CASE REPORT

Rare paratesticular aggressive angiomyxoma with negative oestrogen and progesterone receptors in a male patient

Azfar Neyaz, Nuzhat Husain, Nidhi Anand, Pallavi Srivastava

Department of Pathology, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow, Uttar Pradesh, India

Correspondence to
Professor Nuzhat Husain,
drnuzhathusain@hotmail.com

Accepted 15 May 2018

SUMMARY

Aggressive angiomyxoma (AAM) is a rare mesenchymal myxoid tumour localised to the pelvis and/or perineum in adult females in reproductive age group. AAM is very rare in males, with <50 cases described in literature, and involves scrotum, spermatic cord and perineum. It is slow growing, with a marked tendency for local recurrence after excision, but without metastatic potential. We present a rare case of a paratesticular AAM in a man aged 53 years. Tumour cells were immunoreactive for desmin, smooth muscle actin (SMA), vimentin, CD34 and were negative for S100. Unlike AAMs in females which express oestrogen receptor (ER) and/or progesterone receptor (PR) in >90% cases, the tumour cells in our case were negative for ER and PR, suggesting that the hypothesis that these markers play a role in tumour development and pathogenesis, does not apply in males. Androgen receptor positivity was noted in 2%–5% tumour cells.

BACKGROUND

We describe an interesting rare case of a paratesticular aggressive angiomyxoma (AAM), presenting as a scrotal swelling, highlighting unusual morphological features. AAMs are very rare in males. Our case showed some inadequately described features in literature including an intense tumour lymphocytic reaction presenting in gross evaluation as solid white separate nodules adjacent to main gelatinous

growth. Furthermore, our case, along with few other cases in males described in the literature, had a negative hormone (oestrogen receptor (ER)/progesterone receptor (PR)) receptor status unlike AAM in females where these receptors are expressed.

CASE PRESENTATION

A man aged 53 years presented with a large, slowly growing left scrotal swelling since 3 years. The patient had no history of pain, injury, fever or urinary tract symptoms. The swelling did not cause any significant discomfort except for a feeling of heaviness and the patient had not undergone any prior treatment. During physical examination on palpation, the swelling was firm to soft, non-transilluminated, non-tender, measuring 15×10 cm and was seen occupying the whole scrotum. It was mobile with well-defined contours. There was no history of any abdominal lump, altered bowel or bladder habits, cough or a history suggestive of distant metastasis.

INVESTIGATIONS

Serum tumour biomarkers including α -fetoprotein, β -human chorionic gonadotropin, lactate dehydrogenase and prostate-specific antigen levels were all within normal limits. CT revealed an extratesticular well-demarcated space occupying homogeneous low-density mass with a heterogeneous enhancement effect and a moderate hydrocoele. There was no radiological evidence of lung or bone involvement.

Gross evaluation of the high orchiectomy specimen revealed a partially encapsulated and lobular mass measuring 16.5×12.0 cm, arising in the paratesticular region and encircling the spermatic cord. Cut surface showed two different components: one was soft, glistening, lobular and gelatinous while the other part was firm nodular solid grey-white. Testis measured 6.0×4.5×4.0 cm and was unremarkable (figure 1). Microscopic evaluation of multiple sections of the gelatinous component showed widely scattered small spindle and stellate fibroblasts without atypia along with dilated, thick-walled vessels embedded in a myxoid paucicellular stroma. The cells were small, oval to spindle-shaped, with centrally placed mildly pleomorphic nuclei and ill-defined cytoplasm. No nuclear atypia or mitosis was evident (figure 2A–D). Sections from the solid-white nodular growth showed an intense

Figure 1 Macroscopic findings: cut surface of the tumour shows two different components: one soft, glistening, lobulated, gelatinous measuring 10.0×8.0 (black arrow) and the other firm, nodular, solid grey-white measuring 6.5×4.0 cm (encircled). Unremarkable testis measured 6.0×4.5×4.0 cm (asterisk).

To cite: Neyaz A, Husain N, Anand N, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-222164

Figure 2 Histological findings: photomicrographs of aggressive angiomyxoma demonstrating a relatively uniform population of small mesenchymal cells in myxoid matrix (A), mature vessels of varying calibre (B), infiltration of adipose tissue (C), tumour infiltrating spermatic cord (D), interface of tumour displaying intense lymphocytic infiltrate (E and F).

inflammatory infiltrate (figure 2E and F). Sections from the testicular parenchyma showed seminiferous tubules with mild atrophic changes and evidence of spermatogenesis. The tunica vaginalis and tunica albuginea were unremarkable. On immunohistochemistry, tumour cells were positive for vimentin, CD34, SMA, desmin (focal positive) and negative for S100, β -catenin, mouse double minute 2 homolog (MDM-2), ER and PR (figure 3). Androgen receptor (AR) expression was evident in approximately 2%–5% nuclei. Histological and immunohistochemical features were consistent with a diagnosis of aggressive angiomyxoma. Invasion of adjacent structures except spermatic cord was not observed and surgical margins were free of tumour.

DIFFERENTIAL DIAGNOSIS

In the preoperative phase, a specific diagnosis was difficult and clinical differential diagnoses included an inguinal hernia, hydrocoele, spermatocele, testicular and paratesticular neoplasia.

TREATMENT

A high inguinal orchidectomy was performed.

OUTCOME AND FOLLOW-UP

The postoperative period was uneventful. The patient was discharged 10 days postsurgery. On follow-up, no clinical and imaging signs of local recurrence and distant metastasis were observed in 12 months.

DISCUSSION

Steeper and Rosai in 1983, for the first time first described aggressive angiomyxoma. AAM is a locally invasive tumour

of mesenchymal tissue with a preferred location in the pelvis and perineal region, occurring predominantly in females in the reproductive age group.¹ AAM in males is very rare with <50 reported cases worldwide. In a review of 24 cases in males, Chihara *et al*,² have reported that 38% cases are located in the scrotum, 33% in the spermatic cord, 13% in the perineal region and 8% in intrapelvic organs.² Patients usually present with a long history of disease due to the slow growing nature of the tumour. The term aggressive implies a neoplastic character with a locally infiltrative course and frequent recurrences, rather than a malignant potential.³ Definitive preoperative diagnosis is difficult, and differential diagnosis includes non-neoplastic aetiologies like an inguinal hernia and hydrocoele along with testicular and paratesticular neoplasia.⁴ Ultrasonography does not identify the presence of a tumour precisely. Angiomatous and myxomatous characteristics of the tumour are better revealed by scrotal MRI. Further MRI and CT with contrast can sometimes demonstrate a distinctive 'swirled' appearance of the stroma.⁵ On gross evaluation, AAM is usually partially circumscribed, ill-demarcated, lobulated, soft, grey coloured tumour with a smooth contour and gelatinous appearance.⁶ Our case had two different appearances in the mass, one with a typical gelatinous texture and the other a solid white nodular growth, the morphology of which has been discussed briefly. Conspicuous thick and thin-walled vessels of variable sizes, poorly defined tumour margins, abundant myxoid matrix, foci of adipose tissue, myofibroblasts and fibroblast-like cells, cytologically bland nuclei and sparse mitoses are characteristic histological findings.⁶ Thick-walled vessels and a conspicuous vasculature help to distinguish AAM from other malignant and benign myxoid soft tissue tumours of the genital tract and perineum including myxoma, myxoid neurofibroma, angiomatous fibrosarcoma, spindle cell lipoma, myxoid liposarcoma and leiomyoma.⁷ Further negativity for S100, β -catenin, MDM-2 as well as lack of cellular atypia ruled out other differential diagnoses.⁸ In our case, in addition to these histological features the microscopic evaluation of the distinct solid white nodular areas in the growth showed an intense lymphocytic reaction around the tumour, not well described in earlier reports. The diagnosis and distinction of AAM from other benign and malignant myxoid soft tissue tumours is mainly based on morphology and the exclusion of mimicking lesions with the help of immunohistochemistry. It is a difficult task, given the absence of exclusively specific diagnostic markers. Immunoreactivity for desmin, SMA, MSA, vimentin, CD34 is noted in tumour cells, at least focally.⁶ Several previous reports have demonstrated positive expression of ER and/or PR in a majority

Figure 3 Immunohistochemical findings: neoplastic cells with positive vimentin (A), positive CD34 (B), positive SMA (C) and focal positive desmin (D) immunoreactivity. Neoplastic cells were negative for oestrogen (E) and progesterone receptors (F).

of the cases occurring in females (>90%).⁶ However, data of hormone receptor expression in male AAM are sparse. In a small series of four cases of males with AAM, Idrees *et al* reported hormone receptor positivity (one case of ER+, three cases of PR+) in the males.⁹ Silverman *et al* have described two AAMs in males, which did not express ER or PR hormone receptors but stained for AR.¹⁰ Our case showed positive AR expression in a small percentage of nuclei. Chihara *et al* have reported a case in which 80% of the tumour cells expressed AR and 20% expressed PR, but no expression of ER was observed.^{2 11} With reference to the expression of sex hormone receptors such as ER and AR and the peculiar localisation of AAMs to the pelvis and genital region in women and scrotum in men, it has been postulated that the onset and maintenance of growth in AAMs may be related to the occurrence of these hormone receptors in the tumour. Furthermore, it is known that the pelvic and perineal tissues show immunohistochemical localisation of ER and AR, which may be represented in the tumour.^{2 12} Wide local excision with tumour-free surgical margins is the treatment of choice. Due to the risk of late recurrence, close follow-up remains necessary. A yearly follow-up using imaging modalities has been proposed along with clinical supervision.¹³

Learning points

- ▶ Aggressive angiomyxoma (AAM) is a rare mesenchymal benign myxoid tumour, described almost exclusively in adult females and can in rare instances occur in males.
- ▶ Tumour cells are usually immunoreactive for desmin, SMA, MSA, vimentin, CD34 and are negative for S100.
- ▶ In contrast to females, where oestrogen receptor (ER) and/or progesterone receptor (PR) is almost always expressed, ER and PR staining is usually negative in males.

Contributors All authors made a significant contribution to this study. AN: manuscript preparation, documentation, acquisition of data. NH: compilation and manuscript editing. NA: conception and design. PS: acquisition of data and reports.

This manuscript has not been submitted for publication; it has not been accepted for publication and has not been published in any other journal. All authors have read and approved the final version of the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2018. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Steeper TA, Rosai J. Aggressive angiomyxoma of the female pelvis and perineum. Report of nine cases of a distinctive type of gynecologic soft-tissue neoplasm. *Am J Surg Pathol* 1983;7:463–75.
- 2 Chihara Y, Fujimoto K, Takada S, *et al*. Aggressive angiomyxoma in the scrotum expressing androgen and progesterone receptors. *Int J Urol* 2003;10:672–5.
- 3 Tsang WY, Chan JK, Lee KC, *et al*. Aggressive angiomyxoma. A report of four cases occurring in men. *Am J Surg Pathol* 1992;16:1059–65.
- 4 Rao SN, Dais E, Prabhu S, *et al*. Aggressive angiomyxoma of the epididymis - a case report. *Indian J Urol* 2001;18:96–7.
- 5 Srinivasan S, Krishnan V, Ali SZ, *et al*. "Swirl sign" of aggressive angiomyxoma—a lesser known diagnostic sign. *Clin Imaging* 2014;38:751–4.
- 6 Fetsch JF, Laskin WB, Lefkowitz M, *et al*. Aggressive angiomyxoma: a clinicopathologic study of 29 female patients. *Cancer* 1996;78:79–90.
- 7 Iezzoni JC, Fechner RE, Wong LS, *et al*. Aggressive angiomyxoma in males. A report of four cases. *Am J Clin Pathol* 1995;104:391–6.
- 8 Sato K, Ohira M, Shimizu S, *et al*. Aggressive angiomyxoma of the liver: a case report and literature review. *Surg Case Rep* 2017;3:92.
- 9 Idrees MT, Hoch BL, Wang BY, *et al*. Aggressive angiomyxoma of male genital region. Report of 4 cases with immunohistochemical evaluation including hormone receptor status. *Ann Diagn Pathol* 2006;10:197–204.
- 10 Silverman JS, Albukerk J, Tamsen A. Comparison of angiofibroblastoma and aggressive angiomyxoma in both sexes: four cases composed of bimodal CD34 and factor XIIIa positive dendritic cell subsets. *Pathol Res Pract* 1997;193:673–82.
- 11 Dehuri P, Gochhait D, Srinivas BH, *et al*. Aggressive Angiomyxoma in Males. *J Clin Diagn Res* 2017;11.
- 12 McCluggage WG, Patterson A, Maxwell P. Aggressive angiomyxoma of pelvic parts exhibits oestrogen and progesterone receptor positivity. *J Clin Pathol* 2000;53:603–5.
- 13 Rao KS, Rao KA, Praveen S, *et al*. Aggressive angiomyxoma of scrotum presenting as scrotal lymphedema in a case of postoperative carcinoma penis. *Indian J Surg* 2015;77:170–1.

Copyright 2018 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>. BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow