Uterine endometrial stromal sarcoma with smooth muscle and glandular differentiation

W G McCluggage, A J Cromie, C Bryson, A I Traub

Abstract
This report describes a uterine tumour exhibiting areas of both endometrial stromal and smooth muscle differentiation. There was extensive intravascular permeation within the myometrium as well as extrauterine vascular involvement. The endometrial stromal component had a myxoid appearance and the smooth muscle component exhibited the typical features of intravenous leiomyomatosis. An additional feature was the presence of numerous benign endometrial-type glands within the neoplasm. In many areas a “zoning” phenomenon was present, with endometrial glands surrounded by endometrial stroma, which was in turn surrounded by smooth muscle. This unique combination of endometrial glands, endometrial stroma, and smooth muscle has, to the best of our knowledge, not been described previously and adds to the morphological spectrum of mixed endometrial stromal-smooth muscle tumours. This report discusses the differential diagnosis of this lesion, which has been designated a low grade endometrial stromal sarcoma with smooth muscle and glandular differentiation. (J Clin Pathol 2001;54:481–483)

Keywords: uterus; endometrial stromal sarcoma; smooth muscle neoplasm; intravenous leiomyomatosis

Case report
A 45 year old woman, para 5+3, presented with a four year history of menorrhagia unresponsive to medical treatment. Vaginal examination revealed a 10–12 weeks size mobile uterus. Total abdominal hysterectomy was performed with preservation of both ovaries at the patient’s request. At surgery, the uterus was enlarged to 12 weeks in size and the rest of the pelvis appeared normal.

PATHOLOGICAL FINDINGS
The uterus with attached cervix weighed 220 g and measured 11 cm in length. An 8 cm maximum diameter intramural mass was present, which projected into the endometrial cavity. This mass was focally firm and white in appearance with other softer tan coloured areas. Several cystic areas containing altered blood were present within the mass. Several satellite nodules were present within the myometrium surrounding the main mass. A 6 cm length of right fallopian tube was present.

Histology showed the main lesion to contain areas of both endometrial stromal and smooth muscle differentiation. The endometrial stromal component, which made up approximately 30% of the tumour, was composed of small ovoid to spindle shaped cells with scanty cytoplasm set in a myxoid stroma (fig 1A). There was little nuclear pleomorphism and a formal mitotic count revealed 2–3 mitoses/10 high power fields. Within most of these areas, benign endometrial glands were present intimately surrounded by the endometrial stroma (fig 1B). Several of the endometrial glands were cystically dilated and contained altered blood within the lumen, these areas corresponding to the cystic foci identified grossly. The remainder of the neoplasm was composed of typical smooth muscle (fig 1C), which showed no nuclear pleomorphism or mitotic activity. In many areas there was a characteristic “zoning” phenomenon, with glands surrounded by endometrial stroma, which was in turn surrounded by smooth muscle (fig 1D). Histology of the satellite lesions showed well circumscribed nodules lying within dilated vascular channels. Some of these nodules were composed entirely of smooth muscle, which usually exhibited extensive hyalinisation, with thick walled blood vessels (fig 2A). Other nodules contained a mixture of endometrial glands, endometrial stroma, and smooth muscle, again
exhibiting a zoning phenomenon (fig 2B). Histology of a section taken from the fallopian tube showed dilated paratubal venous channels containing smooth muscle nodules. Immunohistochemical staining for desmin (Dako, Ely, UK) showed diffuse strong cytoplasmic immunoreactivity of the typical smooth muscle elements but little or no staining of the endometrial stromal component. Factor VIII staining (Dako) confirmed that the satellite nodules were situated within dilated vascular channels.

The surface endometrium showed proliferative activity and no important lesions were seen within the cervix.

Discussion

The lesion we describe contained a large component of both endometrial stroma and smooth muscle. The existence of such hybrid neoplasms is recognised in the World Health Organisation classification of uterine tumours. The fact that such tumours exist is not surprising because it has been suggested that multipotential cells are present in the uterus that can differentiate into endometrial stroma and smooth muscle. In our case, the endometrial stromal component was perhaps slightly unusual in that it had a myxoid appearance, rather than exhibiting the dense cellularity usually associated with neoplasms of this differentiation. However, the existence of myxoid endometrial stromal tumours has recently been emphasised. The smooth muscle elements exhibited extensive hyalinisation and contained numerous thick walled blood vessels, especially within the intravascular component, characteristic of the features often seen in intravenous leiomyomatosis. Staining for desmin highlighted the strongly positive smooth muscle elements contrasting with the negative endometrial stromal components.

An unusual feature was the presence of many benign endometrial glands within the lesion, both within the main mass and within the intravascular component. There was often a characteristic zoning phenomenon, with glands surrounded by endometrial stroma, which in turn was surrounded by smooth muscle. Glandular structures may uncommonly be found within endometrial stromal neoplasms. These are usually focal and inconspicuous but can rarely be extensive, and differ from the foci of

Figure 1 (A) Endometrial stromal component containing ovoid to spindle shaped cells in a myxoid stroma. (B) Benign endometrial glands are surrounded by endometrial stroma. (C) Typical smooth muscle elements. (D) A “zoning” phenomenon is present with endometrial glands surrounded by endometrial stroma, which in turn is surrounded by smooth muscle.

Figure 2 (A) Dilated vascular channel containing smooth muscle with hyalinisation and thick walled blood vessels. (B) Dilated vascular channel containing tumour exhibiting “zoning” phenomenon.
epithelioid or sex cord-like differentiation, which are more commonly seen.12–14 As far as we are aware, glandular elements have not been described previously in mixed endometrial stromal-smooth muscle neoplasms, although sex cord-like differentiation has. An endometrial stromal nodule with both smooth and skeletal muscle components has also been described.15 The designation stromyomoya has previously been used, but this is misleading because it implies a benign neoplasm. We have used the designation low grade endometrial stromal sarcoma with smooth muscle and glandular differentiation to emphasise the potential for tumour recurrence and/or metastasis, which may be late. The tumour involved paratubal blood vessels and it is possible that residual tumour still involves pelvic veins. A case has been reported of a low grade endometrial stromal sarcoma with extensive smooth muscle differentiation resembling intravenous leiomyomatosis and exhibiting extension to the inferior vena cava and cardiac chambers.16

Alternative diagnoses considered included an adenosarcoma. However, adenosarcoma characteristically is a well circumscribed polyoid mass arising from the endometrium and without a tendency for extensive intravascular permeation. Moreover, it usually exhibits a "club-like" pattern of growth, with papillary fronds and periglandular stromal condensation creating a cellular cambium layer just beneath the glandular component. Although both endometrial stromal and smooth muscle differentiation can be found in adenosarcoma, the presence of unequivocally benign smooth muscle elements and of a zoning phenomenon is unusual. An unusual morphological variant of adenomyosis was also considered because this is characterised by endometrial glands and stroma surrounded by hypertrophic smooth muscle. Moreover, intravascular growth can occur in adenomyosis. However, such pronounced intravascular growth is uncommon in adenomyosis, as is an intravascular smooth muscle component without endometrial glands and stroma, which was seen focally in our case. In addition, extravesical involvement of blood vessels around the fallopian tube would be unusual in adenomyosis. Intravenous leiomyomatosis with entrapped endometrial glands and stroma was also considered.17 However, although occasional entrapped benign endometrial glands with stroma have been described in intravenous leiomyomatosis,18 in our case the endometrial glandular and stromal components were so extensive throughout the lesion that we prefer to interpret this as an endometrial stromal sarcoma with smooth muscle and glandular differentiation.

In summary, we describe an unusual uterine endometrial stromal sarcoma exhibiting extensive smooth muscle and glandular differentiation. This adds to the morphological spectrum of mixed stromal neoplasms of the uterus.

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