Uterine Leiomyoma with Peculiar Skeletal Muscle Like and Rhabdoid Cells - Case Discussion and Literature Review

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Case Report

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ABSTRACT

Tumors with skeletal muscle differentiation (rhabdomyoma, rhabdomyosarcoma) and extra-renal rhabdoid tumors have been reported in uterus but cases of uterine leiomyoma with skeletal muscle like cells or cells resembling those of extra-renal rhabdoid tumors are rare. We describe clinical and pathological features of one such case of typical uterine leiomyoma in which histopathology showed presence of rounded, polygonal, and strap cells having abundant eosinophilic cytoplasm with round to oval nuclei, some of which were eccentric in position referred to as rhabdoid cells. Intra and extra-cytoplasmic hyaline globules were observed in these cells. However, no cross striations were seen. Immunohistochemistry confirmed their smooth muscle origin (positive for desmin and h-caldesmon while negative for cytokeratin, myogenin, myoglobin, and myo D1). We also review the pertinent literature and emphasize that presence of such cells may lead to problems in differential diagnosis. Their appropriate recognition is important so that overtly aggressive management of a benign tumor is avoided.

KEYWORDS: leiomyoma, skeletal muscle like cells, uterus

INTRODUCTION

Presence of skeletal muscle like cells or cells resembling those of extra-renal rhabdoid tumors is rarely reported in uterine leiomyomas[1-3], although tumors with true skeletal muscle differentiation (rhabdomyoma, rhabdomyosarcoma) and extra-renal rhabdoid tumors have been described in uterus[4-7]. The presence of these cells can cause diagnostic difficulties in separating them from epithelioid smooth muscle tumors, smooth muscle tumor of uncertain malignant potential, or tumors with skeletal muscle differentiation. We report clinical and pathological features of one such case which showed skeletal muscle like cells or rhabdoid cells, review the pertinent literature, and discuss the potential problems in differential diagnosis and its therapeutic implications.

CASE REPORT

Clinical findings: A 45-year-old lady presented to our gynecological OPD with complaint of bleeding per vagina for three years. An endometrial sampling was performed to know the etiology and she was diagnosed as simple hyperplasia on histopathology. Subsequently, she underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy.

Pathology: On gross examination an intramural leiomyoma measuring 3 cm in maximum diameter was identified with whitish whorled appearance. There was no hemorrhage or necrosis. Rest of the specimen was unremarkable except for two small simple cysts in right ovary. Microscopic examination confirmed the presence of simple hyperplasia of endometrium along with focal adenomyosis. The leiomyoma identified grossly showed rounded, polygonal or strap cells having abundant deeply eosinophilic cytoplasm (Fig. 1). They have round to oval and some eccentric nuclei with nuclear enlargement and prominent nucleoli. Intra and extra-cytoplasmic hyaline globules were observed in some cells (Fig. 2). No cross striations were seen. There was no significant mitosis, atypia, or necrosis. On immunostaining, these cells stained positively for vimentin, desmin, and h-caldesmon (Fig. 3), and were negative for cytokeratin, myogenin, and...
myo D1 proving them to be of smooth muscle origin. A diagnosis of leiomyoma with skeletal muscle like or rhabdoid cells was rendered. The patient is doing well after one and half year of follow-up.

DISCUSSION

Skeletal muscle like cells or cells resembling those of extra-renal rhabdoid tumors are rarely seen in uterine leiomyomas. They have distinctive appearance on light microscopy and are referred to as “rhabdoid cells”. They show round, polygonal, or strap shape with abundant deeply eosinophilic cytoplasm and may contain intra / extra cytoplasmic globules / inclusions having fibrillar or occasionally hyaline appearance. They do not display cross striations and have eccentric round to oval nuclei with vesicular to coarse chromatin and conspicuous nucleoli. Two out of the three tumors studied by Watanabe et al[8] in 2003 contained these cells like the present case including intense immunoreactivity for vimentin and desmin. However, h-caldesmon was focal rather than diffuse, and cytokeratin stained a few cells in one case. They interpreted them as exhibiting immature smooth muscle differentiation mimicking smooth muscle cells of the fetal uterus and were designated leiomyoblastoma. In another report[9] on eight atypical (bizarre) leiomyomas, the authors described these cells. Only one of them was examined ultrastructurally and an association of rhabdoid cells with atypical bizarre leiomyomas was suggested. Since all of their cases were obtained from consultive files of difficult cases, they did not review a series of typical leiomyomas. Our case reveals the occurrence of rhabdoid cells in a typical leiomyoma. Recently an analysis of 10 typical and two atypical leiomyomas describe the occurrence of these cells highlighting the presence of intra-cytoplasmic inclusion bodies. Two of their cases showed these bodies in more than 80% of tumor cells[10].

Since filamentous components of the smooth muscle cells of leiomyomas and myometrium comprise myofilaments and intermediate filaments and usually show positive reaction for SMA, desmin, and vimentin, pathogenetically the inclusion bodies found in the present and previously reported cases may be related to abnormal aggregates of actin or intermediate filaments, with a disordered equilibrium between synthesis and turnover of filament protein. In the study of Dundr et al[10], two types of inclusions were found by electron microscopy. One of them was characterized by a filamentous structure with various proportions of intermediate and actin filaments. These inclusions were eosinophilic, PAS negative, and at least at the periphery actin, desmin, and h-caldesmon positive. Another type of inclusions was composed of dense granular material without apparent fibrillar structure. These inclusions were basophilic, or unstained on H&E, were PAS positive and showed negative immunohistochemical staining. They suggest that the dense granular bodies may represent...
progression of the aggregation of filaments leading to loss of the filamentous structure, or they could be related to globules named Thanatosomes related to cell injury and apoptosis\[11,12\].

The primary differential diagnosis of tumors with rhabdoid cells is tumors with skeletal muscle differentiation. We found two previous case reports of leiomyomas with skeletal muscle cells in the literature, and both documented convincing histologic, immunohistochemical, and ultrastructural evidence of true skeletal muscle differentiation\[6,7\]. However, bona fide skeletal muscle differentiation in uterine tumors is most commonly observed as a rhabdomyosarcomatous component in a malignant mixed mullerian tumor or mullerian adenosarcoma. Pure uterine rhabdomyosarcomas occur but are most commonly of cervical origin\[4,13\]. These can be distinguished from present case morphologically (presence of pleomorphism, mitosis, and cross striations) and immunohistochemically (Myo D1, myogenin positive). Rhabdomyoma is another differential diagnosis, but they occur exclusively in lower female genital tract.

Pure malignant rhabdoid tumors of uterus are rare \[6,7,14\] and this diagnosis is one of exclusion as rhabdoid phenotype is reported in endometrial stromal sarcoma, epithelioid smooth muscle tumors, leiomyosarcoma, and malignant mixed mullerian tumor\[15-18\]. Although our case revealed clearly benign features and has background population of typical leiomyoma cells, the rounded cells seen were similar to extra-renal rhabdoid tumors. Extra-renal rhabdoid tumors exhibit hyaline eosinophilic globular inclusions, vesicular nuclei, central prominent nucleoli, and are positive for vimentin and cytokeratin. In our case, these cells were positive for vimentin, and smooth muscle markers, but not cytokeratin. That the rhabdoid cells in our case demonstrated evidence of smooth muscle differentiation support that these cells likely represent variant expression of the smooth muscle phenotype and would be expected to have the benign outcome of the leiomyomas.

In cases where the rhabdoid morphology is diffuse and the immunophenotype is equivocal, molecular analysis of the hSNF5 / INI1 gene or immunostaining for the INI1 product may assist in revealing the correct diagnosis\[19\].

Other neoplasms in the differential diagnosis include epithelioid smooth muscle tumors and smooth muscle tumors of uncertain or low malignant potential. The cells of epithelioid smooth muscle tumors characteristically are devoid of rhabdoid phenotype and have granular eosinophilic or clear cytoplasm and central nuclei in contrast to more fibrillar cytoplasm and eccentrically placed nuclei. In addition epithelioid smooth muscle tumors often are immunoreactive for cytokeratin, and negative for smooth muscle markers. Absence of high mitosis and true necrosis separate the case described from smooth muscle tumors of low malignant potential.

**CONCLUSION**

Presence of peculiar skeletal muscle like cells or cells resembling extra-renal rhabdoid tumor in uterine leiomyoma represent smooth muscle cells with an unusual phenotype. This entity must be kept in mind and needs to be distinguished from uterine tumors with rhabdomyomatous or rhabdosarcomatous differentiation or extra-renal rhabdoid tumors since such cells can cause diagnostic dilemma leading to erroneous diagnosis and overtly aggressive management.

**REFERENCES**


