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Case report

Malignant rhabdoid tumour of the uterus: an immunohistochemical and ultrastructural study

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Summary. Malignant rhabdoid tumours (MRTs) are highly aggressive neoplasms which most frequently occur in the kidney of young children. Several cases of primary MRT occurring in extra-renal sites have been reported, particularly in the soft tissues. We report a case of primary MRT of the uterus, a very rare site for this neoplasm, with morphological, immunohistochemical and ultrastructural features corresponding to restrictive morphological criteria for MRT. The possible differential diagnoses were considered.

Key words: Malignant rhabdoid tumour – Uterus – Immunohistochemistry – Ultrastructure

Introduction

The term malignant rhabdoid tumour (MRT) was first introduced in 1981 to specify a highly aggressive neoplasm with distinctive morphological features, characterized by eosinophilic periodic acid-Schiff (PAS)-positive cytoplasmic inclusions and eccentrically placed nuclei with a prominent nucleolus (Haas et al. 1981).

MRTs have most frequently been reported as arising in the kidney (Haas et al. 1981; Weeks et al. 1989a). However, as the recent review by Kodet et al. (1991) reveals, they have also been seen in several extra-renal locations such as the soft tissues, central nervous system, liver, bladder, heart, tongue, skin, prostate gland, adnexa and vulva, while Lemos and Hamoudi (1978) reported a case in the thymus. Further examples of this rare neoplasm can be found in the reports of Russo and Taylor (1986), Carter et al. (1989) and Matias et al. (1991).

To our knowledge, only one previous case of primary MRT of the uterus has been reported (Cho et al. 1989); the present investigation describes the clinical and morphological features of a further case of a primary endometrial MRT.

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Case history

A 39-year-old woman was hospitalized in June 1987 after 3 weeks of abnormal uterine bleeding and lower abdominal pain. On pelvic examination, the uterus was found to be enlarged and firm. After an endometrial curettage that revealed a possible stromal neoplasm of uterine origin, a total abdominal hysterectomy, bilateral salpingo-oophorectomy and sampling of para-aortic and iliac lymph nodes were carried out. Following surgery, a pelvic radiation (55 Gy) was performed. One year later, the patient developed ascites and a CT scan revealed multiple metastases to the right lung, liver and abdomen. A cycle of adjuvant chemotherapy was administered. The patient died with cachexia in November 1988, 17 months after the histological diagnosis. No autopsy was requested.

Materials and methods

The tissue obtained for histology was fixed in 10% buffered formalin, embedded in paraffin and stained with haematoxylin and eosin (H & E), PAS before and after diastase digestion, Gomori silver impregnation, Masson's trichrome and alpha-naphthol-esterase.

For immunohistochemistry, the ABC (avidin biotin peroxidase complex) staining procedure (Hsu et al. 1981) was used, as detailed previously (Doglioni et al. 1987).

The specificity, working dilution and sources of the primary antisera are reported in Table 1.

For the ultrastructural immunolocalization of vimentin, 1 mm^3 tissue fragments were retrieved from the formalin-fixed paraffin-embedded block, dewaxed, and re-embedded in Epon 812 resin. Ultra-thin sections were immunostained with an indirect immunogold procedure (gold particle size 10 nm), as reported previously (Viale et al. 1985).

Results

A partly necrotic polypoid mass, measuring 8.5 cm at its greatest axis, was found in the 500-g uterus. The

Table 1. Antibodies and antisera used in the study

Reagent	Dilution	Source
Anti-CKs (lu-5 mAb)[a]	1/5	Boehringer Mannheim Biochemicals, Indianapolis Ind. U.S.A.
Anti-CKs (CAM 5.2 mAb)[a]	1/20	Becton-Dickinson, Mountain View, Calif., U.S.A.
Anti-vimentin (v9 mAb)	1/20	Boehringer Mannheim Biochemicals
Anti-desmin (D33 mAb)	1/10	Sanbio, Am Uden, Holland
Anti-smooth muscle actin (1A4 mAb)	1/3000	Sigma, St. Louis, Mo., U.S.A.
Anti-T cells (UCHL1 mAb)	1/100	Dakopatts, Copenhagen, Denmark
Anti-B cells (L26 mAb)	1/100	Dakopatts
Anti-K chains (poly)[a]	1/2000	Dakopatts
Anti-λ chains (poly)[a]	1/2000	Dakopatts

mAb, Monoclonal antibody; poli, polyclonal antiserum
[a] Proteolytic digestion with trypsin

neoplastic tissue surrounded residual endometrial glands and invaded the myometrium to a depth of more than 50% of the thickness of the myometrial wall. The neoplasm consisted of a diffuse proliferation of monomorphic polygonal cells separated by occasional fibrotic trabecula (Fig. 1). The eosinophilic cytoplasm contained a spherical hyalin inclusion (Fig. 2), which was weakly PAS-positive, diastase resistant. The nucleus was round, oval or kidney-shaped and often possessed a prominent nucleolus. Mitotic figures were numerous. With Gomori staining, the stroma revealed thickened reticulum fibres surrounding clusters of neoplastic cells. Immunohistochemically, the cytoplasmatic inclusions were strongly positive with anti-vimentin antiserum (Fig. 3, inset) whereas all other immunostaining was negative.

At the ultrastructural level, the cytoplasm of most of the neoplastic cells contained large paranuclear aggregates of intermediate filaments of approximately 10 nm, arranged in concentric whorls and labelled with immunogold after incubation with anti-vimentin antiserum (Fig. 3). Thick and thin myofilaments, tonofilaments and desmosome-like intercellular junctions were not found.

Discussion

Since the first description of MRT of the kidney (Haas et al. 1981), a series of extra-renal cases have been reported which are fairly heterogeneous both on morphological and clinical grounds. From the histological standpoint, all the authors apart from Dervan (1987) agree in considering the presence of a prominent nucleolus to be an important marker of MRT, whereas PAS positivity of the cytoplasmic inclusions varies from strong to weak and can even be negative. Moreover, with immunohistochemistry, the differences are even more evident. In fact, with the exception of vimentin, expression of the major cell markers varies considerably among the various extra-renal cases and with respect to the more homogeneous renal MRT cases (Blatt et al. 1986; Sotelo-Avila et al. 1986; Harris et al. 1987; Kent et al. 1987; Perrone et al. 1989; Schmidt et al. 1989; Tsokos et al. 1989). From the clinical standpoint, Haas et al. (1981) described MRT as being characterized by early infantile onset and rapidly lethal progression. However, the mean age of the extra-renal cases is higher (mean 12 years). Balaton et al. (1987) described a case occurring in a 59-year-old man and nine cases of long survivors have been reported (Tsuneyoshi et al. 1985; Sotelo-Avila et al. 1986; Kent et al. 1987; Perrone et al. 1989; Schmidt et al. 1989; Tsokos et al. 1989).

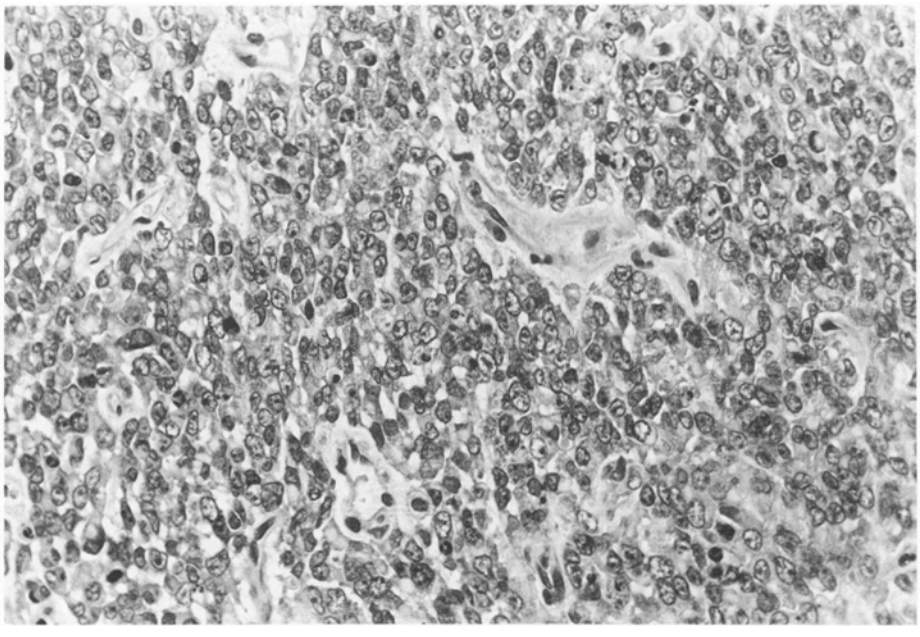

Fig. 1. The monomorphic proliferation of neoplastic cells was separated by fibrotic trabecula. H & E, ×250

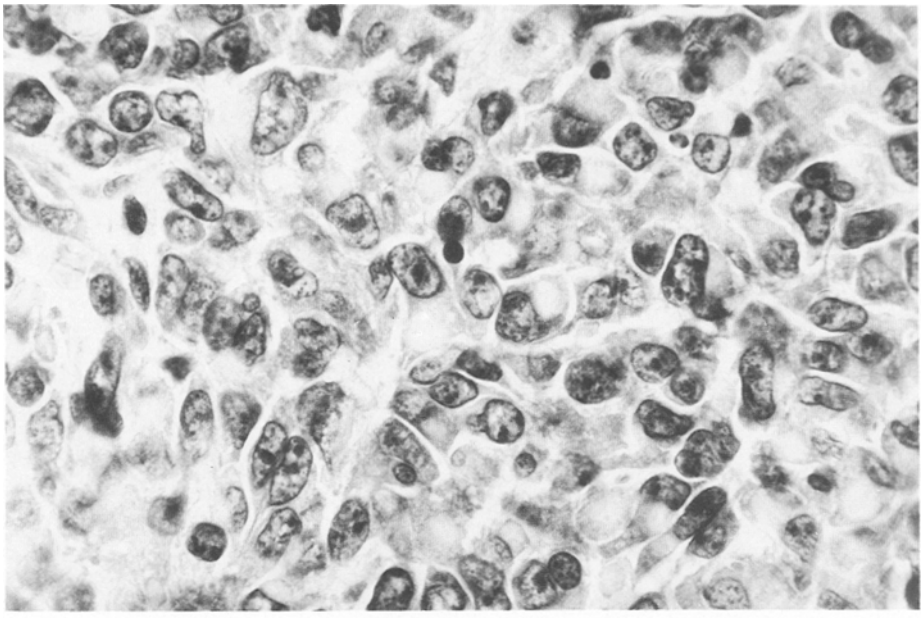

Fig. 2. At higher power, in most neoplastic cells, hyalin cytoplasmic inclusions, often in paranuclear position, are clearly evident. H & E, ×1000

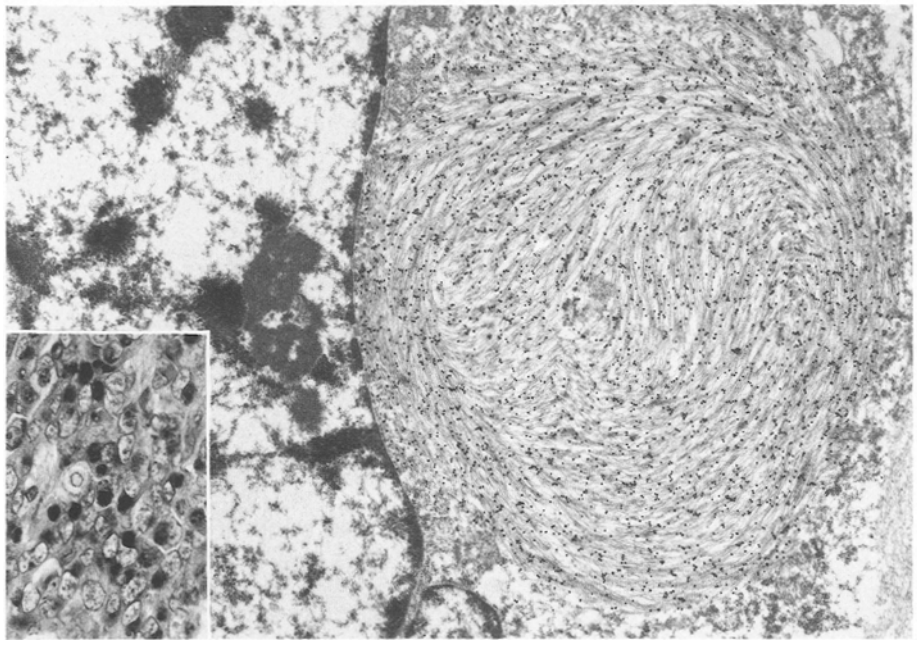

Fig. 3. The neoplastic cells contained large paranuclear aggregates of vimentin filaments arranged in concentric whorls. Immunogold, ×11350. *Inset:* strongly cytoplasmic positivity with anti-vimentin antiserum, often in a ball-like position. ABC, ×500

It is possible to claim that not all the cases reported in the literature fit the initial definition of rhabdoid tumour, and recently some authors have in fact proposed the term "pseudo-rhabdoid" (Weeks et al. 1989b) for those tumours which partially resemble MRTs; in fact it is known that "rhabdoid cells" can be reported in several specified soft tissue tumours (Tsuneyoshi et al. 1987).

Our case is a malignant and highly aggressive tumour of the endometrium which corresponds to Beckwith's restrictive morphological criteria for MRT (Haas et al. 1981), all the main histological, immunohistochemical and ultrastructural characteristics of the entity being present.

Only one case of primary MRT of the uterus (Cho et al. 1989) has been reported. It was characterized by a concomitant involvement of the vaginal tract and a short period of follow-up. In the uterus, MRT must be differentiated from several stromal and epithelial lesions as well as from haematological disorders. The presence of benign endometrial glands could suggest the diagnosis of adenosarcoma, but in our case the epithelial component was constituted by residual endometrial glands. In high-grade stromal sarcoma there are no characteristic cytoplasmic inclusions (Akhtar et al. 1975), the neoplastic cells are always separated by a well-developed reticulin network and the immunohistochemical findings are more complex than in classical MRT (Dabbs and

Park 1988; Devaney and Tavassoli 1991; Farhood and Abrams 1991). Furthermore, the morphology combined with the complete absence of histochemical and immunohistochemical signs of muscular and lymphoid differentiation exclude the possibility either of an epithelioid leiomyosarcoma or of high-grade non-Hodgkin's lymphoma. Finally, as regards a possible diagnosis of endometrial carcinoma, in which McNutt et al. (1985) reported the ultrastructural presence of whorled perinuclear aggregates of intermediate filaments, the absence in our case of any other signs of epithelial differentiation seems to exclude this hypothesis.

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