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Aggressive angiomyxoma of the pelvis with high Ki-67 expression: a case report and literature review

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Summary

Purpose: As a benign tumor, aggressive angiomyxoma (AA) of the pelvis has a high local recurrence rate within several years after surgery. Radiation therapy has been proved to be ineffective for preventing recurrence. Ki-67 is a famous marker of cell proliferation for many cancers. High Ki-67 expression was correlated with radiosensitivity in other cancers. For aggressive angiomyxoma, Ki-67 expression and its relationship with radiosensitivity were rarely reported. Therefore, the authors present a case of AA with high Ki-67 expression. *Materials and Methods:* A 30-year-old woman presented with menorrhagia and a slowly growing mass on the right side of the pelvis. She was diagnosed with AA based on clinical features, radiological investigation, histopathology, and immunohistochemical stains. The tumor was excised successfully. Staining for Ki-67 was approximately 30% positive. After the excision, the patient was treated with a total dose of 48 Gy in 24 fractions using three-dimensional conformal radiation therapy. *Results:* The patient had local recurrent tumor at 16 months of follow-up after the surgery. *Conclusion:* AA of the pelvis has a high local recurrence rate within several years after surgery. Whether the recurrence was associated with high Ki-67 expression needs more clinical cases observations in the future.

Key words: Aggressive angiomyxoma; Case report; Ki-67; Pelvis; Radiotherapy.

Introduction

Aggressive angiomyxoma (AA) is an uncommon deep mesenchymal tumor that occurs in the vulva and perineal regions in women of reproductive age [1]. AA was first described by Steeper and Rosai in 1983 [2]. They indicated that AA is a rare type of soft tissue tumor characterized by local infiltration, microvascular growth, and small spindle cell proliferation within abundant myxoid stroma [2].

Ki-67 is a famous marker of cell proliferation for many cancers. High Ki-67 expression was correlated with poor prognosis and high radiosensitivity in other cancers [3]. For AA, Ki-67 expression and its relationship with radiosensitivity were rarely reported in previous reports. The authors report here a case of AA in the pelvis with high Ki-67 expression.

Case Report

A 30-year-old woman presented with menorrhagia and a slowly growing mass on the right side of the pelvis. The mass lasted for three years and had gradually increased in size and extended to the centre of the pelvis recently. Computed tomography of the pelvis showed a hypoattenuating tumor measuring 6.4×7.6 cm. The tumor was originating from the retrovesical space. The uterus and rectum were extruded. Tumor infiltration to adjacent tissues was not observed. Magnetic resonance imaging revealed that the mass was well-defined (Figure 1). The mass was isointense to muscle on T1-weighted images and high-intensity to muscle on T2-weighted images, with apparent enhancement on T1-weighted images after contrast administration. Furthermore, the mass presented a whorled pattern of signal intensity, particularly on the T2-weighted and contrast enhancement images. The patient underwent tumor resection using open retrovesical approach. The mass was elastic, covered by thin membrane, and located between the uterus and rectum. The mass was then successfully excised . The resected tumor was elastic, soft, and had a smooth surface. Histologically, the tumor was composed of bland spindle cells with round to ovoid nuclei. The cells were separated from each other by abundant myxoid (Figure 2) which contained numerous non-arborizing blood vessels, particularly capillaries and medium-sized arteries. Immunohistochemically, the tumor cells exhibited positive for vimentin, α-smooth muscle actin, CD34, HHF-35, estrogen receptor, and progesterone receptor. The tumor cells were negative for desmin and S100 protein. Staining for Ki-67 was approximately 30% positive (Table 1). The diagnosis of AA was achieved based on clinical features, radiological investigation, histopathology, and immunohistochemical stains. After the excision, the patient was treated with a total dose of 48 Gy in 24 fractions using three-dimensional conformal radiation therapy. During follow up, the patient was completely asymptomatic in the first ten months. However, follow-up computed tomography showed that the patient had a local recurrent tumor at 16 months after surgery.

Discussion

AA is a benign, slow-growing, locally infiltrative but non-metastasizing tumor that mainly occurs in the pelvis

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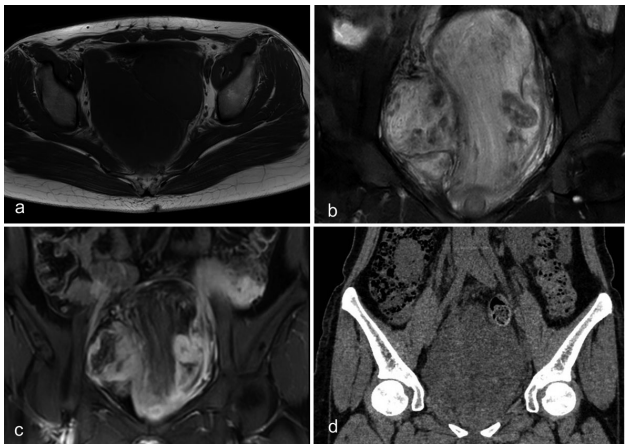

Figure 1. — Baseline magnetic resonance imaging and follow-up computed tomography of the mass. (a) Transverse T1-weighted image of the pelvis shows an isointense mass arising from retrovesical space. The uterus and rectum were extruded with no infiltration. (b) Coronal fat-suppression T2-weighted image of the pelvis shows a hyperintense mass with swirled internal architecture. (c) Coronal contrast-enhanced fat-suppression T1-weighted image shows a mass with inhomogeneous enhancement and whorled pattern. (d) Recurrence of the mass was detected on a follow-up computed tomography, which shows the size of the recurrent mass was even slightly larger than that of the baseline mass.

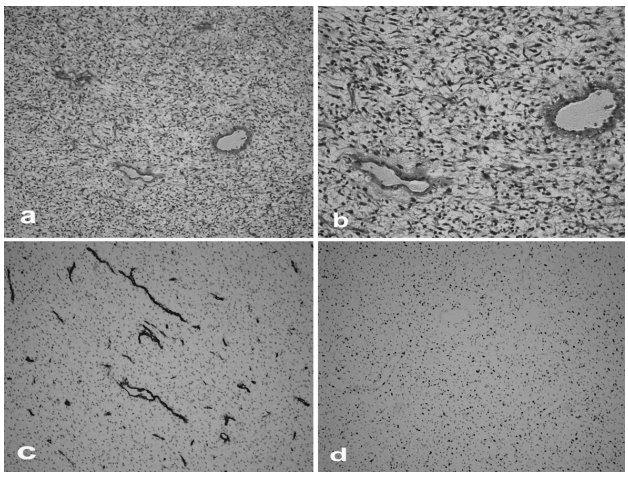

Figure 2. — Histological and immunohistochemical sections of the mass. Figure 2(a) shows spindle shaped cells lying in the abundant myxoid stroma containing scattered vessels with thickened and dilated walls (H&E staining, original magnification ×200). Figure 2(b) shows swollen nuclei with minimal cytoplasm (H&E staining, original magnification ×400). (c) The tumor cells exhibit positive nuclear staining for CD34. (d) The tumor cells shows approximately 30% positive nuclear staining for Ki-67.

and perineum in women of reproductive age [4]. Occasionally, AA can occur in men with a man-to-woman ratio of 1:6. AA is usually soft, large, cystic, and prone to local recurrence. The magnetic resonance imaging features of AA of the pelvis include isointensity or hypointensity on T1-weighted images and hyperintensity on T2-weighted images [5]. The swirled or layered internal architecture on T2-weighted images and contrast-enhancement T1-weighted images had been reported as a typical feature of AA [6]. Histologically, AA is composed of stellate and spindle-shaped cells distributed in a myxoid matrix background [7]. The lesion is supplied by blood vessels with variable caliber [7]. The vessels characteristically demonstrate thickened and hyalinized walls [7]. Immunohistochemically, the tumor cells are usually positive for vimentin, CD-34, desmin, smooth muscle actin, and estrogen and progesterone receptors. The tumor cells are usually negative for cytokeratin and S-100 protein [8].

Table 1. — *Immunostaining of the tumor cells.*

Vimentin	Strongly positive
Desmin	Negative
S-100	Negative
Cytokeratin	Weakly positive
Estrogen receptor	Positive
Progesterone receptor	Positive
CD34	Strongly positive
Actin	Positive
Bcl-2	Positive
Neurofilament	Positive
Ki-67	Approximately 30% positive

The differential diagnoses of AA of the vulva include myxoid liposarcomas, rhabdomyosarcomas, malignant fibrous histocytomas, and angiomyofibroblastomas. Myxoid liposarcoma and rhabdomyosarcomas usually occur in younger patients [9]. Malignant fibrous histocytomas and angiomyofibroblastomas tend to infiltrate or invade into adjacent tissues [9]. None of these tumors would be expected to show whorled internal architecture on T2-weighted images or contrast-enhanced T1-weighted images.

Complete surgical excision is usually the primary treatment choice. However, the local recurrence rate is significant. It has been reported that the local recurrence rate could reach up to 70% in the first three years after surgery [10]. Adjuvant treatments such as radiation therapy and chemotherapy were shown to be ineffective because of the low mitotic activity of AA [1]. Hormonal therapy may be effective in shrinking the tumor before surgery and preventing the recurrence [11]. Adjunct therapy using arterial embolization can be considered in case of partial resection of the tumor [12].

As a marker of cell proliferation, Ki-67 was rarely reported in AA in previous reports [4]. Silverman *et al.* reported a case of AA with multiple recurrences who had a Ki-67 index of 10-20% in “hot spots” of the primary tumor tissue and up to 30% in recurrent tumor tissue [13]. However, Ki-67 was negative for an AA case in another report [4]. Previous studies suggested that high expression of Ki-67 was a predictive marker of radiosensitivity for many

cancers [14]. For example, couture *et al.* reported that low expression of Ki-67 (< 20%) was a significant factor in local failure for patients with tumors of the oral cavity who are treated by radical radiotherapy ($p = 0.01$) [15]. The tumor cells of this case had a Ki-67 index of 30%. After the excision, this patient was treated with a total dose of 48 Gy in 24 fractions using three-dimensional conformal radiation therapy. However, follow-up computed tomography showed that this patient had local recurrent tumor at 16 months after surgery. Radiation therapy has been proved to be ineffective for preventing local recurrence of AA of the pelvis. This case further suggests that radiation therapy may be also ineffective for preventing local recurrence of AA with high Ki-67 expression.

Conclusion

In conclusion, AA is a benign, slow-growing, locally infiltrative but non-metastasizing tumor that mainly occurs in the pelvis and perineum in women of reproductive age. Complete surgical excision is usually the primary treatment choice. AA of the pelvis has a high local recurrence rate within several years after surgery. Adjuvant treatments including hormonal therapy and arterial embolization can be considered to prevent the recurrence. However, whether the recurrence of aggressive angiomyxoma was associated with high Ki-67 expression needs more clinical cases observations in the future.

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