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Case report

Extraspinal ependymoma in the sacrococcygeal region

A case report with ultrastructural, immunohistochemical and cytophotometric studies

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Summary. We describe on a primary, subcutaneous sacrococcygeal ependymoma presenting in a young female patient. Detailed immunohistochemical and electron microscopic examinations were performed. Out of the 40 similar cases reported in literature this is the first in which the determination of DNA content was also used to predict biological behaviour. The tumour proved to be aneuploid with low proliferative capacity in spite of absent histological signs of malignancy. It is suggested that DNA determination may be helpful in establishing prognosis and that it may contribute to a better understanding of the biological behaviour of this tumour.

Key words: Extraspinal ependymoma – DNA content versus histological picture

Introduction

Extraspinal ependymoma is a rare and potentially malignant tumour metastasizing in some 20% of cases. It is usually localized subcutaneously in the sacrococcygeal region. The most frequently observed histological type is the myxopapillary variant. The precise histogenetic classification of this tumour does not usually present any difficulty, due to the availability of immunohistochemical and electron microscopical criteria for diagnosis. However, one cannot disregard the observation of Helwig and Stern (1984) who concluded from the analysis of 32 cases that there was no clinical or histological clue that would allow a reliable prediction for the development of metastases. This has inspired us to examine whether the determination and evaluation of DNA content provide evidence for a potentially malignant character of the tumour.

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Case report

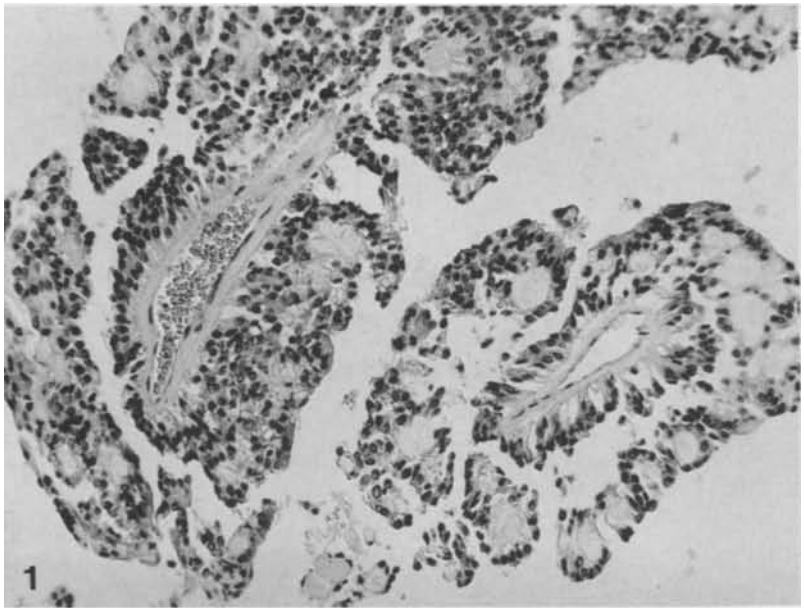
M.E. was a female patient aged 19 years. At the age of 17 she bore a child. She had not suffered from any previous illness. In summer 1987, gynecological examination was performed for therapeutic abortion and this revealed a fist-sized mass retrorectally. The sacrum was destroyed causing disordered urination and temporary incontinence. Due to increasing symptoms she was directed to the National Institute of Oncology. Surgery was performed on 28 January, 1988.

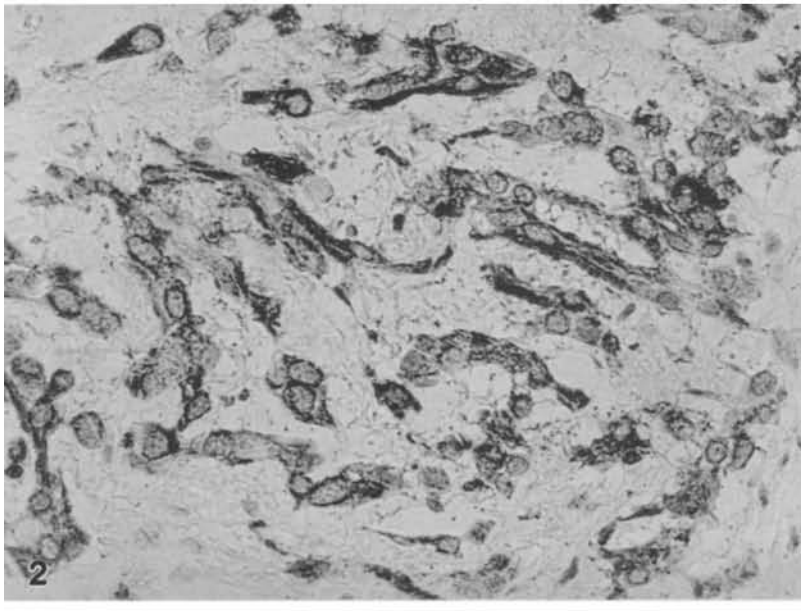
The lumbosacral region of the vertebral column was exposed surgically. The lumbosacral muscles were detached from L_V and from the sacral vertebrae. Immediately beneath the fascia a scarlet, soft tumour became visible. It extended upwards to the intervertebral space of L_V and caudally it involved the lower portion of the dural sac. It penetrated into the gluteal muscle and the pelvis. The gluteal muscles were infiltrated over an area of 5 cm diameter. The macroscopically visible tumour could not be removed completely, so this intervention was palliative. The patient was discharged after primary wound-healing on the 15th postoperative day. Two months later the surgical area was irradiated by telecobalt irradiation: total dose 50 Gy, distributed over 12 and 13 days with one week interval.

CT examination performed on 28 April 1988 revealed that dorsally the bony structure of the three upper segments of the sacrum were destroyed and fragmented. Distally, the entire bony structure of the sacrum had disappeared; in its place some minor bone fragments were detected. On the right a small area of the sacroiliac joint was also involved. Deep in the pelvis, a 5×6 cm solid soft tissue shadow could be discerned. Distant metastases were not found. Her complaints have intensified. Now, seven months after surgery, she has become addicted to major analgesics. Persistent pains at rest make us consider a reoperation and additional irradiation.

Material and methods

The biopsy specimen was fixed and processed routinely. Special stains were PAS and the "Stains-all" reaction. For the immunohistological examination the indirect peroxidase-anti-peroxidase technique (Sternberger et al. 1970) was used with the polyclonal glial fibrillary acidic protein (GFAP), S-100 protein antisera and the monoclonal vimentin and cytokeratin





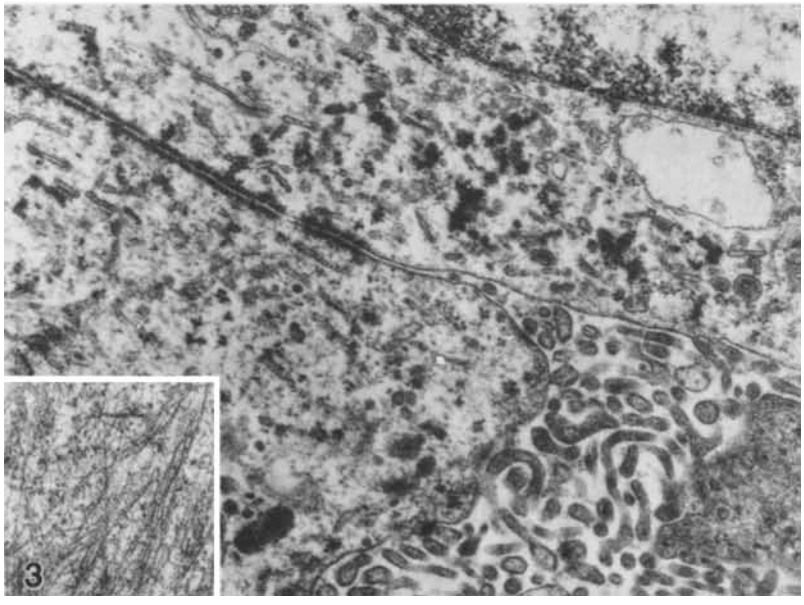


Fig. 1. Perivascular pseudorosettes characteristic of extramedullary ependymoma. Cells are fairly uniform, nuclei are round (H.E. ×170)

Fig. 2. Strong GFAP positivity in the cytoplasm of tumour cells (Immuno-peroxidase reaction for GFAP and nuclear staining with H. ×350)

Fig. 3. Electronmicrograph of tumour cells. Microvilli seen on the cell surface. Striking presence of elongated desmosomes between the adjoining cells. *Insert:* Fine cytoplasmic filaments responsible for GFAP positivity (×18000, insert: ×26000)

48 K; 56 K; 58 K; 64 K antisera (Heintel, Wien, Austria). The immunohistochemical reactions were performed on paraffin sections of the tumour. For electron-microscopy, material was taken from formalin fixed specimen. Cytophotometry was carried out on imprint smears. Following Feulgen staining (hydrolysis: 1 NHCl, 60 °C, 9 min) measurements were performed with an MPM 1K computercontrolled cytophotometer (Carl Zeiss, Oberkochen FRG).

Results

The microscopic picture showed dominance of solid cellular tumour tissue in the slightly myxous matrix. Nuclei were fairly uniform and round, mitotic forms were seldom observed. The cytoplasm was finely vacuolised. Tumour cells were grouped in bundles or arranged in a network. In addition, in some minor areas papillary structures and characteristic perivascular pseudorosettes were seen (Fig. 1). Vascular invasion was absent. PAS reaction showed diffuse positivity of varying intensity in the cytoplasm of tumour cells. With the "Stains-all" reaction a small amount of acidic mucopolysaccharides could be demonstrated as indicated by the bluish-green colour reaction.

Immunohistochemistry showed that the cytoplasm of the tumour cells gave intensive positive reaction with GFAP (Fig. 2) and Vimentin; reaction against S-100 protein, however, was less positive and not present everywhere. Reaction to cytokeratin was completely negative.

On electronmicroscopy the tumour cells were generally cuboidal. In some places they formed distinct lumina with tight junctions between the adjacent cells. Formation of various junctional complexes and elongated desmosomes could be observed. Microvilli protruded into the luminal region (Fig. 3). Sparsely, mitochondria, free polyribosomes, rough endoplasmic reticulum and microtubules were present in the cytoplasm. In some cells large aggregates of fine cytoplasmic filaments could also be identified. Our diagnosis "extramedullary ependymoma" was confirmed by immunohistochemical and electron microscopical evidence.

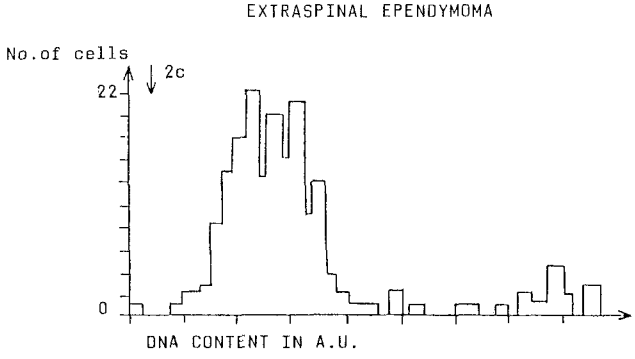


Fig. 4. Most of the tumour cells form one subpopulation, their DNA value is significantly different from the 2c normal value. DNA index: 1.53 that indicates aneuploidy

Results of DNA cytophotometry are summarized in Fig. 4. They demonstrate aneuploidy (DNA index: 1.53) with one subpopulation and low proliferating activity.

Discussion

Extraspinal ependymoma usually occurrs in young patients. This potentially malignant tumour usually appears in the sacrococcygeal region, and is most frequently diagnosed as a primary subcutaneous sacrococcygeal mass either connected or not connected with the spinal cord (Anderson 1966; Helwig and Stern 1984). Histologically papillary or myxopapillary forms mixed with solid areas are seen. Most of the cells are cuboidal occuring in clusters without notable polymorphism. Often they are arrayed around a central cavity. The solid parts contain characteristic perivascular pseudorosettes in fairly high number. Immunohistochemical reactions show strong GFAP, vimentin positivity and somewhat weaker positivity for S-100 protein. The immune reaction is, however, negative for cytokeratin (Helwig and Stern 1984). On ultrastructural level numerous binding elements, basal membrane, some microvilli and microfilaments and a few microtubules become visible (Rutherford et al. 1987; Vagaiwala et al. 1979).

Radical surgery is not always feasible, as in our case, because of the special localization of the tumour. It is supposed that operative manipulation exposes vascular channels to loose tumour cells, and this is responsible for distant metastases (Wilff 1972). Helwig and Stern (1984) failed to find any reliable clinical or histological indicator of metastasis formation although the recurring behaviour of the tumour and its metastasizing capacity in some 20% of the cases in 5 to 15 years make such an indicator highly desirable. The determination of DNA content is a useful aid in this respect. From the flow cytometric study of soft tissue tumours Kreichbergers and coworkers (1987) have concluded that all aneuploid tumours are malignant. Similar observations were made by Federspiel et al. (1987) who analysed 66 gastrointestinal smooth muscle tumours for DNA content but found only the leiomyosarcomas to show aneuploidy. In some malignant soft tissue tumours, for example alveolar soft part sarcoma, however, Persson et al. (1988) have observed diploid and tetraploid values in an analysis of 10 cases. This fact indicates that even diploid or polyploid tumours may be malignant. However, to the best of our

knowledge no paper has been published on an aneuploid soft tissue tumours with benign biological course as may happen in case of epithelial tumours for example in situ carcinomas and severe dysplasias. The same is true for bone tumours (Mellin and Grundmann 1989). In our own case it was also the aneuploidy that demonstrated the potentially malignant character of the tumour.

This finding emphasizes the need for close and long follow up. Combined surgical and radiotherapy of the tumour and the surgical removal of possible solitary pulmonary metastasis may give a chance of a longer survival (Helwig and Stern 1984; Wolff et al. 1972).

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