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Immunohistochemical study of sarcoma-like mural nodules in a mucinous cystadenocarcinoma of the ovary

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Summary. We describe an ovarian mucinous cystadenocarcinoma with several sarcoma-like mural nodules (SLMN). The distinction between these lesions and foci of anaplastic carcinoma is important because of the poor prognosis of the latter. We have studied the potential value of immunohistochemistry in the differential diagnosis of these two lesions. In contrast to an anaplastic carcinoma, which was largely composed of keratin-positive cells, SLMN were negative or only focally positive. Therefore, in distinguishing SLMN from foci of anaplastic carcinoma, keratin stains may be added to other gross and microscopical differential features, such as size, demarcation, and presence or lack of obvious carcinomatous elements.

Key words: Ovary – Mucinous tumour – Sarcoma-like mural nodules – Anaplastic carcinoma – Immunohistochemistry

Introduction

Mucinous cystic tumours of the ovary, whether benign, borderline or malignant, may be associated with sarcoma-like mural nodules (SLMN) that resemble gingival epulis or giant cell tumours of bone (Prat and Scully 1979b). Although the clinico-pathological features of the nodules and the follow-up of several patients suggest that these lesions are reactive rather than neoplastic, their exact nature remains controversial. It is obvious, however, that their distinction from true sarcomatous mural nodules (Prat and Scully 1979a) and foci of anaplastic carcinoma (Prat et al. 1982) – also described in association with mucinous ovarian tumours – is extremely important, since each of these lesions carries a different prognosis. The uniform sarcomatous appearance of the former and the lack of circumscription and occasional presence of vascular invasion in the latter usually allow us to separate them. However, difficulties in differential diagnosis have been enhanced by the existence of tumours containing both SLMN and foci of anaplastic carcinoma (Fujii et al. 1985), as well as of nodules exhibiting morphological features of both lesions. Kenney et al. (1984) tried to classify tumours with giant cells in four categories based on whether or not the neoplasms were predominantly giant cell tumours (Groups I and II) or whether there was another associated neoplasm in the vicinity of the giant cell tumour (groups III and IV). The SLMN found in the wall of ovarian mucinous cystic tumours belong to group IV.

We describe an ovarian mucinous cystadenocarcinoma with several SLMN. The potential value of immunohistochemistry in the differential diagnosis of these lesions is discussed.

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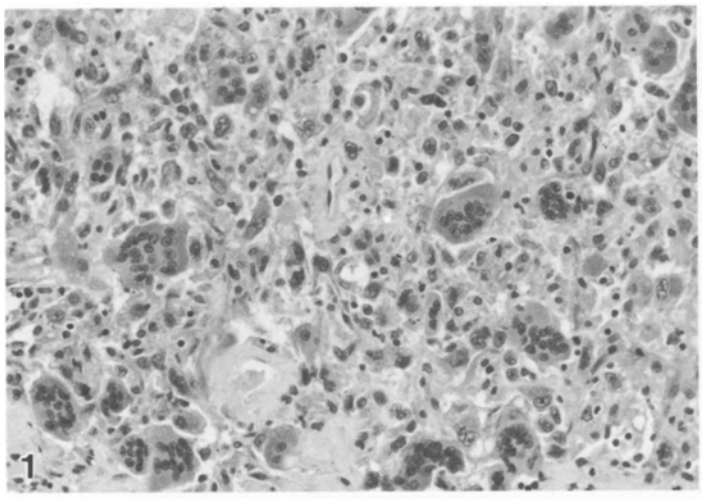
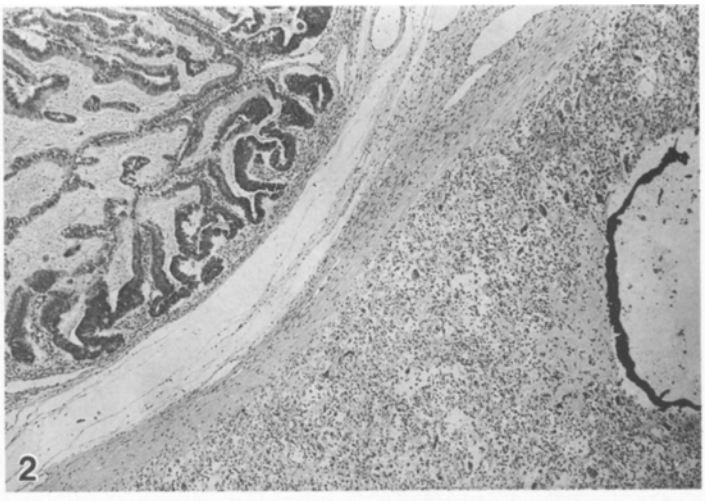
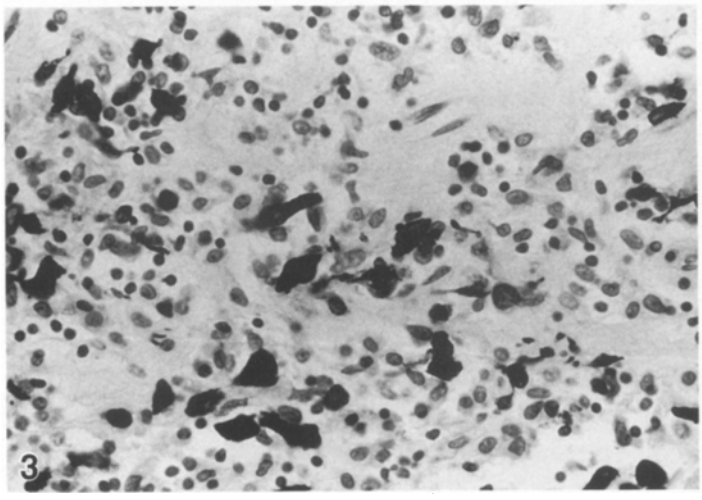
Case report

A 22-year-old woman complained of abdominal swelling of 3–4 months' duration. Pelvic examination revealed a left adnexal mass. At laparotomy, there was a 40-cm cystic ovarian tumour which ruptured during removal. A unilateral salpingo-oophorectomy and contralateral ovarian biopsy were performed. The tumour was a large multilocular cyst. Its outer surface was largely smooth with scattered haemorrhagic fibrous tags. Five reddish brown nodules, ranging from 0.5 to 1.5 cm in diameter, were found on the inner surface of the cyst wall. On microscopical examination, the cyst was partly lined by a single layer of mucinous epithelium with numerous goblet cells. In other areas, the epithelium showed stratification up to 3–4 layers and papillary infolding. The cells contained large hyperchromatic nuclei with one or two prominent nucleoli. There were also atypical glands in a back-to-back distribution exhibiting a cribriform pattern. Numerous nests of luteinized stromal cells were found around the tumour glands.

The mural nodules appeared well-circumscribed. They were composed of granulation tissue with abundant chronic inflammatory cells, such as lymphocytes, plasma cells and histiocytes. Haemosiderin-laden and foamy macrophages were prominent in some areas. Admixed with these elements were many epulis-like multinucleated giant cells as well as spindle-shaped and some pleomorphic "mono" and "multinucleated" cells (Fig. 1). The epulis-like cells were concentrated around areas of haemorrhage and contained







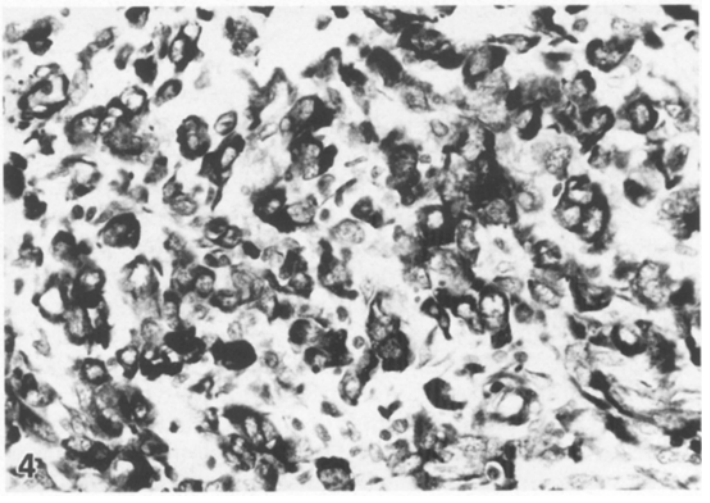


Fig. 1. Representative histology of a sarcoma-like mural nodule. It is composed of epulis-like multinucleated cells admixed with mononucleated cells, several of them atypical, as well as inflammatory cells. H&E, ×200 (Reduced to 85%)

Fig. 2. The mucinous epithelium displays positive stain for antikeratin CAM 5.2. The sarcoma-like mural nodule appears largely negative. Notice a ruptured epithelial cyst within the nodule. ABC, ×100 (Reduced to 85%)

Fig. 3. Sarcoma-like mural nodule. Only occasional mononucleated cells stained positively with anti-keratin CAM 5.2. ABC, ×400 (Reduced to 85%)

Fig. 4. Focus of anaplastic carcinoma in an ovarian mucinous tumour. The cells stained strongly positive for anti-keratin CAM 5.2. ABC, ×400 (Reduced to 85%)

several round to oval nuclei which appeared uniform. In contrast, some of the mononucleated cells were atypical and had hyperchromatic nuclei which contained mitotic figures. Some of these cells also exhibited degenerative changes such as nuclear pyknosis and cytoplasmic eosinophilia. Some of the nodules appeared partly fibrous and even hyalinized. One of the nodules contained remnants of a ruptured epithelial cyst. There was no evidence of capsular or vascular invasion in any of the mural nodules.

Immunohistochemical techniques (ABC) demonstrated a positive staining for wide spectrum keratin (WSK), CAM 5.2, epithelial membrane antigen (EMA), carcinoembryonic antigen (CEA) and CA 19.9 in the mucinous epithelial component of the tumour (Fig. 2). In three of the nodules, both the epulis-like giant cells and the pleomorphic cells were positive for vimentin, negative for WSK and CAM 5.2 and focally positive for CEA. The remaining two nodules, however, showed, in addition, a focal positive staining for WSK, CAM 5.2, CEA, CA 19.9 and EMA in some of the mononucleated cells (Fig. 3). These cells were negative for alcian blue stains. None of the pleomorphic or atypical cells were positive for keratin. A few of the giant epulis-like and pleomorphic cells were also positive for muramidase.

The patient is alive without evidence of disease 3 years after surgery.

We compared the pathological and immunohistochemical features of the SLMN with those of a previously reported ovarian mucinous tumour with mural foci of anaplastic carcinoma (Prat et al. 1982). The latter lesion contained a higher number of pleomorphic cells, was poorly demarcated and had evidence of vascular invasion. The cells contained bizarre hyperchromatic nuclei and had abundant eosinophilic cytoplasm. No epulis-like giant cells were found. The pleomorphic cells were strongly positive for CAM 5.2 (Fig. 4) and vimentin, focally positive for WSK and negative for EMA, desmin and CA 19.9. The surface epithelial component stained positively for WSK, CAM 5.2, EMA, CEA, and was negative for vimentin, desmin and CA 19.9.

Discussion

Mucinous cystic tumours of the ovary are occasionally associated with SLMN (Prat and Scully 1979b). These consist of a heterogeneous population of giant multinuc-

leated cells of the epulis type, oval to spindle-shaped mononucleated cells and inflammatory cells, and almost always contain foci of haemorrhage and necrosis. The SLMN may exhibit three morphological patterns: pleomorphic and epulis-like, pleomorphic and spindle-celled, and giant cell histiocytic. Each of these patterns differs histologically from true ovarian sarcomas (Prat and Scully 1979a) and from foci of anaplastic carcinomas (Prat et al. 1982) also found in the walls of some ovarian mucinous tumours. Despite their marked cellular pleomorphism and high mitotic rate, their gross circumscription and the survival of all the patients with SLMN who have been followed (Prat and Scully 1979b) suggest that the nodules represent a reactive rather than a neoplastic lesion. We have found identical reactions to those of SLMN in various malignant (renal cell carcinoma, high-grade uterine sarcoma) as well as benign tumours. They probably represent inflammatory reactions to haemorrhage, mucin or tumour products and do not have, by themselves, any prognostic implication.

The immunohistochemical findings in the five mural nodules of the present case also support the reactive nature of these lesions. In fact, the majority of the cells of these nodules stained positively for vimentin and muramidase and negatively for keratin and other epithelial markers. However, focal positivity for WSK, CAM 5.2 and CEA was encountered in a few mononucleated cells within two nodules. Furthermore, in one of them, keratin-positive cells were present in the vicinity of a ruptured epithelial cyst, suggesting that they had spilled off the wall of the cyst into the stroma. This finding, together with the focal positivity for CEA in the giant cells, supports the idea that SLMN result from an unusual reaction to intramural haemorrhage or to the mucinous content of the cyst.

Although the distinction between foci of anaplastic carcinoma and true sarcomatous nodules may not prove to have prognostic significance, both types of nodules should be separated from SLMN because of the favourable prognosis of the latter (Prat and Scully 1979b). From a histological viewpoint, the small size and sharp demarcation of the SLMN, the lack of vascular invasion and the absence of obvious sarcomatous and carcinomatous elements are all features in favour of a benign, reactive lesion.

Immunohistochemistry may be useful in distinguishing the different types of nodules that may develop in the wall of ovarian cystic tumours. However, only a few cases have been studied (Brujin et al. 1987; Clarke 1987) and most of them were foci of anaplastic carcinoma, malignant mixed mullerian tumours or pure sarcomatous lesions. Puts et al. (1987) studied three ovarian mucinous cystadenocarcinomas containing mural nodules. Although two of the tumours probably belong to the malignant mixed mullerian category, the mural nodule of the third was composed of spindle-shaped cells admixed with multinucleated giant cells; both spindle and giant cells were positive for vimentin. The authors contended that the features of this mural nodule were identical to those of the pleomorphic and spindle-celled variant of SLMN.

In distinguishing SLMN from foci of anaplastic carcinoma, stains for intermediate filaments are useful but not conclusive. Whereas the cells of the SLMN were positive for vimentin and only focally positive for keratin, the anaplastic foci of a mucinous cystadenocarcinoma were largely composed of keratin-positive cells. Kessler et al. (1990) described the immunohistochemical features of two sarcoma-like mural nodules with foci of anaplastic carcinoma in an ovarian mucinous cystadenocarcinoma. The nodules were composed of spindle and polygonal cells admixed with inflammatory and multinucleated, epulis-like, giant cells. In some areas, obvious foci of invasive carcinoma merged imperceptibly with the sarcoma-like tissue. The epithelial component of the tumour and some of the atypical spindle and polygonal cells within the stroma stained positively for keratin. The spindle and multinucleated giant cells that lacked atypicality were negative for keratins and positive for vimentin.

The focal keratin positivity observed in some of the SLMN cells can have several explanations. First, since SLMN always arise in close association with mucinous epithelium, the positive stain can be attributed to entrapped cells that possibly spilled from the ruptured epithelial surface. However, it may represent a focal inappropriate expression or a cross-reaction with other type of intermediate filaments, such as actin, which share certain epitopes with keratins. In fact, similar phenomena have been observed in other mesenchymal lesions such as smooth muscle tumours or the post-operative spindle cell nodules of the urinary tract (Wick et al. 1988).

In contrast to true sarcomatous nodules, SLMN usually occur in young women and are characterized by small size, sharp demarcation, lack of vascular invasion and heterogeneous cell population (Lange 1990). In some cases, however, distinction between the two lesions can be extremely difficult. Furthermore, true sarcomas can also contain inflammatory cells and occasionally giant cells of the epulis type. Immunohistochemistry does not help in the differential diagnosis, since both SLMN and true sarcomas are negative for keratins and positive for vimentin (de Nictolis et al. 1990).

Thus, we conclude that, although SLMN may contain a few keratin positive cells, a strong and diffuse positivity for keratin should be interpreted as evidence of anaplastic carcinoma. Therefore, in distinguishing SLMN from foci of anaplastic carcinoma, keratin stains could be added to other gross and microscopical differential features, such as size, demarcation, and presence or lack of obvious carcinomatous elements.

References

Brujin JA, Smit V, Que DJ, Fleuren GJ (1987) Immunohistology of a sarcomatous mural nodule in an ovarian mucinous cystadenocarcinoma. Int J Gynecol Pathol 6:287–293

Clarke TJ (1987) Sarcoma-like mural nodules in cystic serous ovarian tumors. J Clin Pathol 40:1443–1448

Fujii S, Konishi I, Kobayashi F, Okamura H, Yamabe H, Mori T (1985) Sarcoma-like mural nodules combined with a microfocus of anaplastic carcinoma in mucinous ovarian tumor. Gynecol Oncol 20:219–233

Kenney RM, Prat J, Tabernero M (1984) Giant-cell tumor-like proliferation associated with a papillary transitional cell carcinoma of the renal pelvis. Am J Surg Pathol 8:139–144

Kessler E, Halpern M, Koren R, Dekel A, Goldman J (1990) Sarcoma-like mural nodules with foci of anaplastic carcinoma in ovarian mucinous tumor: clinical, histological and immunohistochemical study of a case and review of the literature. Surg Pathol 3:211–219

Lange JM (1990) Diagnostic dilemmas in gynecologic and obstetric pathology. Semin Diagn Pathol 7:146–155

Nictolis M de, Loreto C di, Cinti S, Prat J (1990) Fibrosarcomatous mural nodule in an ovarian mucinous cystadenoma: report of a case. Surg Pathol 3:309–315

Prat J, Scully RE (1979a) Sarcomas in ovarian mucinous tumors. Cancer 44:1327–1331

Prat J, Scully RE (1979b) Ovarian mucinous tumors with sarcoma-like mural nodules. Cancer 44:1332–1344

Prat J, Young RH, Scully RE (1982) Ovarian mucinous tumors with foci of anaplastic carcinoma. Cancer 50:300–304

Puts J, Moesker O, Aldeweireldt J, Vooijs GP, Ramaekers FCS (1987) Application of antibodies to intermediate filament proteins in simple and complex tumors of the female genital tract. Int J Gynecol Pathol 6:257–274

Wick MR, Brown BA, Young RH, Mills SE (1988) Spindle cell proliferations of the urinary tract. An immunohistochemical study. Am J Surg Pathol 12:379–389