

Ovarian leiomyoma with myxoid stroma

A. MOULLA², N. MAGDY^{1,3}, M. EL-BAHRAWY^{1,4}

¹ Department of Histopathology, Imperial College London, UK; ² Department of Histopathology, University Hospital Coventry, UK; ³ Department of Histopathology, National Cancer Institute, Egypt; ⁴ Department of Pathology, Faculty of Medicine, Alexandria University, Egypt

Key words

Myxoid leiomyoma • Ovary • Stromal tumors

Summary

Ovarian smooth muscle tumours are rare. Notable myxoid change in smooth muscle tumours is uncommon, and raises diagnostic issues that need to be considered on evaluating a spindle cell lesion with notable myxoid change. There is only one case of

myxoid leiomyoma of the ovary previously reported. We here report a case of ovarian leiomyoma with areas of myxoid stroma and discuss the relevant differential diagnosis and histological features to be assessed in such a lesion.

Introduction

Ovarian smooth muscle tumors, both benign and malignant, are rare, based on our experience and that in the literature, even allowing for the fact that sporadically encountered benign examples would not warrant reporting. There are fewer than 150 cases reported over a wide age range, from 3 to 103 years-old, mean 43 years-old. Most are unilateral. Rarely bilateral leiomyomas have been reported in young women 16 to 38 years of age^{1,2}. There is only one sizable series¹. In that report it was documented that histologically ovarian leiomyomas demonstrate a similar spectrum to their uterine counterparts, including leiomyoma with bizarre nuclei, mitotically active leiomyoma, cellular leiomyoma, epithelioid leiomyoma and lipoleiomyomas¹. Myxoid leiomyoma of the ovary is a very rare entity with only one case described in the literature to date¹. We have recently encountered an additional case of ovarian leiomyoma with myxoid stroma and report it herein along with a brief consideration of myxoid ovarian tumors, which, like myxoid tumors elsewhere may cause diagnostic difficulty.

Case report

A 23 years-old woman presented with abdominal pain and investigation revealed a right ovarian cyst that was

suspicious for malignancy with MRI imaging. The patient underwent right salpingo-oophorectomy.

Macroscopically. The ovary was replaced by a well circumscribed mass with a smooth outer surface measuring 60 x 45 x 35 mm. The cut surface was mainly solid, pale brown with firm gritty white areas. An adjacent small cyst was seen, measuring 18 mm.

Microscopically. The majority of the tumour consisted of bundles of smooth muscle fibres with delicate spindle cells dispersed in an amorphous, pale, blue matrix (Figs. 1A-D). No notable nuclear atypia and no necrosis were seen and the mitotic count was < 1/50 HPF. On immunostaining the tumour cells expressed vimentin, smooth muscle markers (SMA, desmin, h-Caldesmon, and calponin, CD56 (Figs. 1E-J), being negative for inhibin, cytokeratin, S100, WT-1 and CD34. The macroscopically described cyst adjacent to the lesion is a mature cystic teratoma.

Discussion

Myxoid degeneration is seen in 3% to 13% of leiomyomas. The myxoid stroma in a leiomyoma arises from myxoid degeneration of collagen surrounding smooth muscle nodules. Myxoid leiomyoma was first emphasised in female genital tract neoplasia by Tavassoli and Norris in 1979 in vulval cases^{3,4}.

Myxoid leiomyomas are composed of anastomosing fas-

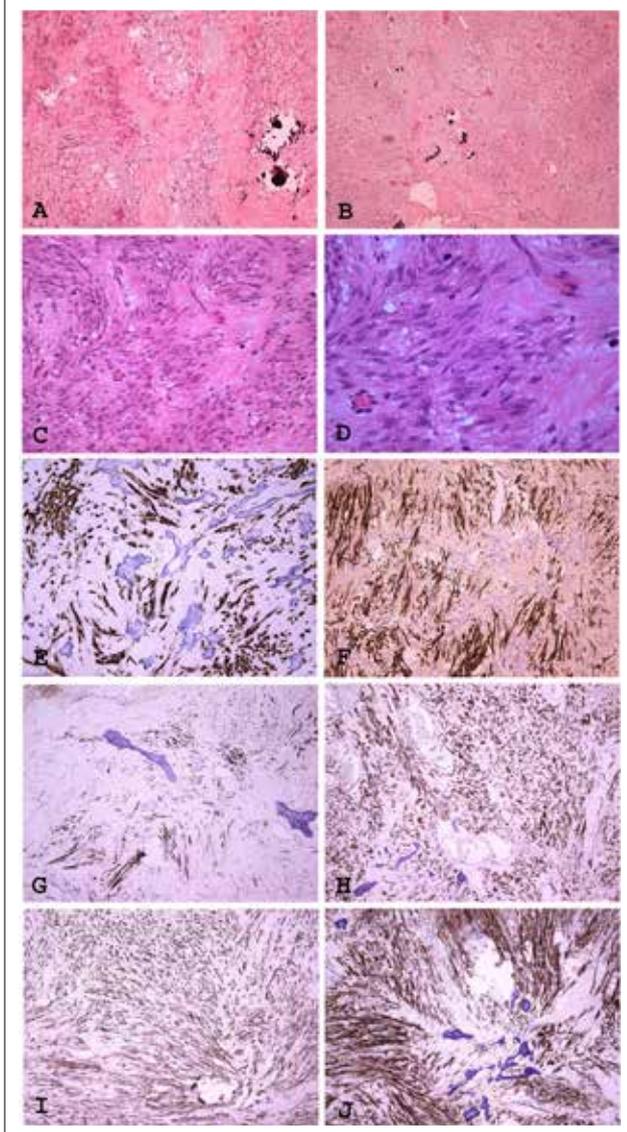
Acknowledgements

The authors thank Dr Robert Young, Massachusetts General Hospital, USA, for his valuable advice in the preparation of the manuscript.

Correspondence

Alexandra Moulla, Department of Histopathology University Hospital Coventry, Clifford Bridge Rd, Coventry CV2 2DX, UK - Tel. + 44 (0)7710 653153 - E-mail: alexandra@giuntoli.com

Fig. 1. Myxoid leiomyoma. A and B; Interlacing bundles of smooth muscle fibres in a background of myxoid stroma (A and B: X100, C: X 200, D: X400), E; h-caldesmon, F; SMA, G; Desmin, H; Calponin, I; vimentin and J; CD56 (E-J X200).



cicles of fusiform smooth muscle cells. There is abundant cellular material rich in acid mucins. The tumour tends to have large vessels. There is no cytological atypia. Mitotic figures are usually $< 2/10$ HPF⁵.

It is most important to distinguish myxoid leiomyoma from myxoid leiomyosarcoma, which can be challenging in some cases. Myxoid leiomyosarcoma shows abundant myxoid stroma that separates the smooth muscle fibres with nuclear enlargement, pleomorphism, infiltrative growth, high mitotic count, higher ki67 and p53 expression. The myxoid leiomyosarcomas are either hypercellular or variably cellular. The hypocellular foci contain mucin pools or have myxoid matrix that imparts a reticular appearance. Sometimes the stroma is myxohyaline which is alcian blue positive. The neoplastic cells are arranged in bundles or

fascicles or even individually within the myxoid matrix. The tumour cells have eosinophilic cytoplasm and elongated cigar-shaped hyperchromatic nuclei. Geographic tumour cell necrosis is observed in 48% of cases and lymphovascular invasion in 36% of cases. Myxoid leiomyosarcoma diagnosis is established if the tumour border is infiltrative and there is at least one of the following criteria:

- ≥ 2 mitoses /10 HPF;
- moderate or severe atypia;
- coagulative tumour necrosis⁶.

As recommended by Lerwill et al.¹, in the ovary, 2 or more of the following criteria in a smooth muscle tumour should raise the diagnosis of leiomyosarcoma:

- significant nuclear atypia;
- mitotic index 10 or more mitoses/10 HPF;
- necrosis.

In the uterus the presence of tumour cell necrosis would preclude placing a smooth muscle tumour with significant atypia and mitotic activity in a benign category.

In the absence of tumour cell necrosis mitotic count of ≥ 5 mitoses/10 HPF in a cytologically atypical ovarian tumour warrants a diagnosis of leiomyosarcoma, a threshold lower than applied by Bell et al (10 mitoses/10 HPF) in uterine smooth muscle tumors, although others diagnose sarcoma in the uterus when mitotic counts are below 10 mitoses/10 HPF provided there is significant atypia¹⁷. Another very characteristic feature in leiomyosarcoma is the absence of large thick walled blood vessels, which are usually present in myxoid leiomyoma⁴.

Another lesion to be considered in the differential diagnosis is myxoma of the ovary, which appears with loose myxomatous stroma, scattered spindle cells without pleomorphism and without mitotic activity. The tumour cells express vimentin but are negative for desmin, cytokeratin and S100.

Ovarian leiomyomata are frequently confused with the more common fibroma, which often shows edema, but rarely myxoid change. The tumour cells are positive for CD56, SMA, WT1, occasionally S100 and CD34.

We should consider in differential diagnosis the apoplectic leiomyoma which consists of stellate to ovoid zones with hypercellular periphery and central haemorrhage, necrosis and hyalinization. The hypercellular areas can sometimes show increased mitoses $\sim 14/10$ HPF but no cytological atypia. There is edema and cyst formation in 95% and 42% of cases respectively. The hypercellular areas show spindle cells with nuclear pyknosis and mitoses are distributed only at the periphery and are not diffusely distributed as in leiomyosarcoma cases⁸.

Sclerosing stromal tumor of ovary is another lesion which appears with a pseudolobular pattern of growth and widespread areas of sclerosis with myxoid-fibrotic stroma and focal cystic spaces. There are two cell populations, spindle and round cells and hemangiopericytoma like vessels. The immunohistochemistry shows positivity of tumour cells for vimentin, inhibin and SMA⁹.

Finally we should consider the inflammatory myofibroblastic tumour where there are myofibroblastic and fibroblastic spindle cells with an inflammatory infiltrate of lymphocytes, plasma cells, eosinophils, and histiocytes. The background has abundant blood vessels. Immunohistochemically the tumour cells are positive for Vimentin, SMA, and calponin and in 1/3 of cases for desmin and keratin¹⁰. ALK overexpression by immunohistochemistry may assist in distinction between myofibroblastic tumour and myxoid leiomyosarcoma as it is present in the former and negative in 85% of myxoid leiomyosarcomas.

ALK rearrangements may be helpful in confirming the diagnosis. Although documented in several other tumors like PNST and rhabdomyosarcomas, distinction from these entities is possible both on the basis of morphology and immunoprofile⁶. In molecular studies 40% of uterine leiomyomas have detectable chromosomal abnormalities as t12,14 (q15, q23-24) rearrangements involving the short arm of chromosome 6 and chromosome 7. Specific mutations of the MED12 protein have been noted in 70% of uterine leiomyomas^{11 12}. Genetic changes in ovarian leiomyomas have not been studied.

In conclusion, we report the second case of leiomyoma with myxoid stroma encountered in the ovary, and discuss the differential diagnosis and approach to distinguish this benign entity from other neoplasms, which would significantly influence patient management.

References

- ¹ Lerwill MF, Sung R, Oliva E, et al. *Smooth muscle tumors of the ovary: a clinicopathologic study of 54 cases emphasizing prognostic criteria, histologic variants, and differential diagnosis*. Am J Surg Pathol 2004;28:1436-51.
- ² Daniel Y, Lessing JB, Bar-Am A, et al. *Treatment of bilateral multiple primary ovarian leiomyomas during pregnancy by way of conservative surgery: a case report*. Eur J Obstet Gynecol Reprod Biol 1997;74:125-6.
- ³ Kurman R, Hedrick Ellenson L, Ronnett B. *Blaustein's pathology of the female genital tract*. 6th ed. Springer 2011, pp. 460-471.
- ⁴ Tavassoli FA, Norris HJ. *Smooth muscle tumors of the vulva*. Obstet Gynecol 1979;53:213-7.
- ⁵ Levy G1, Hill MJ, Beall S, et al. *Leiomyoma: genetics, assisted reproduction, pregnancy and therapeutic advances*. J Assist Reprod Genet 2012;29:703-12.
- ⁶ Parra-Herran C, Schoolmeester JK, Yuan L, et al. *Myxoid leiomyosarcoma of the uterus: a clinicopathologic analysis of 30 cases and review of the literature with reappraisal of its distinction from other uterine myxoid mesenchymal neoplasms*. Am J Surg Pathol 2016;40:285-301.
- ⁷ Bell SW, Kempson RL, Hendrickson MR. *Problematic uterine smooth muscle neoplasms: a clinicopathologic study of 213 cases*. Am J Surg Pathol 1994;18:535-58.
- ⁸ Bennett JA, Lamb C, Young RH. *Apoplectic leiomyomas: a morphologic analysis of 100 cases highlighting unusual features*. Am J Surg Pathol 2016;40:563-8.
- ⁹ Ozdemir O, Sarı ME, Sen E, et al. *Sclerosing stromal tumour of the ovary: a case report and the review of literature*. Niger Med J 2014;55:432-7.
- ¹⁰ Nielsen GP, Young RH. *Mesenchymal tumors and tumor-like lesions of the female genital tract: a selective review with emphasis on recently described entities*. Int J Gynecol Pathol 2001;20:105-27.
- ¹¹ Kamra HT, Dantkale SS, Birla K, et al. *Myxoid leiomyoma of cervix*. J Clin Diagn Res 2013;7:2956-7.
- ¹² Levy G, Hill MJ, Beall S, et al. *Leiomyoma: genetics, assisted reproduction, pregnancy and therapeutic advances*. J Assist Reprod Genet 2012;29:703-12.