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Clinicopathological study of cystic and atypical uterine leiomyoma: a rare entity

Estudo clinicopatológico de leiomioma uterino atípico e cístico: uma entidade rara

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ABSTRACT

A 43-years-old Brazilian woman, Caucasian, premenopausal, was attended with a history of lower abdominal pain, distension, and bleeding. Pelvic and transvaginal ultrasound revealed an enlarged uterus with a large, well-defined, uniformly hyperechoic lesion. The patient underwent total hysterectomy and the specimen was sent for anatomopathological evaluation. The histopathological analyses revealed a leiomyoma with extensive cystic degeneration and atypical characteristics, the immunohistochemical study confirmed the benignity of the case. The finding of atypical leiomyoma with cystic degeneration is rare and should be carefully evaluated to exclude malignant diseases.

Key words: uterine neoplasms; pathology; myoma; desmin.

RESUMO

Mulher brasileira, 43 anos de idade, caucasiana, na pré-menopausa, foi atendida devido a história de dor em abdômen inferior, distensão e sangramento. A ultrassonografia pélvica e transvaginal revelou útero aumentado com grande lesão hiperecoica, bem definida e uniforme. A paciente foi submetida à histerectomia total, e a amostra foi enviada para avaliação anatomopatológica. A análise histopatológica revelou quadro de leiomioma com degeneração cística extensa e características atípicas; o estudo imuno-histoquímico confirmou a benignidade do caso. O achado de leiomioma atípico com degeneração cística é raro e deve ser cuidadosamente avaliado para excluir doenças malignas.

Unitermos: *neoplasias uterinas; patologia; mioma; desmina.*

RESUMEN

Mujer brasileña de 43 años, caucásica, premenopáusica, fue atendida con antecedentes de dolor abdominal bajo, distensión y menorragias. La ecografía pélvica y transvaginal reveló un útero agrandado con una lesión grande, bien definida y uniformemente hiperecoica. La paciente fue sometida a histerectomía total y la pieza fue enviada para evaluación anatomo-patológica. Los análisis histopatológicos revelaron un leiomioma con degeneración quística extensa de características atípicas y la inmunohistoquímica confirmó la benignidad del caso. El hallazgo de un leiomioma atípico con degeneración quística es raro y debe evaluarse cuidadosamente para descartar enfermedades malignas.

Palabras clave: *neoplasias uterinas; patología; mioma; desmina.*

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INTRODUCTION

Leiomyomas are also known as myomas or fibroids. They are benign uterine tumors that affect women mostly during reproductive age. This benign tumor is the most common gynecologic neoplasm, it can cause a variety of health complications and is the leading indication for hysterectomy[1, 2]. Despite their benign character, leiomyomas are responsible for high morbidity in the female population and represent a public health problem with high health costs[3, 4].

The symptoms are directly related to size, number, and location, and the most common clinical findings of uterine leiomyoma are abnormal uterine bleeding, pelvic pain, dysmenorrheal, and reproductive changes[5]. Some risk factors should be considered, including black ethnicity, early menarche, nulliparity, family history, systemic hypertension, oral contraceptives, alcoholism, and smoking[6, 7].

The majority of tumors are estrogen and progesterone-dependent, with growth rates related to hormone receptor levels[8, 9]. Accelerated leiomyomas growth overcomes blood supply leading to degenerations, with cystic degeneration accounting for approximately 4% of cases[10]. It can be located at different levels of the wall of the uterus: submucosa, subserosa, intramural or cervical[11].

There are several leiomyoma variants, such as mitotically active, cellular, and atypical leiomyomas. The majority of these variants is rare and has a benign natural history. The pre-operative detection of uterine leiomyosarcoma is difficult due to the clinical similarity with ordinary leiomyomas, making the pathological examination indispensable for the correct diagnosis[12].

Microscopically the atypical leiomyomas are recognized by the absence of coagulative necrosis, low mitotic rate, and the presence of atypical tumor cells in moderate to severe amounts. Although benign, the clinical behavior of this variant is still unclear. The low mitotic activity is a key point in the differentiation of leiomyosarcoma[13, 14].

The authors present an unusual case of a large atypical uterine leiomyoma with cystic degeneration that could be misdiagnosed for malignancy on ultrasonography.

CASE REPORT

A 43-year-old Brazilian woman, premenopausal, with a history of two pregnancies, a cesarean delivery and an abortion, sought medical attention with complaints of abdominal pain, distension, and vaginal bleeding. The patient had been under treatment for depression and systemic arterial hypertension for two years. On physical examination, she presented with good general condition, hydrated, ruddy, eupneic, and no abnormalities. Pelvic and transvaginal ultrasound revealed an enlarged uterus with a large, well-defined, uniformly hyperechoic lesion, approximately 11.5 × 10.1 × 15.6 cm in size, in the myometrium. No evidence of internal calcification was noted (**Figure 1**). The patient was submitted to hysterectomy and the surgical specimen was referred for pathological examination.

The specimen consisted of a globular uterus weighing 1,150 g, measuring 17.5 × 11.5 × 10 cm, with cystic consistency, partially covered by white-gray serosa. The sections showed an intraparenchymal cystic cavity, trabecular pink surface, with 10.5 cm in the longest axis, filled with liquid citrus (**Figure 2**).

Histologically, sections of the uterus showed cystic neoformation with an inner surface composed of anaplastic cells, often giants with irregular or spindle cytoplasm and

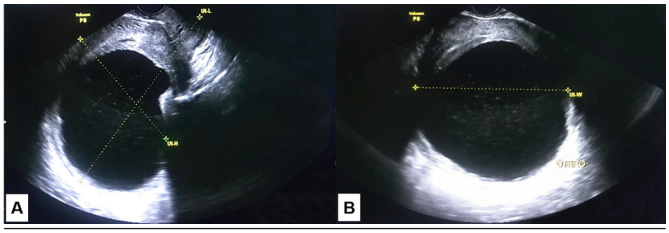

FIGURE 1 – *Abdominal ultrasonography of a 43-year-old female with atypical and cystic retroperitoneal leiomyoma*

The exam shows a well-defined and uniformly hyperechoic mass with a cystic component in the coronal (A) and longitudinal (B) plane.

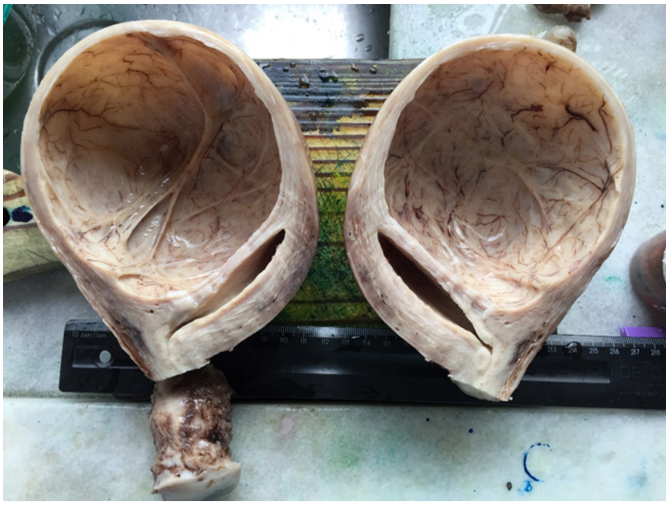

FIGURE 2 – *The macroscopic appearance of the tumor fixed in formalin*

An intraparenchymal cystic cavity with a pink trabecular surface was observed, with liquid citrus filling the cavity.

anisomorphic, rounded or oval nuclei with coarse chromatin, and eosinophilic macronuclei (**Figure 3**). Considering the hypothesis of malignancy, an immunohistochemical study was performed. We found a high expression of desmin and a lower expression of Ki-67 (**Figure 4**), ruling out the malignancy hypothesis and confirming the diagnosis of cystic and atypical leiomyoma in uterine myometrium.

The patient had a good postoperative evolution, is currently well, and in outpatient follow-up.

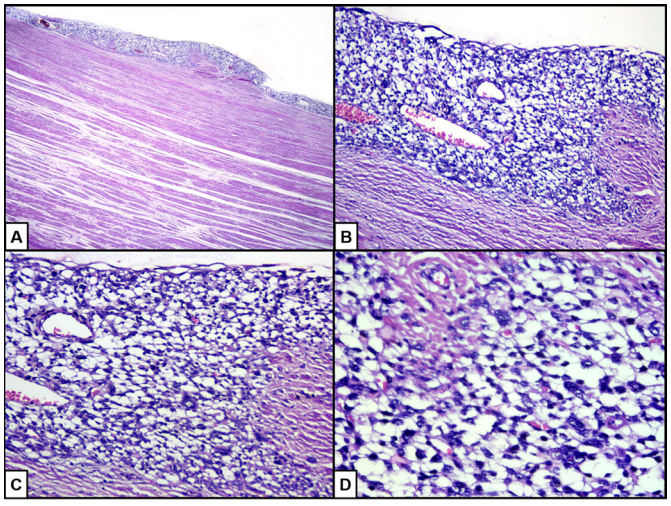

FIGURE 3 – *Histopathology of atypical leiomyoma with cystic degeneration*

A) 40× magnification shows the proliferation of smooth muscle and cystic degeneration at the top of the image; B) 100× magnification showing the cystic neoformation; C) 400× magnification showing cystic neoformation with anaplastic cells; D) 1000× magnification showing anaplastic cells with anisomorphic nuclei.

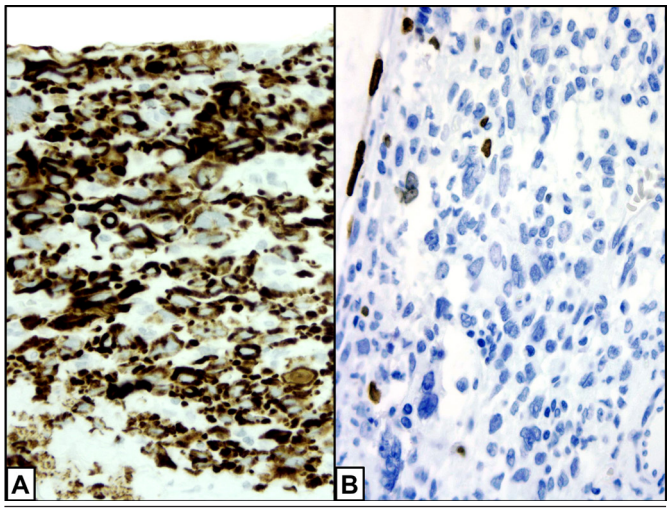

FIGURE 4 – *Immunohistochemical analysis of atypical leiomyoma with cystic degeneration*

A) 400× magnification shows high positivity for desmin; B) 400× magnification shows low positivity for Ki-67 indicating low proliferation rates.

DISCUSSION

Uterine leiomyomas are noncancerous growths in the uterus. In general, they are asymptomatic and occasionally identified during routine gynecological examinations. Atypical leiomyomas are uterine smooth-muscle tumors of controversial nature for clinicians and pathologists and in cases of degeneration, can lead to errors of diagnosis[2, 12].

In the study, we describe the reported case of a 43-years-old woman with an cystic and atypical tumor in the uterus, it is known that the tumor shows a preference for middle-aged women, the average age of 45 years[15, 16]. The original pathological specimen showed areas similar to smooth muscle neoplasm interspersed with foci of atypical cells.

Large uterine tumors such as those observed in this case, in addition to causing pain due to compression of structures, may also rupture or twist causing acute abdomen as observed in previous studies[17, 18].

Despite the atypical findings, most atypical leiomyomas show benign behavior. However, most patients undergo total hysterectomy[19]. Although in cases of large leiomyomas as shown in this work, a total hysterectomy is essential to avoid complications, this surgery is associated with morbidity and mortality, besides generating a major economic impact on the health care delivery system[4].

The diagnosis of leiomyomas is based on imaging findings, that is, through magnetic resonance or ultrasound tests. The use of imaging exams of leiomyomas and their variants allows a classification of the location and pre-treatment planning[12]. A transvaginal ultrasound (TVUS) is one of the main exams when there is a suspicion of uterine masses, however, degenerative changes can present heterogeneous changes, therefore the performance of histopathological exams is essential[20, 21].

Secondary changes of leiomyomas can occur, such as myxoid, hyaline, red, and cystic degeneration[22, 23]. These changes usually are caused by variations in the blood flux[24]. In case the of cystic degeneration, some authors considered it to be a sequel of edema, observed in 4% of leiomyomas of the uterus[24].

Considering that the exposed case presented a large tumor mass with a cystic cavity containing citrus liquid, the hypothesis that cystic degeneration arises from intense edema, can be considered.

The presence of cystic degeneration in atypical leiomyoma is extremely rare[25]. Degenerating leiomyomas that are atypical may

be confused with leiomyosarcomas, adenomyosis, hematometra, uterine sarcoma, and ovarian masses in ultrasonography evaluation[10]. Therefore, histopathological examination and immunohistochemistry are essential for the differentiation process, as verified in this report.

The immunohistochemistry technique is an important tool to assist in distinguishing tumors, as they reveal strong immunoreactivity against actin, desmin, and vimentin[26]. Because of this, in this work, tissue desmin marking was performed, a specific smooth muscle marker, and Ki-67 marking, a test that measures the rate of cell proliferation. It is possible to rule out the suspicion of malignancy in the case and confirming its atypical character.

CONCLUSION

Although ultrasound is an important diagnostic modality in the suspicion of leiomyomas, changes in this neoplasm may be present in an unusual way, making the initial diagnosis difficult. In this case, the use of histopathology and immunohistochemistry helps to detect atypical cases such as the one presented here.

In the presence of pelvic masses, with or without symptoms, an accurate investigation is essential, especially in cases with a cystic component, which can be confused with several pathologies. The exclusion of leiomyosarcoma and other malignancies is essential to improve patient quality of life.

REFERENCES

1. Rice KE, Secrist JR, Woodrow EL, Hallock LM, Neal JL. Etiology, diagnosis, and management of uterine leiomyomas. J Midwifery Womens Health. 2012; 57(3): 241-47.

2. Bulun SE. Uterine fibroids. N Engl J Med. 2013; 369(14): 1344-55.

3. Flake GP, Andersen J, Dixon D. Etiology and pathogenesis of uterine leiomyomas: a review. Environ Health Perspec. 2003; 111(8): 1037-54.

4. Cardozo ER, Clark AD, Banks NK, Henne MB, Stegmann BJ, Segars JH. The estimated annual cost of uterine leiomyomata in the United States. Am J Obstet Gynecol. 2012; 206(3): 211.e1-9.

5. Wegienka G, Baird DD, Hertz-Picciotto I, Harlow SD, Hartmann KE. Uterine leiomyomata (fibroids): are bleeding symptoms more likely to be reported after diagnosis? J Clin Epidemiol. 2004; 57(3): 318-20.

6. Wise LA, Palmer JR, Harlow BL, et al. Risk of uterine leiomyomata in relation to tobacco, alcohol and caffeine consumption in the Black Women's Health Study. Hum Reprod. 2004; 19(8): 1746-54.

7. Ross RK, Pike MC, Vessey MP, Bull D, Yeates D, Casagrande JT. Risk factors for uterine fibroids: reduced risk associated with oral contraceptives. Br Med J (Clin Res Ed). 1986; 293(6543): 359-62.

8. Robboy SJ, Bentley RC, Butnor K, Anderson MC. Pathology and pathophysiology of uterine smooth-muscle tumors. Environ Health Perspect. 2000; 108 Suppl 5: 779-84.

9. Hall JM, Couse JF, Korach KS. The multifaceted mechanisms of estradiol and estrogen receptor signaling. J Biol Chem. 2001; 276(40): 36869-72.

10. Aydin C, Eriş S, Yalçin Y, Sen Selim H. A giant cystic leiomyoma mimicking an ovarian malignancy. Int J Surg Case Rep. 2013; 4(11): 1010-12.

11. Lellis-Júnior GC, Tavares MA, Kunzmann NG, et al. Miomas uterinos. Rev Med Minas Gerais. 2011; 21(4 Supl 6): S1-S143.

12. Arleo EK, Schwartz PE, Hui P, McCarthy S. Review of leiomyoma variants. AJR Am J Roentgenol. 2015; 205(4): 912-21.

13. Kalogiannidis I, Stavrakis T, Dagklis T, et al. A clinicopathological study of atypical leiomyomas: benign variant leiomyoma or smooth-muscle tumor of uncertain malignant potential. Oncol Lett. 2016; 11(2): 1425-28.

14. Coindre JM. Grading of soft tissue sarcomas: review and update. Arch Pathol Lab Med. 2006; 130(10): 1448-53.

15. Naz Masood S, Masood Y, Mathrani J. Diagnostic dilemma in broad ligament leiomyoma with cystic degeneration. Pak J Med Sci. 2014; 30(2): 452-54.

16. Sharma P, Zaheer S, Yadav AK, Mandal AK. Massive broad ligament cellular leiomyoma with cystic change: a diagnostic dilemma. J Clin Diagn Res. 2016; 10(4): ED01-ED2.

17. Takai H, Tani H, Matsushita H. Rupture of a degenerated uterine fibroid as a cause of acute abdomen: a case report. J Reprod Med. 2013; 58(1-2): 72-74.

18. Bastu E, Akhan SE, Ozsurmeli M, et al. Acute hemorrhage related to spontaneous rupture of an uterine fibroid: a rare case report. Eur J Gynaecol Oncol. 2013; 34(3): 271-72.

19. Manxhuka-Kerliu S, Kerliu-Saliu I, Sahatciu-Meka V, Kerliu L, Shahini L. Atypical uterine leiomyoma: a case report and review of the literature. J Med Case Rep. 2016; 10: 22.

20. Ahamed KS, Raymond GS. Answer to case of the month #103. Large subserosal uterine leiomyoma with cystic degeneration presenting as an abdominal mass. Can Assoc Radiol J. 2005; 56(4): 245-47.

21. Karasick S, Lev-Toaff AS, Toaff ME. Imaging of uterine leiomyomas. AJR Am J Roentgenol. 1992; 158(4): 799-805.

22. Funaki K, Fukunishi H, Tsuji Y, Maeda T, Takahashi T. Giant cystic leiomyoma of the uterus occupying the retroperitoneal space. J Radiol Case Rep. 2013; 7(12): 35-40.

23. Murase E, Siegelman ES, Outwater EK, Perez-Jaffe LA, Tureck RW. Uterine leiomyomas: histopathologic features, MR imaging findings, differential diagnosis, and treatment. Radiographics. 1999; 19(5): 1179-97.

24. McLucas B. Diagnosis, imaging and anatomical classification of uterine fibroids. Best Pract Res Clin Obstet Gynaecol. 2008; 22(4): 627-42.

25. Siti-Aishah MA, Noriah O, Malini MN, Zainul-Rashid MR, Das S. Atypical (symplastic) leiomyoma of the uterus--a case report. Clin Ter. 2011; 162(5): 447-50.

26. Sarnat HB. Vimentin/desmin immunoreactivity of myofibres in developmental myopathies. Acta Paediatr Jpn. 1991; 33(2): 238-46.

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