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Case Report

Aggressive angiomyxoma of the vulva

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Abstract

Background. Aggressive angiomyxoma is a rare soft tissue tumour that carries a high risk of local relapse. It is a slowly growing and locally infiltrating tumour.

Case. We describe the case of an aggressive pelvic-perineal angiomyxoma arising in a 36-year-old woman. The patient had a mass that grew before, during and after her pregnancy. Transperineal surgery was performed. The resection margins were free of disease.

Conclusion. Our case confirms what has previously been published concerning the possible hormone-dependence of this neoplasm. Given the positive estrogen and progesterone receptor status of this tumour, we will consider hormonal treatments in the case of a future relapse.

Keywords: Aggressive angiomyxoma; Soft tissue tumour; Vulva

Introduction

Aggressive angiomyxoma is a rare soft tissue tumour that carries a high risk of local relapse [1]. About 150 cases have been published in the literature since 1983, when it was first described by Steeper and Rosai [3] as a slowly growing myxoid neoplasm [2]. It almost exclusively involves the genital, perineal and pelvic regions of women of child-bearing age and has its median incidence in the fourth decade [1]. However, there have also been rare cases diagnosed in perimenopausal women, men and children, and it has been found not only in the pelvic soft tissue, but also in the retroperitoneum, vesica, vagina, vulva, perineum and scrotum [4]. It is a slowly growing and locally infiltrating tumour [1]. Local relapses, which occur in 30–40% of the cases, often appear many years (sometimes decades) after the first excision [1]. The literature also includes two cases diagnosed in pregnant women and a third relapsing during pregnancy [5].

Case report

We here report the case of an aggressive pelvic-perineal angiomyxoma arising in a 36-year-old woman (VB), whose recent and remote medical history included no diseases worthy of note. She had only one at time pregnancy. Her body weight increased all through the pregnancy 15 kg. She underwent a cesarean section because of a breech presentation in January 2002. She noted a small mass at the level of the right labium majus, which grew extremely slowly before and during the pregnancy, but very rapidly after the birth.

For this reason, she underwent surgical excision of the nodule (a suspected lipoma) on August 5, 2003. Unexpectedly, the histological diagnosis of the excised mass (a 10 g

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oval nodule with a maximum diameter of 4.5 cm) was aggressive angiomyxoma.

Further diagnostic investigations were carried out, including nuclear magnetic resonance (NMR) and computed tomography (CT). NMR revealed a mass with a maximum diameter of 6.5 cm in the adipose tissue on the right side of the pelvic fossa, between the obturator and levator muscles of the anus, extending towards the right side of the perineum. The examination also showed a limited dislocation of the ampulla of the rectum, the involvement of the

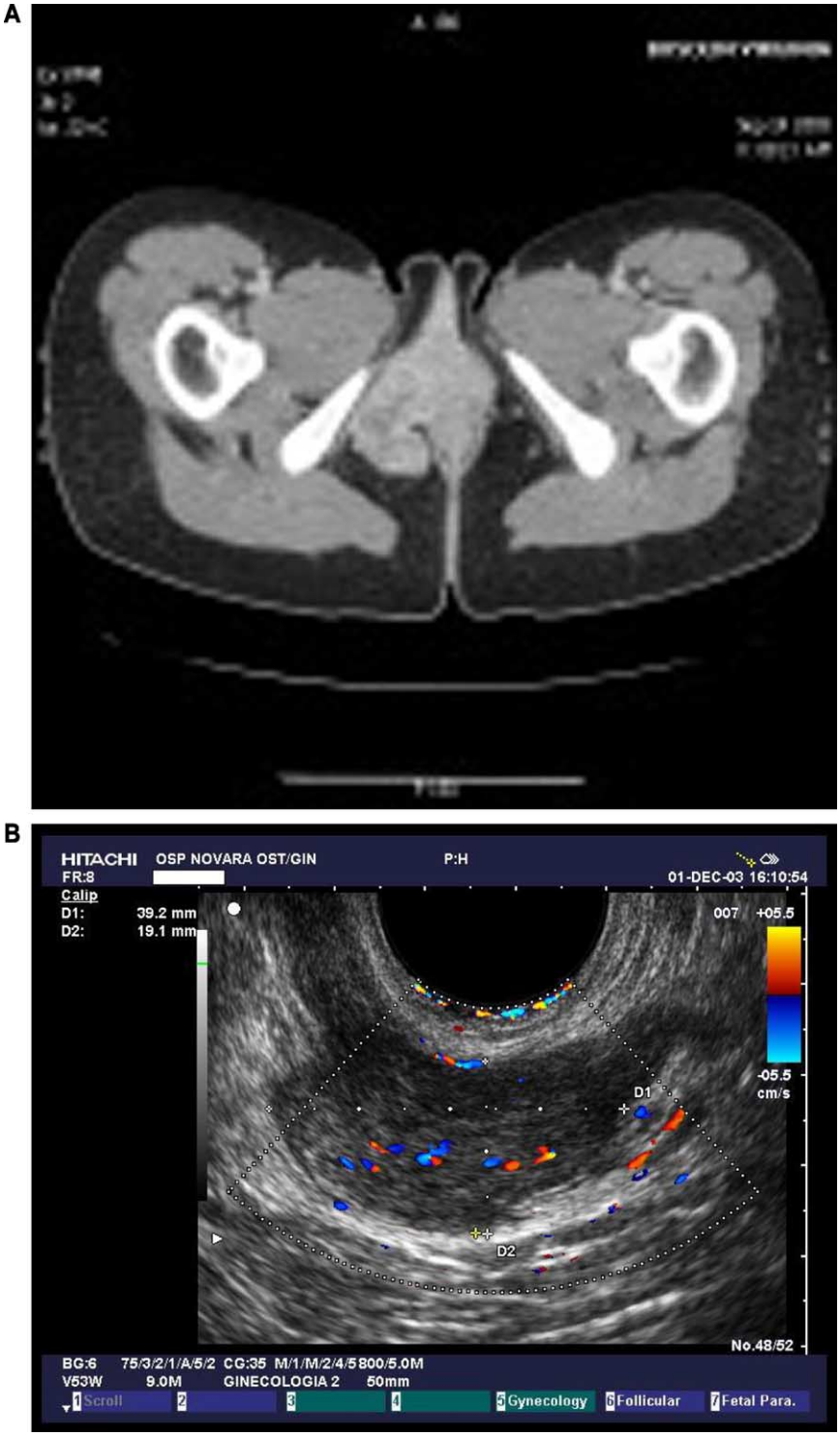

Fig. 1. CT of the pelvis (A) revealed the presence of a solid formation characterised by uneven late contrast enhancement on the right, in the adipose tissue between the internal obturator and levator muscles of the anus. Transperineal echography (B) revealed an ovoid mass with a homogeneous echotexture and poorly defined margins; colour-Doppler demonstrated irregular, thin and randomly dispersed vessels in the central area of the tumour.

right wall of the vagina, and an extension to the homolateral labium majus.

Contrast CT of the pelvis revealed the presence of a solid formation characterised by uneven late contrast enhancement on the right, in the adipose tissue between the internal obturator and levator muscles of the anus. This formation was 6.5 cm long cranio-caudally, extended into the perineal adipose tissue of the medial region of the thigh and then seemed to be displaced contralaterally and infiltrate the right lateral wall of the vagina and the homolateral labium majus (Fig. 1A).

Transperineal echography did not show any infiltration of the perineal muscles; transperineal ultrasonography revealed an ovoid mass with a homogeneous echotexture and poorly defined margins; colour-Doppler demonstrated irregular, thin and randomly dispersed vessels in the central area of the tumour (Fig. 1B).

A gynecological examination performed in December 2003 revealed an uninfiltrated vaginal wall, a soft and relatively immobile neoplasm with a diameter of about 8 cm that did not reach the upper part of the ischio-rectal fossa and a rectal wall that was neither infiltrated nor dislocated. This finding was confirmed by a transperineal echogram taken during the second admission.

For this reason, transperineal surgery was performed on December 2, 2003. A right peri-labial incision was made and the neoplasm was removed after an external sphincterotomy; the fossa was drained and the external anal sphincter was reconstructed (Fig. 2). The postoperative course was uneventful.

Upon macroscopic examination, the tumour was a 40 g grey-pink, lobulated and poorly circumscribed mass with a maximum diameter of about 15 cm. When sectioned, the surface had a soft, myxoid appearance with irregular borders.

The tumour was fixed in buffered formalin for 48 h and extensively sampled. After fixation, small samples were embedded in paraffin and routinely processed for histologic examination and immunohistochemistry.

Histological staining included hematoxylin–eosin (H&E), Masson's trichrome and Gomori's method for reticular fibres. The sections were also immunostained for vimentine, S100, smooth-muscle specific actin (SM-actin), desmin, CD 34, Mib 1 and estrogen and progesterone receptors.

Vimentine (Immunotech, Marseille, France, dilution 1:50)
Actin (DAKO, Carpinteria, CA, USA, dilution 1:100)
S100 (Biogenex, San Ramon, CA, USA, dilution 1:50)
Desmin (Biogenex, dilution 1:40)
CD 34 (Neo markers, Fremont, CA, USA, dilution 1:60)
Mib 1 (Immunotech, dilution 1:100)
Estrogen (DAKO, dilution 1:35)
Progesterone (DAKO, dilution 1:50)

H&E staining showed that the neoplasm was paucicellular and consisted of small, spindle-shaped cells with a poorly defined eosinophilic cytoplasm and bland nuclei. These were merged in an abundant myxoid and edematous stroma containing medium-sized to large vessels with thick and occasionally hyalinised walls (Fig. 3A). The neoplastic cells were frequently clustered around the vessels in a whorl fashion.

Despite a careful search, no mitotic figures were identified.

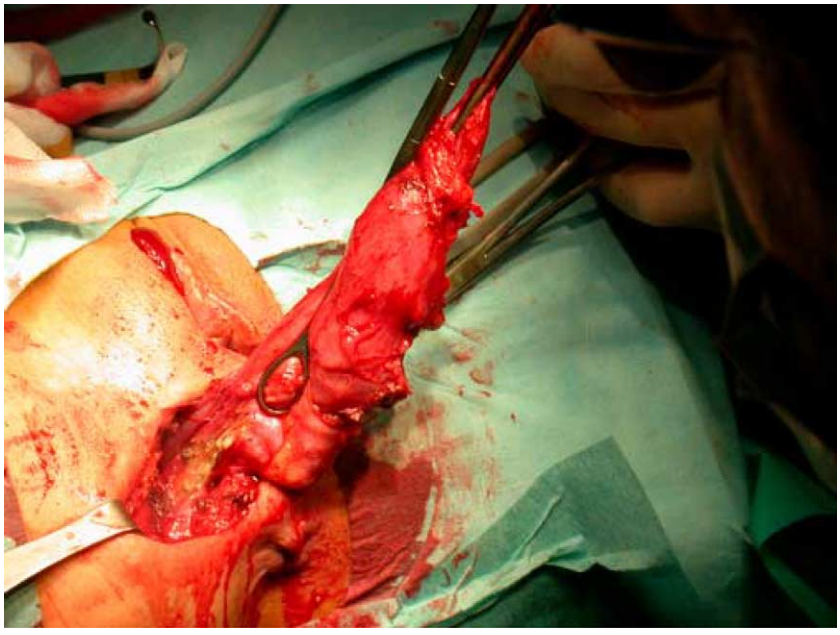

Fig. 2. A right peri-labial incision was made and the neoplasm was enucleated after an external sphincterotomy; the fossa was drained and the external anal sphincter was reconstructed.

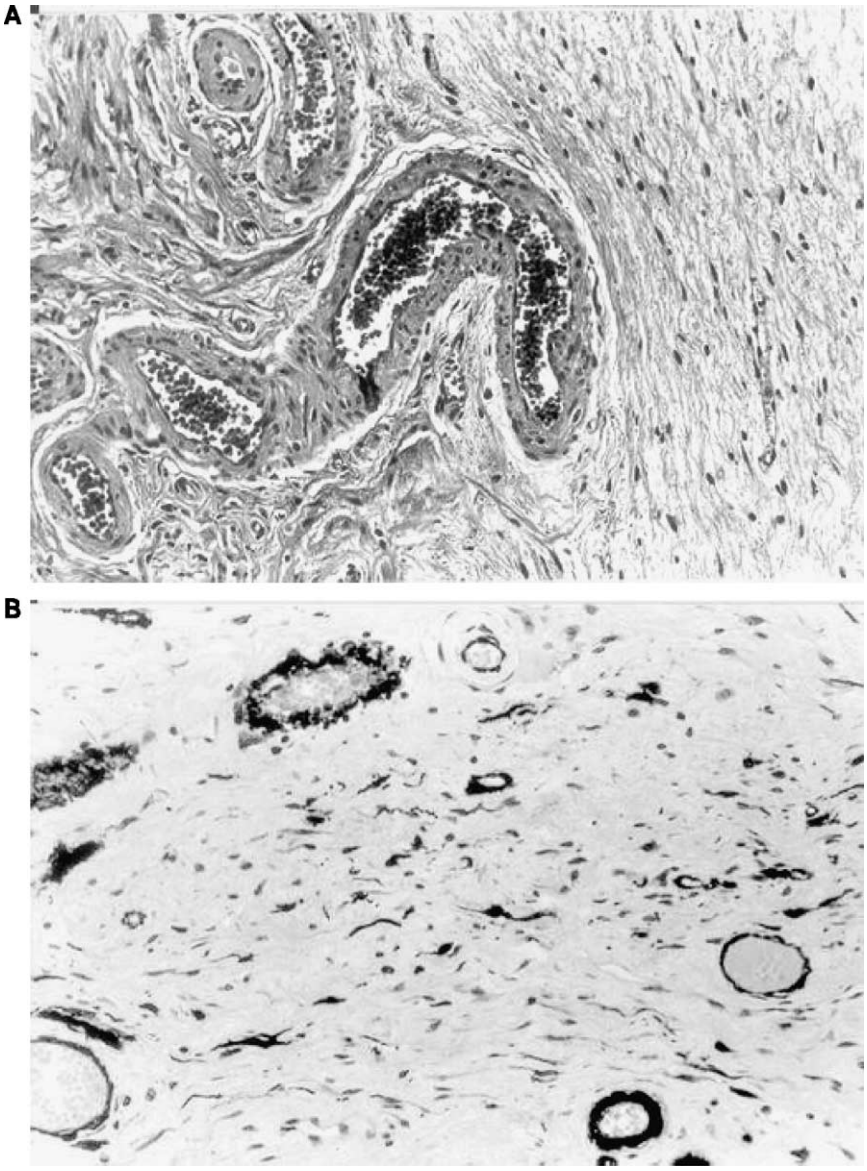

Fig. 3. Micrographs of neoplastic histologic sections: (A) on H&E examination a cluster of medium-sized arterioles are in close contact with spindle-shaped neoplastic cells, that (B) strongly stained with anti-SM actin antiserum. (original magnification 200×).

The neoplasm invaded the surrounding fatty tissue, the epithelial duct of Bartholin's gland and neural elements although surgical margins, identified as burned tissue, were pathologically negative.

Immunohistochemistry revealed strong positivity for vimentin, SM actin and desmin, whereas S100 and CD34 were negative (Fig. 3B). Estrogen and progesterone antisera disclosed positively stained nuclei in about 90% of neoplastic cells.

On the basis of these findings, a diagnosis of deep (aggressive) angiomyxoma was formulated. The main differential diagnoses included myxoid neoplasms (myxoid neurofibroma, low grade myxofibrosarcoma, myxoid liposarcoma, myxoid malignant fibrous histocytoma and superficial angiomyxoma), cellular angiofibroma, angiomyofibroblastoma and benign conditions such as chronic fibrosis or edema of the labia.

Discussion

Rosai and Steeper [3] first described a very slowly growing myxoid neoplasm of the genitals and perineal and pelvic region in 1983.

The pathogenesis of aggressive angiomyxoma is not clear. Recent studies have demonstrated a translocation at the level of chromosome 12 with a consequent aberrant expression of the HMGIC protein involved in DNA transcription [1].

The diagnosis of aggressive angiomyxoma is not usually made by the clinician, but by the pathologist. The most

frequent clinical diagnoses include Bartholin's cyst, labial cyst, polyp, Gartner's duct cyst, pedunculated soft tissue tumours or perineal herniation. In the case we report, the initial diagnosis was vulvar lipoma [5].

The sizes of the neoplasms described in the literature vary from 5 to 23 cm [6].

The largest (giant) aggressive myxoma was described in 1998 by Chen, who published a case report concerning a 38-year-old woman with a mass of 57 × 47 × 23 cm that had developed slowly over about 8 years, but particularly during pregnancy [7].

Our patient had a mass that grew extremely slowly before and during her pregnancy, but very rapidly after the birth of the fetus. This was probably due to the fact that patient's body weight increased significantly during the pregnancy (15 kg) and so the soft tissue's expansion masked the tumour growth.

The immunohistochemical study of our case revealed positive estrogen and progesterone receptors, with negative proliferative index (Mib1) indicating a low rate of proliferation.

Fishman et al. [8] described a case of a 37-year-old woman with a diagnosis of aggressive angiomyxoma who was weakly estrogen-positive and progesterone-negative, and relapsed during pregnancy. On the other hand, Htwe et al. [9] found that a 41-year-old woman diagnosed as having aggressive angiomyxoma during pregnancy with positive progesterone receptors and negative estrogen receptors.

As described in previous case reports, this tumour frequently requires a combined abdomino-perineal approach [7]. After the histological diagnosis of the first surgical excision, several investigations were undertaken to evaluate the topography of the tumour more precisely with the aim of making a complete but as conservative an excision as possible with the second operation, given the young age of the patient.

The right perilabial incision allowed confirmation of the clinical and echographic findings, and so, as there was a clear cleavage between the neoplasm and the levator muscle of the anus, perineal access was sufficient.

The resection margins were free of disease.

Given the topographical variability of this genital tumour, no standardised surgical procedure has been described in the literature, but all of the authors have underlined the importance of the complete eradication of the disease.

Positive lesion margins are certainly a very important factor when considering the possibility of relapse because of the local infiltration capacity of the tumour, even though a broad resection with tumour-free margins does not totally prevent a recurrence [4].

It has been reported that a recurrent aggressive angiomyxoma can be treated using GnRH agonists, which leads to NMR-detected disease remission and makes it possible to avoid further destructive surgery [4,10]. Given the positive estrogen and progesterone receptor status of the tumour here described, we consider hormonal treatments in the case of a future relapse.

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