Aggressive angiomyxoma of the pelvis with a cellular nodule composed of tumor cells showing epithelioid features

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Abstract

A 49-year-old female was admitted to a nearby hospital with a chief complaint of genital bleeding. Abdominal ultrasonography revealed an intrapelvic mass, and she was referred to our hospital. Computed tomography and magnetic resonance imaging revealed a huge mass in the pelvic cavity. T2-weighted images (Figure 1A) and diffusion-weighted images (Figure 1B) showed high intensity consistent with a tumor. Under the diagnosis of an ovarian tumor, the operation was performed, and the mass was found to arise from the retroperitoneum. Total resection was completed, and the surgical margin was found to be histopathologically negative. After the operation, the patient was regularly monitored. No apparent recurrence was detected on magnetic resonance imaging 1 year after operation. Macroscopic examination revealed a myxedematous tumor (size, 18×13×5 cm; Figure 2A). The cut surface showed a yellowish-white and elastic hard nodule (size, 1.5×1.5 cm) (Figure 2B). Microscopically, the tumor was composed of spindle-shaped cells sparsely scattered in the myxedematous background along with vessels of varying calibers (Figure 3A). Higher magnification demonstrated that the spindle-shaped cells had bland nuclei (Figure 3B). Mitotic figures were not apparent. The tumor infiltrated into the surrounding tissue and entrapped adipose tissue and peripheral nerves. The nodule showed alternating areas of hypercellularity and moderate cellularity and consisted of round to polygonal tumor cells with abundant eosinophilic cytoplasm, which are cells showing epithelioid features (Figure 3C). Although the nuclei of the tumor cells inside the nodule were enlarged, they did not show sufficient atypia to be diagnosed as malignant (Figure 3D). Only a few mitotic figures were identified when the whole nodule was searched.

Results of the immunohistochemical study in both areas were the same, and the results were positive for desmin (Figure 3E,F), cSMA, estrogen receptors, and progesterone receptors (Figure 3G,H) and negative for AE1/AE3, EMA, S100, CD34, HMB45, and Melan A. The MIB-1 labeling index was less than 1% in most areas of the tumor and 5.8% (58 positive cells per 1000 tumor cells) in the nodule when counting cells with more than moderate nuclear positivity. On the basis of the macroscopic, microscopic, and immunohistochemical findings, this case was diagnosed as AAM with a cellular nodule showing epithelioid features. The cellular nodule was considered benign judging from its degree of nuclear atypia, inconspicuous mitotic figures, and the MIB-1 labeling index.

Discussion and Conclusions

AAMs are rare, slow-growing tumors with a high recurrence rate ranging from 25% to 47%,2,5 and they have propensity to occur almost exclusively in the pelvic and perineal region.2,4 The high recurrence rate is due to the infiltrative growth of AAMs. Complete surgical resection of the tumor is the primary treatment, and a postoperative follow-up is neces-

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sary. In this case, the surgical margin was negative and no recurrence was observed 1 year after operation. Hormonal therapy using gonadotropin-releasing hormones has been used as an alternative treatment for achieving the resolution of AMMs.6,7

The differential diagnosis of AAM includes angiomyofibroblastoma, cellular angiofibroma, superficial angiomyxoma, fibroepithelial stromal polyps, and myxoid leiomyoma.6 Of these, the most important lesion is angiomyofibroblastoma, which is a recently described, benign, myxoid, and vascular soft tissue tumor of the vulva. In the original description, angiomyofibroblastomas located in the superficial soft tissue and they were usually smaller than 5 cm, and well demarcated. These features contrast with the larger size (often >10 cm) and infiltrative characteristics of AAMs.8

Histopathological examination reveals angiomyofibroblastomas contain hypocellular and perivascular hypercellular areas composed of bland mesenchymal cells that appear more plump or epithelioid than those of AAMs. As with AAMs, mitotic figures are not easily detected.8 The recurrence rate for angiomyofibroblastomas is reported to be much lower than that for AAMs.8 Cellular angiofibromas are much more recently described uncommon mesenchymal tumors with benign nature occurring mainly in the genital region.10 They are commonly well delineated, situated in the superficial soft tissue, and consist of bland spindle-shaped cells arranged without any characteristic pattern.10 They are not as large as AAMs, and their size was reported to range from 1 to 9 cm in a recent study.11

The histopathological findings of our case displayed typical morphology in most areas of the tumor, but the presence of a cellular nodule inside AAM was an unusual finding. In both areas, typical immunohistochemical expression patterns were observed; positivity was observed for demin, αSMA, estrogen receptors, and progesterone receptors. Hormone receptor expression is considered a characteristic feature of AAMs.6 However, it is also detected in angiomyofibroblastomas and cellular angiofibromas.12,13

Recently, the presence of the high mobility group A (HMGA2) gene rearrangement in AAMs by cytogenetic analysis and fluorescent in situ hybridization has been demonstrated.14 HMGA2 belongs to a family of transcriptional factors that function in embryogenic development and is not ordinarily expressed in adult tissues.14 Chromosomal translocation involving 12q13-15 that influences the HMGA2 gene has also been reported in other mesenchymal neoplasms, including lipomas, liposarcomas, leiomyomas, and pulmonary hamartomas.15 It is suggested that at least some AAMs have the same molecular genetic background as other common mesenchymal tumors described above.14 These findings have led to research into the usefulness of HMGA2 immunohistochemistry in mesenchymal tumors. One recent study investigated HMGA2 immunohistochemical expression in various tumors and evaluated its value as a discriminatory marker. Strong nuclear reaction was observed in 90% of AAMs compared with weaker positivity in 27% of fibroepithelial stromal polyps and no staining in angiomyofibroblastoma.16 In the present study, immunohistochemistry for HMGA2 was not necessary in the differential diagnosis because of the typical morphology, other than the presence of a nodule, and the typical immunohistochemical reaction for classical markers. However, if it is difficult to differentiate AAMs particularly from angiomyofibroblastomas, immunohistochemistry for HMGA2 is recommended. To the best of our knowledge, the presence of a cellular nodule inside AAM has not been documented in the literature.

Interestingly, the nodule was composed of
epithelioid cells with the same immunohistochemical pattern as those outside the nodule. High signal intensity on the diffusion-weighted image was suspected to reflect higher cellularity in the nodule.

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