CYTOLOGY OF MALIGNANT MIXED MESODERMAL TUMOUR OF THE UTERUS: EXPERIENCE OF 10 CASES

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Summary: The value of cytology as a diagnostic tool in uterine MMMT has been tested in order to reach an earlier diagnosis.

From 10 endocervical scrapings we were able to obtain 7 positive smears, two of them diagnostic for mixed tumour at first examination, 1 detected upon revision.

In one case the positive smear was obtained from a direct scraping of the neoplasia protruding through the cervical os.

INTRODUCTION

Malignant Mixed Mesodermal Tumours (MMMT) are very uncommon and aggressive neoplasms of the female genital tract. In the uterus they are seen practically always in post-menopausal patients, in whom they present with uterine bleeding and enlargement.

Generally, they are large, soft, polypoid growths usually involving the posterior wall and the fundus, sometimes protruding from the cervix ([1]).

Histologically they are biphasic neoplasms characterised by the presence of both epithelial and stromal malignant components, hence the designation "mixed". The epithelial component is usually rapresented by an adenocarcinoma of endometrioid type at different grade of differentiation but also rare types of endometrial adenocarcinoma can be present. The stromal component may be of homologous type (composed of sarcomatous elements indigenous to the uterus) (fig. 1) or of heterologous type (composed of elements differentiating towards skeletal muscle, cartilage, bone or fat) (fig. 2). The epithelial and the stromal components can be strictly intermingled or in isolated nodules.

The characteristic cytologic features of MMMT of the uterus in routine vaginal and cervical smears have not been well documented. This paper presents the cytodiagnostic findings of 10 MMMT of the uterus as found in routine vaginal and cervical smears in order to reach an earlier diagnosis.

MATERIAL AND METHODS

During the six-year period from 1980 to 1986, 13 women were treated at Gynaecological Department, Pavia University, for uterine MMMT (9 cases were of homologous type; 4 cases of heterologous type). Specimens for cytologic examination were obtained from the vagina, ectocervix and endocervix of 10 patients and stained routinely with Papanicolaou's method.

Positive smears were observed in 7 patients; 6 patients had neoplastic elements and one severe dysplastic squamous cells.

Clinical records and follow-up were studied with all available cytologic and histologic material.

RESULTS

At the time of the diagnosis the age of patients with uterine MMMT, who had cytologic examination ranged from 59 to 85 years with a mean age of 71.3. Initial symptoms noted were increased abdominal girth, pelvic mass, pain or discomfort in

pelvic area and vaginal bleeding. Clinical findings include obesity, hypertension, hormonal treatments after menopause and diabete mellitus. Physical examination revealed enlarged uterus and palpable abdominal mass. In one patient the tumour protruded through the cervical os. The stage of presentation was IA (3 cases), IB (5 cases), and III (2 cases).

The cytologically positive smears obtainel from 7 patients (4 with MMMT homologous type; 3 with MMMT heterologous type) showed in two cases definite sarcomatous elements in addition to adenocarcinoma, making possible the diagnosis of mixed tumour. In four cases only a malignant epithelial component, i.e., adenocarcinoma, which was virtually indistinguishable from endometrial adenocarcinoma, was present. In one case we found severe dysplastic squamous cells.

The revision of slides made possible an additional diagnosis of mixed tumour from the group of previously diagnosed as adenocarcinoma because of the detection of anaplastic tumour cells in addition to adenocarcinoma.

One of the two smears originally diagnosed as mixed tumour was obtained from the patient with neoplasm protruding through the cervical os; the other from a patient with a nodule of 4 cm in diameter localized in the left cornus mainly constituded of a rabdomyoblastic component.

All but one of the 7 patients with positive cytologic specimens, were treated with total abdominal hysterectomy and biloteral salpingo-oophorectomy. One of them had post-operative radiation and chemotherapy and is NED 9 months from the diagnosis. The other 6 patients died during the first year after surgery.

In one case of MMMT homologous type, autopsy was performed. Metastatic sites included: vagina, urinary bladder, omentum, mesenteric lymphnodes, liver, right lung, pericardium, left cervical lymphnodes. Both histologic components were found in metastatic sites.

Cytological findings.

The malignant epithelial component observed in 6 of our cases, resembled that of endometrial adenocarcinoma in various stages of differentiation. Epithelial neoplastic cells were arranged in strips or scattered in groups in relation to the degree of differentiation and to the level of conservation. Well preserved cells ranged in size from 8 to 15μ and had a central nucleus and high cytoplasmic ratio. Well differentiated elements had chromatin finely arranged while in less differentiated ones it appeared in hyperchromatic clumps. A single round amphophylic macronucleolus was often detected (fig. 3). Badly preserved cells showed several small intracytoplasmic vacuoles, indicating degenerative phenomena, which tended to coalesce until they filled the entire cytoplasm, masking the nuclear structure.

The sarcomatous component observed in 3 of our cases, presented as isolated or coupled pleomorphic cells, of uneven size and shape ranging from round to fusiform. Their cytoplasm was pale, basophilic with indistinct borders blended into the background of the smears and sometimes with bipolar processes. Single nucleus, relatively large showed variable chromatin patterns from vescicular to finely arranged or very hyperchromatic. Prominent nucleoli were often detected (figg. 4a - b). Multinucleated tumour cells and atypical mitoses were found only in the case of neoplasm protruding through the cervical os. In our cases we did not find heterologous elements.

DISCUSSION

A recent suggestion that the frequency of uterine MMMT has increased ([2]) and the above mentioned survival rates have

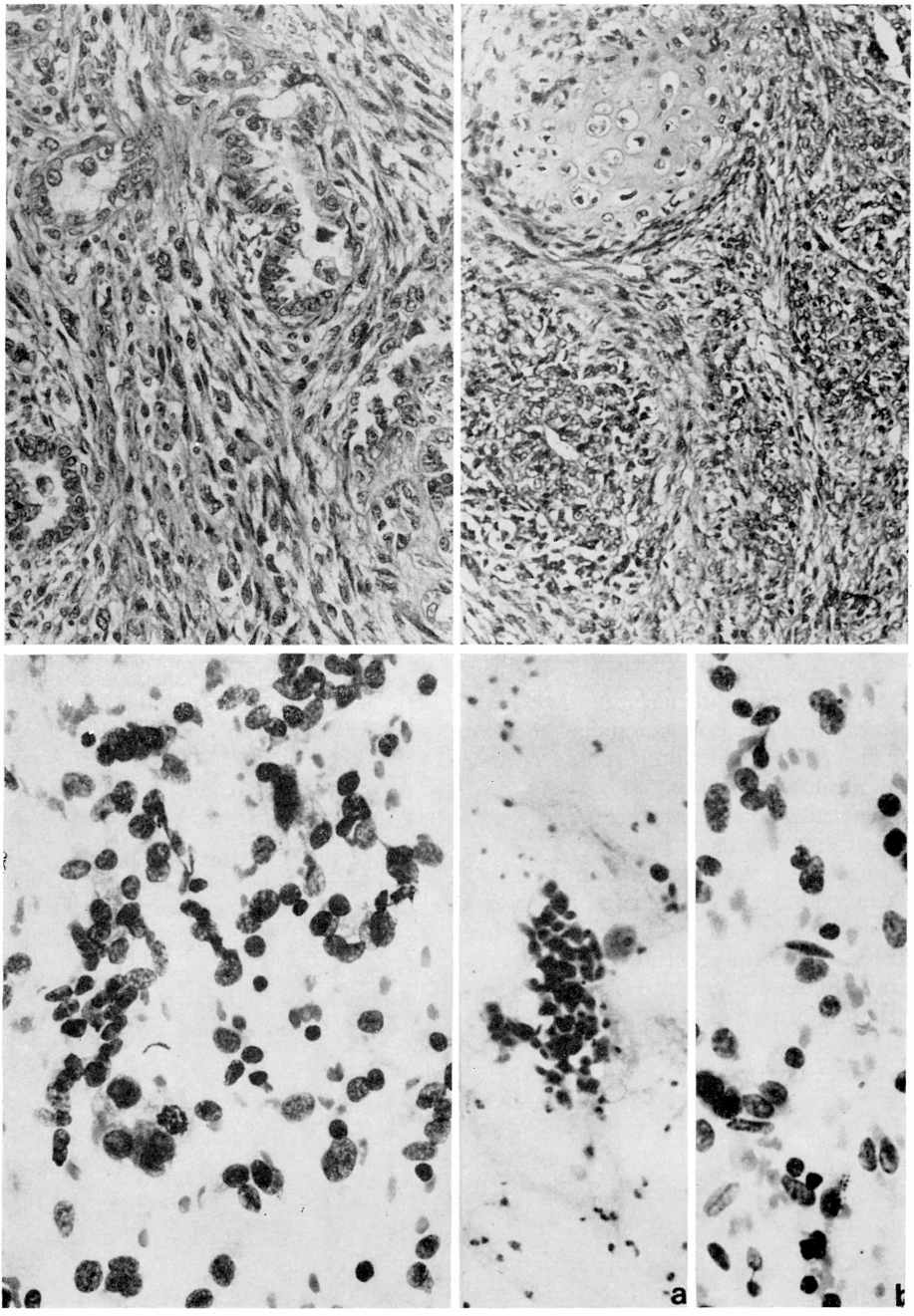

Fig. 1. — Epithelial and stromal component in MMMT homologous type (EE ×400).

Fig. 2. — Chondrosarcomatous differentiation in MMMT heterologous type (EE ×400).

Fig. 3. — Epithelial neoplastic cells with chromatin arranged in hypercromatic clumps. Atypical mitotic figure is present (PAP ×400).

Fig. 4. — *a*) Neoplastic cell likely of mesenchymal origin, with abundant cytoplasm and macronucleolus (PAP × 400). *b*) Solitary sarcomatous element with bipolar cytoplasmic processes (PAP ×400).

stimulated much research towards discovery of widely adoptable diagnostic methods such as exfoliative cytology.

While uterine sarcomas almost exclusively originate submucosally and infrequently shed cells before reaching considerable size, uterine MMMT as a result of extensive inflammatory and degenerative phenomena, tend to exfoliate more than other mesenchymal neoplasms. This characteristic is confirmed by the high incidence of mixed tumour diagnosis on cervical smears in the series of Parker ([3]) (66%), White ([4]) (53%) and Hajdu ([5]) 80%) as well in our series (70%; one case after revision). Hajdu and Hajdu ([5]) and Massoni and Hajdu ([6]) stated that there are no characteristic cytologic features of this tumor, but MMMT should be suspected by the presence of bizarre spindle shaped cells and malignant glandular cells. An-Foraker and Kawada ([7]) emphasized the difficult diagnosis of MMMT because of the variety of cellular elements that can often be misinterpreted; endometrial aspiration smears, preserving heterologous elements, better can improve the diagnostic accuracy.

In our series the greatest number of neoplastic cells was detected in the endocervical scrapings (except for the case in which the neoplasm protruded to the cervical os). Since we tend to push the swab over the OUS, our samples are the result of a direct scraping of tumoral mass. Therefore by using the latest tools for endometrial scraping such as Perma or Endocyte curettes we shall be able to increase the number of positive smears improving the amount and the cytologic preservation of epithelial and mesenchymal cells as An-Foraker and Kawada suggest.

According to our data, we think that a cytological diagnosis of MMMT may be possible even in the preclinical period of tumour development, by repeating smears when we detect neoplastic cells and badly preserved elements which may suggest a mesenchymal component, and performing an endometrial scraping in such cases.

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