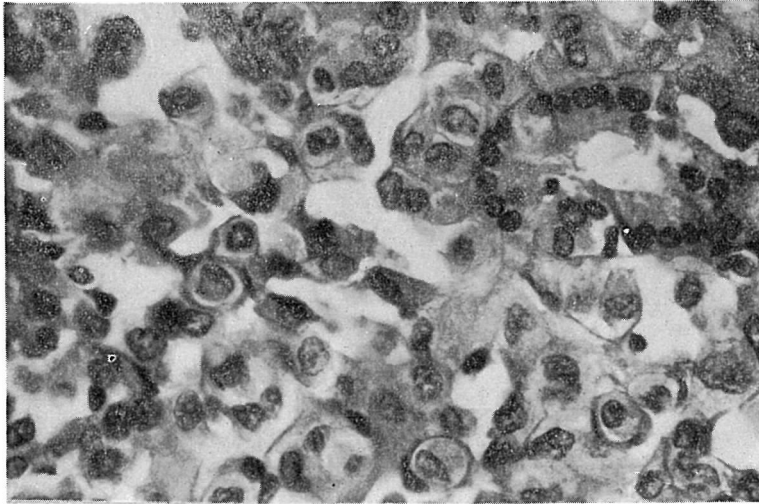


Fig. 8. Mesothelial tumor cells have the vesicular cytoplasm. On the upper right, micro-follicle is noted. H.E. stain. $\times 400$.

ronidase digestion, but the colloidal materials, which were weakly stained by the alcian blue, were not removed.

The metastatic lesions were observed in the whole alimentary tract. The lymph nodes in the supraclavicular, mediastinal and retroperitoneal regions were involved by the epithelial and mesenchymal elements and necrosis of the tumor cells were remarkable.

DISCUSSION

Although diffuse pleural mesothelioma is regarded as a tumor in which distant visceral metastases are unusual, the present case showed the numerous metastatic foci such as to the lymph nodes, both lungs, liver, right kidney, thyroid gland, pancreas, gastrointestinal tract, diaphragm and right chest wall. Roberts⁵⁾ described distant visceral metastases in 15 of the 32 cases (47%), in which the commonest metastatic sites are the hilar and mediastinal lymph nodes and opposite lung.

The most striking characteristic of the diffuse mesothelioma is the remarkable structural variation from areas to areas. Histopathologically, there are three groups of mesothelioma: tubulopapillary, fibrous and bimorphic pattern. In this case, most areas showed tubulopapillary pattern and solid sheets of epithelial-like cells. For the differentiation of the peripheral pulmonary adenocarcinoma from diffuse pleural mesothelioma, histochemical techniques is useful. PAS reaction is nearly negative

except for fine cytoplasmic granularity, but the tumors are stained for acid mucopolysaccharide by colloidal iron and alcian blue stain. These acid mucopolysaccharide can be digested by prior treatment with testicular hyaluronidase. These histochemical studies are regarded to be very helpful for the diagnosis of pleural mesothelioma²⁻⁴).

Metastasis of one tumor to another is quite uncommon. Richardson and Katayama⁶) found 40 cases in which the host tumor was malignant, and 56 in which the host tumor was benign. Three additional cases of tumor to tumor metastasis have been reported recently by Majmuder⁷), Theologides and Lee⁸). The criteria for the acceptance of the tumor to tumor metastasis are as follows⁹): (1) more than one primary malignant tumor exist and they must be a true neoplasm. (2) The recipient tumor must be a true neoplasm. (3) The foreign malignant tumor must be a true metastasis with established growth and invasion in the host tumor and not a "collision" (contiguous invasion) or a simple static embolism. In this case, the host tumors are the giant- and micro-follicular adenoma of thyroid gland and the foreign malignant tumor is the diffuse pleural mesothelioma.

SUMMARY

Diffuse pleural mesothelioma in a 68-year-old Japanese woman was reported. Although diffuse pleural mesothelioma rarely shows the distant visceral metastasis, the disseminated metastases in various organs, such as the lymph nodes, both lungs, diaphragm, right chest wall, liver, kidney, pancreas, and gastrointestinal tract, were noted in the present case. The metastasis of diffuse pleural mesothelioma to the giant- and micro-follicular adenomas of thyroid gland was also noted.

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REFERENCES

- 1) *Annual of the Pathological Autopsy Cases in Japan*. vol. 18. Edited by The Japanese Pathological Society. 1976.
- 2) Fisher, E.R. and Hellstrom, H.R.: The periodic acid-Schiff reaction as an aid in the identification of mesothelioma. *Cancer*, 13 : 837-841, 1960.
- 3) Laurini, R.N.: Diffuse pleural mesothelioma with distant bone metastasis: A case report. *Acta. Path. Microbiol. Scand., Section A*. 82 : 296-298, 1974.
- 4) Wagner, J.C., Mundy, D.E. and Harington, J.S.: Histochemical demonstration of hyaluronic

- acid in pleural mesotheliomas. *J. Path. Bacter.*, 84 : 73-78, 1962.
- 5) Roberts, G.H.: Diffuse pleural mesothelioma: A Clinical and pathological study. *Brit. J. Dis. Chest*, 64 : 201-211, 1970.
 - 6) Richardson, J.F. and Katayama, L.: Neoplasm to neoplasm metastasis. *Arch. Path.*, 91 : 135-139, 1971.
 - 7) Majmuder, B.: Metastasis of cancer to cancer: Report of a case. *Human Pathology*, 7 : 117-119, 1976.
 - 8) Theologides, A. and Lee, J.C.: Tumor to tumor metastasis. *JAMA*, 219 : 384, 1972.
 - 9) Godwin, M.G.: Diffuse mesothelioma: with comment on their relation to localized fibrous mesothelioma. *Cancer*, 10 : 298-319, 1957.