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CASE REPORT

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Epithelial mesothelioma with deciduoid features

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Abstract A rare case of malignant mesothelioma in a 15-year-old girl is described. The patient presented with secondary amenorrhoea and clinical symptoms resembling those of an ovarian cyst. One large and multiple small peritoneal nodules were found at laparoscopy. Histologically the tumour was characterised by an unusual pattern with a superficial resemblance to decidual reaction, but because of significant mitotic activity the diagnosis of a malignant tumour, epithelial mesothelioma with deciduoid features, was made. The patient died 11 months after diagnosis. Post-mortem examination revealed extensive extraperitoneal spread.

Key words Epithelial mesothelioma · Deciduoid peritoneal mesothelioma · CEA · Calretinin

Introduction

Peritoneal mesotheliomas are rare malignant neoplasms developing primarily in adults and associated with long-term asbestos exposure [12]. They occasionally occur in children [5, 8]. However, two recently described types of mesothelial tumour affect young adults almost exclusively. These are the desmoplastic small round cell tumour with divergent differentiation, preferentially affecting males and the deciduoid mesothelioma, which has been reported exclusively in females. Three cases of the latter subtype of mesothelioma have been published [10, 14].

We now report the fourth case, with immunohistochemical, ultrastructural and autopsy details.

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Clinical history

A previously healthy 15-year-old girl was admitted to hospital in early October 1996 with a 3-month history of secondary amenorrhea. She had never been pregnant, and her menarche had occurred 1 year before presentation. Chest X-ray and laboratory findings were normal. Computerised tomography revealed a relatively circumscribed intrapelvic mass, which was displacing the intestine. Laparoscopy was performed to rule out a cyst of the right ovary, and a large mass was seen amid the intestines on the right side of the abdomen. There were many peritoneal plaques. The uterus, ovaries, fallopian tubes and urinary bladder were normal. The lesion was not attached to the liver, gallbladder or stomach. The peritoneal cavity contained a small amount of slightly blood-tinged ascites.

Following the histological diagnosis the patient was treated by chemotherapy, receiving vincristine, doxorubicin, cyclophosphamide and cisplatin in the first cycle. The second cycle was doxorubicin, cyclophosphamide and cisplatin in combination, while the third and fourth consisted of combinations of vincristine, metothrexate, vepesid and of vincristine, doxorubicin, iphosphamide and vepesid, respectively. After 6 months the tumour showed partial remission and laparotomy was performed. The main tumour mass and the omentum were resected. There was a short remission following the surgery, but distant metastases occurred and the patient died 11 months after the initial recognition of the tumour.

Materials and methods

The surgical specimen was fixed in 10% buffered formalin and processed by the standard technique to paraffin wax. The 5-µm-thick sections were stained with haematoxylin and eosin, periodic acid–Schiff (PAS) without and with diastase digestion (D/PAS), PAS-alcian blue and Gomori's reticulin, all according to standard methods. Parts of the formalin-fixed material were postfixed in 2% glutaraldehyde and 2% osmium tetroxide and embedded in Araldite. Ultrathin sections were stained with lead citrate and uranyl acetate. For immunohistochemical examination deparaffinized tissue sections were stained with a panel of mono- and polyclonal antibodies using the avidin–biotin–peroxidase method. The reagents, their sources, and the results are summarised in Table 1.

Table 1 Immunohistochemical reactions and results in the study of deciduoid mesothelioma (*EMA* epithelial membrane antigen)

Antibody specificity	Source	Tumour cells reactivity	Stromal spindle cells
Cytokeratin (lu-5)	BioGenex	Positive	Negative
EMA	BioGenex	Positive	Negative
CAM 5.2	Becton-Dickinson	Positive	Negative
BerEP4	DAKO	Focal positive	Negative
HMFG2	BioGenex	Focal positive, mainly cytoplasmic	Negative
CEA	BioGenex	Scattered positive cells	Negative
Calretinin	Research Diagnostic Inc	Weak, focal positive cells	Negative
Vimentin	DAKO	Positive	Positive
Desmin	DAKO	Negative	Focal Positive
Smooth muscle actin (1A4)	DAKO	Negative	Negative
S-100 protein[a]	DAKO	Negative	Negative
NSE	DAKO	Weak, positive	Negative
Leu-M1 (CD15)	DAKO	Focal, positive	Negative
CD30	DAKO	Negative	Negative
CD44	DAKO	Negative	Negative
β–HCG	DAKO	Negative	Negative
Progesterone receptor	BioGenex	Negative	Negative
Oestrogen receptor	BioGenex	Negative	Negative
p53 (DO7)	DAKO	Positive	Negative

[a] Polyclonal antibodies, all the others are monoclonal

Pathological findings

The original specimen sent for examination was a 7×5×4 mm block of greyish-white tissue taken from the large mass and a few 1–2 mm diameter fragments of debris from peritoneal plaques.

Histologically, the larger block and the small debris proved to be from the same tumour, composed of large epithelioid-like rounded, ovoid or polygonal cells arranged in solid sheets and trabeculae. Oedematous connective tissue with elongated fibroblast-like cells and a mild, mixed inflammatory infiltrate were seen within the sheets of tumour cells (Fig. 1). The nuclei were large, round or oval vesicular with well-defined, occasionally indented, nuclear membranes. Binucleated forms were occasionally present. The nuclei each contained one to three small or one prominent nucleoli (Fig. 2). Mitoses (including abnormal forms) were present with a frequency of 10–15/10 high power fields. There were occasional large vacuoles or granulocytes in the pale to bright eosinophilic cytoplasm (Fig. 3). The PAS reaction was negative, and no epithelial mucin was demonstrated.

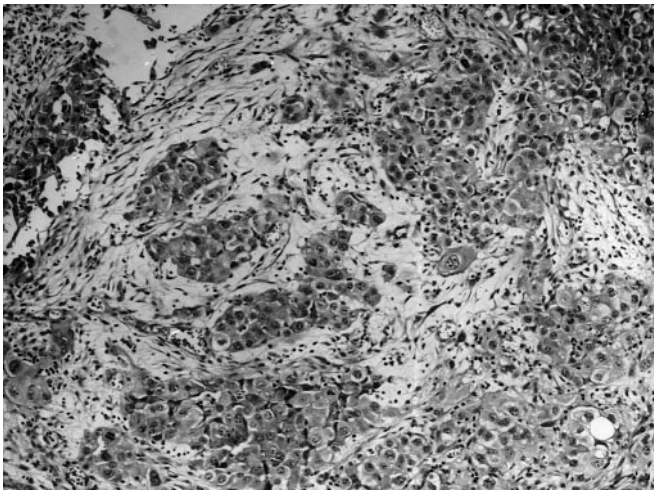

Fig. 1 Large epithelioid tumour cells are present in solid sheets and trabeculae. Within the tumour there is oedematous connective tissue with elongated fibroblast-like cells and a mixed inflammatory infiltrate. HE, ×40

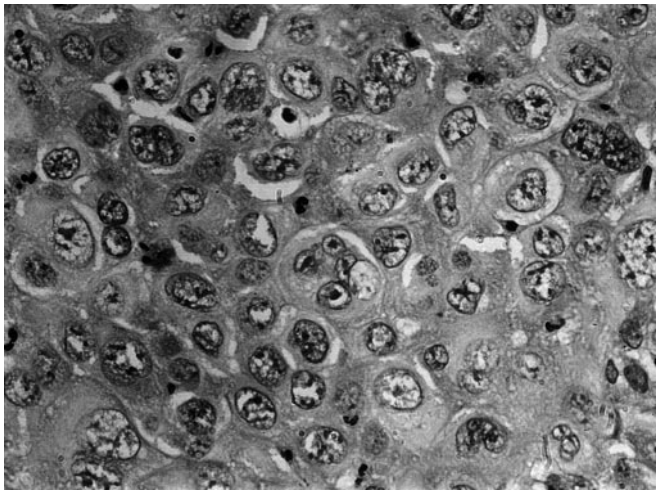

Fig. 2 Large, round or oval vesicular nuclei with a well-defined, occasionally indented, nuclear membrane are seen in pale eosinophilic cytoplasm. HE, ×200

In the plump tumour cells immunohistochemistry revealed diffuse strong positivity for cytokeratin (lu-5), EMA, CAM 5.2 and focal positivity for HMFG2 and Ber-EP4, while the stromal spindle cells were negative

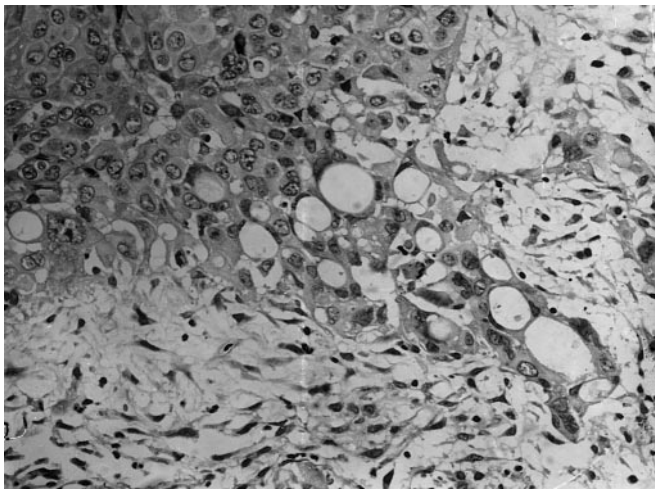

Fig. 3 There are occasional large vacuoles in the cytoplasm. HE, ×100

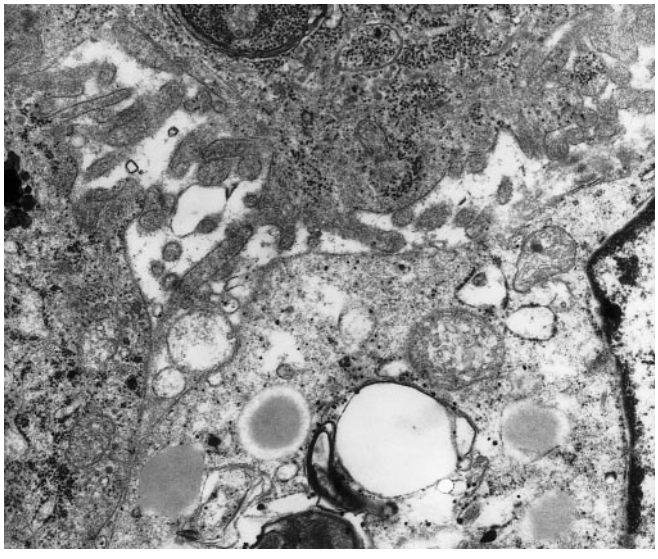

Fig. 4 An intercellular lumen containing long, slender microvilli. In the cytoplasm lipid droplets and lamellar body (*bottom*) are seen. Original magnification ×9500

with these epithelial markers. In the tumour cells focal staining was present with LeuM1 (CD15). Vimentin was positive in both cell types, and only in scattered cells could positivity for CEA be demonstrated. Only scattered tumour cells showed weak calretinin positivity. A weak positive reaction for NSE is interpreted as non-specific. All other markers but p53 were negative in tumour cells (Table 1).

Ultrastructurally, the cytoplasm of the poorly differentiated large tumour cells contained glycogen lakes, lipid droplets and scattered lamellar bodies. The cells were connected by occasional junctional structures and surrounded by basal lamina. The intercellular channels contained a moderate amount of long, slender microvilli (Fig. 4).

The most relevant findings at the post-mortem examination were extensive tumour masses in the abdominal cavity. There were abundant disseminated tumour nodules in the pouch of Douglas. The right ovary was replaced by a tumour measuring 6 cm in its maximum diameter. Remnants of the ovary could not be identified. The left ovary, the uterus, the urinary bladder and the urethra were normal. There were multiple metastases in the lungs and liver. The paratracheal, hilar and retroperitoneal lymph nodes were infiltrated by tumour. Both visceral and parietal pleura were smooth; no plaques or thickening were observed. No other primary tumour was found. The cause of death was respiratory insufficiency caused by multiple pulmonary metastases.

Discussion

Diffuse malignant mesothelioma affects mainly adult males, often after a long latent period of asbestos exposure. Occurrence in children and in young adults is extremely rare. In 1985, Talerman et al. reported one case of malignant peritoneal mesothelioma that had developed in a 13-year-old girl [14]. The lesion was composed of large, anaplastic cells, and an initial diagnosis of deciduosis was made. Nascimento et al. published two similar cases in 1994, and they designated the lesion deciduoid mesothelioma [10]. The common characteristics of these patients and ours are the following: the tumour affected young female patients; there was no connection with asbestos exposure, and all of the patients have died within 1 year after diagnosis (Table 2). One of the patients reported by Nascimento et al. was pregnant, and two of the others were in the perimenarchal period. These data suggest that the neoplastic lesions were connected with hormonal changes, although we, like others, were unable to detect oestrogen or progesterone receptors by immunohistochemistry.

Despite the resemblance to pseudotumoral deciduosis (sheet-like proliferation of large round, ovoid or polygonal cells with pale eosinophilic, slightly foamy or vacuolated cytoplasm, large and vesicular nuclei with a prominent nucleolus) the microscopic appearance was quite similar to the sheet-like subtype of epithelial mesothelioma. We prefer the designation epithelial mesothelioma with deciduoid features. Another tumour it is important to consider in the differential diagnosis is the anaplastic large cell lymphoma, especially in small specimens. The age distribution of this lymphoma is similar to that of deciduoid mesothelioma with a peak in the second decade; the skin, the gastrointestinal tract or soft tissues may be the first sites of presentation [2]. The histological similarities are: large polygonal cells with distinct cell membranes, abundant eosinophilic cytoplasm, vesicular nuclei and the prominent nucleoli. However, in contrast to deciduoid mesothelioma, anaplastic large cell lymphoma stains for T- or B-cell lineage markers and diffusely with CD30, and only occasionally with anticytokeratin antibodies [6, 9].

Table 2 Cases of deciduoid peritoneal mesothelioma

Case	Reference	Age (years)/ sex	Signs	Therapy	Survival
1	[14]	13 F	Abdominal pain	Cyclophosphamide, vincristin, doxorubicin	7 months
2	[10]	23 F	Infertility, pelvic pain	Oestrogen and progesterone	4 months
3	[10]	24 F	Abdominal swelling during pregnancy	Termination of the pregnancy, laparotomy	No data
4	Present case	15 F	Secondary amenorrhoea	Polychemotherapy	11 months

The immunohistochemical profile of our case is contradictory and surprising (Table 1). The focal LeuM1 (CD15), CEA and BerEP4 positivity and the mainly cytoplasmic staining with CAM 5.2 favour the diagnosis of carcinoma. However, a small proportion of epithelial type mesotheliomas reacts with these antibodies, although the staining is usually weak and focal [3, 4, 11]. At the ultrastructural level the presence of numerous long slender microvilli can help distinguish mesothelioma from carcinoma, but some mesotheliomas have been described as having short microvilli or no microvilli [15]. In our case neither the immunohistochemical profile nor the ultrastructural appearance is convincing with regard to a mesothelial origin, so that the differential diagnosis of carcinoma also must be considered. Which type of carcinoma would be likely? At autopsy we found that the right ovary was destroyed by the tumour mass, and no other primary tumour was found. At the time of laparoscopy the reproductive tract was free of macroscopic abnormality, supporting secondary involvement of the ovary. The present tumour shows a superficial similarity with the oxyphilic cell subtype of ovarian carcinoma, but this variant of clear cell carcinoma occurs in middle-aged women with a median age of 55 years [16]. PAS staining was used in our case: no positivity was present and no epithelial mucin was demonstrated.

The facts supporting our diagnosis are an initial multiple-site peritoneal tumour without any other lesion; a dual immunophenotype (strong vimentin *and* epithelial marker positivity); positivity of the calcium-binding protein calretinin [7], albeit only focal and weak; CD44 positivity (observed in the majority of mesotheliomas and in a minority of adenocarcinomas [1]); and the presence of long microvilli, but only in moderate numbers. The extensive extraperitoneal metastases are an unusual feature, but malignant mesotheliomas are sometimes diagnosed from lymph node metastases [13]. The negativity of the epithelial markers in the spindle cells proves that this tumour is a variant of epithelial and not of biphasic mesothelioma (Table 1).

The bad clinical outcome of this variant and the unusual metastatic pattern for an epithelial type of mesothelioma underline the point that the deciduoid appearance distinguishes a unique subtype among epithelial mesotheliomas.

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