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# Congenital malignant mesothelioma

## A case report and electron-microscopic study

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**Abstract.** Malignant mesothelioma was diagnosed in a 16-day-old boy. As far as we know this is the first report of a congenital case of this disease.

**Key words:** Malignant mesothelioma – Neonatal tumour

### Introduction

Malignant mesothelioma is an extremely rare tumour in children, and only 14 cases of peritoneal origin have been reported.

We report a case of malignant peritoneal mesothelioma in a 16-day-old boy. Such widespread metastasis is very uncommon in neonatal tumours. Clinically his condition deteriorated rapidly. The diagnosis was based on light and electron-microscopic findings, especially on the presence of hyaluronic acid and keratin in the cytoplasma. This is thought to be the first congenital case to be reported.

### Case report

A 16-day-old male was admitted on October 9, 1984, to our hospital because of gradual enlargement of the abdomen since birth. During pregnancy his mother had had no history of infection, medication, irradiation, or exposure to asbestos. Delivery was uncomplicated. Physical examination revealed marked abdominal distension, but the liver and spleen were not enlarged, and no abdominal mass was palpable. The left scrotum and inguinal region were enlarged. There were skin tumours 3–10 mm in diameter on the cheek, buttock, and abdomen. Laboratory studies showed severe anaemia (haemoglobin 5.0 g/dl) and normal blood chemistry except for a lactic dehydrogenase level of 730 IU/l. C-reactive protein was +4, alpha-fetoprotein 9400 ng/ml, carcinoembryonic antigen 49.4 ng/ml, and the beta subunit of human chorionic gonadotropin 0.92 ng/ml. Urinary vanillylmandelic acid was not detected. A chest roentgenogram and CT-scan showed a right lung infiltrate and massive ascites. Abdominal paracentesis produced 370 ml bloody fluid. Bone marrow aspiration revealed hypocellularity and no abnormal cells. Chromosome analysis of peripheral blood cells, bone marrow cells, and ascites cells showed a normal karyotype of 46,XY. Laparotomy revealed that the peritoneal cavity contained 120 ml bloody ascitic fluid and numerous small nodules on the surface of the peritoneum, omentum, and mesentery. A golf ball-sized omental mass was excised for histopathological studies. Left orchidectomy was performed because the testis was enlarged and there were some supratesticular masses (Fig. 1). After the operation, the infant was treated with vincristine, vinblastine, bleomycin, and cis-diamine dichloroplatinum, but eventually died at the age of 33 days.

The autopsy findings were as follows: the tumours were disseminated diffusely over the peritoneal surface, tunica vaginalis testis, subserosa of the gastrointestinal tract, and the tissues surrounding the liver and spleen. Only in the left kidney and adrenal gland were solitary lesions present in the parenchyma. Metastatic lesions were found in the right lung, the hilar lymphnodes, and along the pulmonary trunk. The brain was normal. Microscopic examination showed sheet-like, tubular, and papillary cell-proliferation patterns (Fig. 2). The tumour cells had plump, eosinophilic cytoplasm and large nuclei with prominent nucleoli. There were diastase-resistant periodic acid-Schiff-positive granules, and mucicarmine stain was faintly positive. In some vacuoles, Alcian blue stains were positive; these disappeared with hyaluronidase treatment. Immunoperoxidase stains were positive for anti-epithelial membrane antigen and anti-keratin but negative for anti-alpha-fetoprotein, anti-carcinoembryonic antigen, anti-vim-

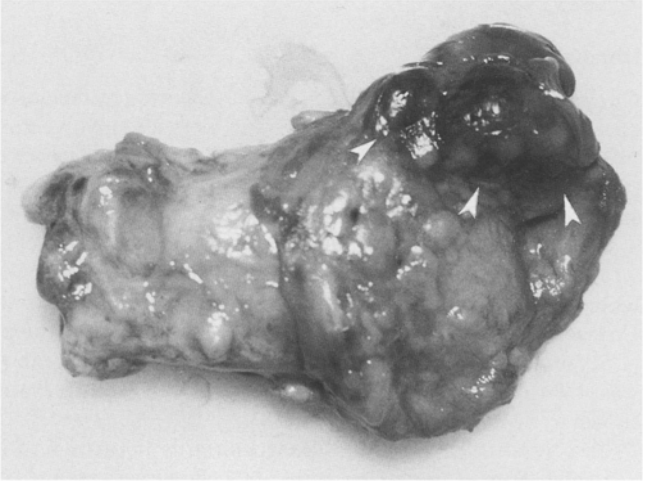

**Fig. 1.** Resected left testis. Supratesticular masses are found, and the tunica albugina testis is thickened

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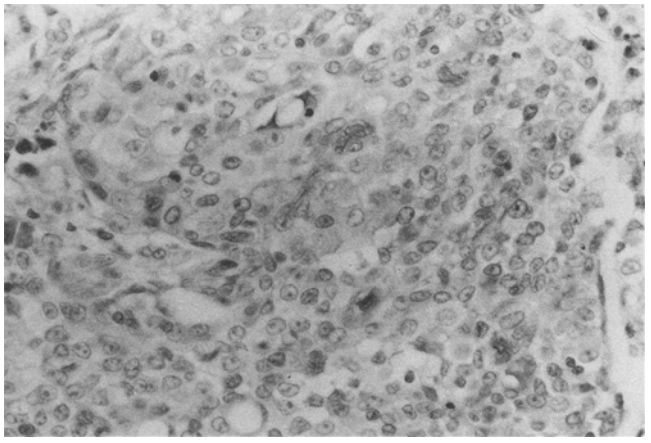

**Fig. 2.** Microscopic findings in tissue surrounding testis. Tumour cells are seen in nests, with tubular structures in some areas. These cells have large nuclei with prominent nucleoli and eosinophilic cytoplasm containing vacuoles. HE stain × 70

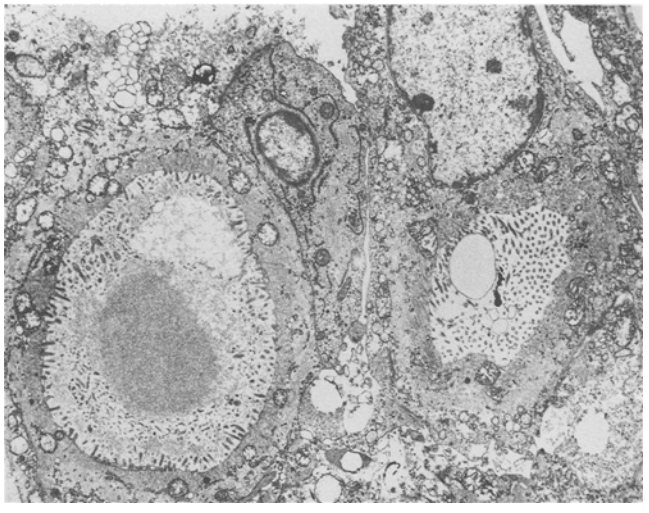

**Fig. 3.** Intracellular lumen surrounded by microvilli with non-structural electron-medium-dense material in it. × 3224

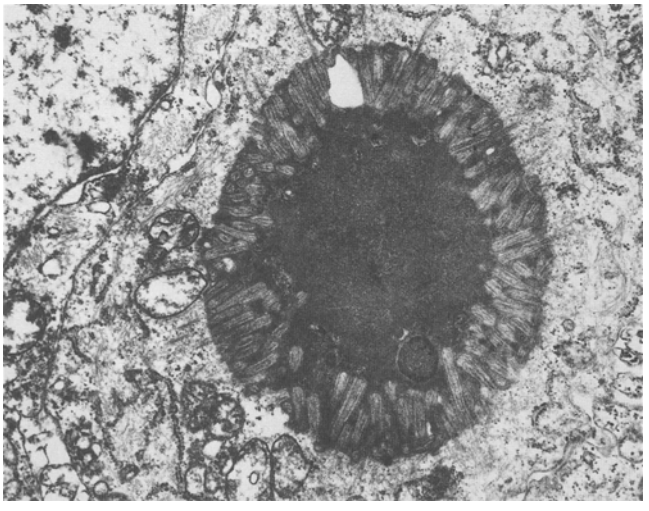

**Fig. 4.** Intracellular vacuole surrounded by microvilli, and homogenous electron-high-dense material in it. There are many intermediate filaments in the cytoplasm. × 11160

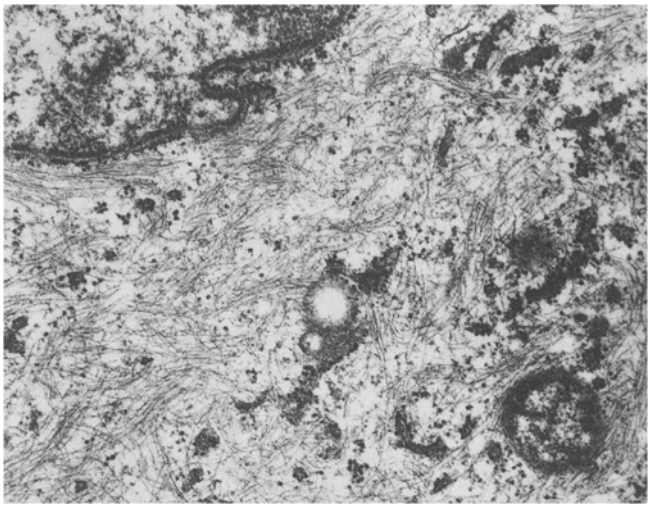

**Fig. 5.** Numerous intermediate filaments in the cytoplasm. × 22320

entin, anti-desmin, and anti-factor VIII-gamma. Electron-microscopic studies disclosed epithelial cells containing many intermediate filaments in the cytoplasm. These cells had intracellular lumens and vacuoles surrounded by numerous microvilli, in which non-structural materials were sometimes seen (Figs. 3, 4, 5).

## Discussion

Malignant mesothelioma is extremely rare in children, and only 14 cases of peritoneal origin have been reported (Table 1). The age of the patients ranged from 2–16 years. They were treated with laparotomy, irradiation, and chemotherapy, but only two lived more than 2 years after the onset.

The pathological diagnosis of mesothelioma is difficult, and special stains are helpful because mesothelioma cells contain hyaluronic acid and keratin. Electron-microscopically, the presence of tonofilaments, microvilli, and glycogen-like granules suggests that the tumour cells are mesothelial in origin.

The differential diagnosis of our patient included embryonal carcinoma and other primary neoplasms with peritoneal metastasis. Such a high level of alpha-fetoprotein is common at this age. Tests for other tumour markers and urinary catecholamine metabolites were negative. Embryonal carcinoma was excluded since the proliferation of tumour cells was clearly separated from the testis, which was initially thought to be the site of origin, and the immunoperoxidase stain was negative for anti-alpha-fetoprotein. No other primary carcinomas could be found. The tumours were predominantly over the peritoneum and omentum. Intrathoracic lesions were thought to represent lymphogenous metastasis. Solitary lesions in the left kidney and adrenal gland were not likely to be caused by infiltration through the capsule, but by haematogenous metastasis. Necrosis and surrounding fibrosis were marked, so it was suspected that the malignant transformation of the mesothelial cells had occurred relatively early in the embryonal stage. The diagnosis of malignant mesothelioma was based on the light and electron-microscopic findings of the surgical and autopsied materials; histochemical study supported this conclusion.

**Table 1.** Malignant peritoneal mesothelioma in children

| Case | Sex | Age | Location | Treatment | Recurrence | Survival outcome | Autopsy | Date of report Author |
|---|---|---|---|---|---|---|---|---|
| 1 | F | 2 years | Peritoneum mesentery | Laparotomy | | 2 weeks died | (+) | 1962 [12] Turpin et al. |
| 2 | F | 5 years | Peritoneum, omentum | Laparotomy, gold | Peritoneum | 6 years alive | | 1964 [6] Kauffman and Stout |
| 3 | F | < 10 years | Peritoneum | Not reported | | Died | | 1970 [8] McDonald et al. |
| 4 | M | 12 years | Peritoneum | Not reported | | Died | | 1972 [3] Grundy and Miller |
| 5 | F | 16 years | Peritoneum | Laparotomy, chemotherapy | | 21 months died | | 1973 [9] Rogoff et al. |
| 6 | F | 3 years | Peritoneum, omentum, liver | Laparotomy, RT, ActD, VCR, CTX | Chest wall, mediastinum, lung | 20 months died | (+) | 1976 [4] Gutman et al. |
| 7 | M | 2 years | Peritoneum, omentum | Laparotomy, NM | | 90 days died | | 1979 [5] Jones and Silber |
| 8 | M | 3 years | Peritoneum | Not reported | | Died | | 1980 [13] Wassermann et al. |
| 9 | M | 11 years | Peritoneum | Not reported | | Died | | 1980 [13] Wassermann et al. |
| 10 | F | 12 years | Peritoneum | Not reported | | Died | | 1980 [13] Wassermann et al. |
| 11 | F | 16 years | Peritoneum, omentum, pelvic organs, intestinal wall | Laparotomy, thiotepa, ActD | Omentum, diaphragm, myometrium, ovary, colon | 10 months died | (+) | 1981 [1] Brenner et al. |
| 12 | M | 2 years | Peritoneum, omentum | Laparotomy, RT, chemotherapy | Abdominal mass | 3 months died | | 1985 [7] Kovalivker and Motovic |
| 13 | F | 8 years | Omentum | Laparotomy, chemotherapy | Peritoneum | 2.5 years alive | | 1985 [7] Kovalivker and Motovic |
| 14 | F | 13 years | Peritoneum, omentum, ovary surface | Laparotomy, CTX, VCR, ADR | Peritoneum, | 8 months died | | 1985 [11] Talerman et al. |
| 15 | M | 16 days | Peritoneum, omentum, adrenal, kidney, testes, pericardium, pleura, lung, skin | Laparotomy, VCR, VBL, BLM, CDDP | | 33 days died | (+) | 1987 This paper Nishioka et al. |

RT: radiotherapy, ActD: actinomycin D, VCR: vincristine, CTX: cyclophosphamide, NM: nitrogen mustard, ADR: adriamycin, VBL: vinblastine, BLM: bleomycin, CDDP: cis-diamine dichloroplatinum

One case of benign congenital mesothelioma has been reported [10]. The youngest patients with malignant mesothelioma were a 1-year-old with a pleural lesion [13] and a 20-month-old with a pericardial tumour [2]. Our patient is thought to be the first case of congenital malignant mesothelioma.

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