

Long-term follow-up of a recurrent multifocal desmoid tumour treated with tamoxifen: A case report

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ABSTRACT

We report a long-term follow-up of a female patient with a multifocal extremity desmoid tumour. She had 3 local recurrences after excision and developed a second unresectable pelvic tumour that has remained unchanged in size for 14 years since starting tamoxifen treatment.

Key words: *extremities; fibromatosis, aggressive; recurrence; tamoxifen*

INTRODUCTION

Fibromatoses are proliferations of highly differentiated fibrous tissue. The deep or musculoaponeurotic types

of fibromatoses are known as desmoid tumours, aggressive fibromatoses, or desmoid-type fibromatoses. Desmoids are insidiously growing tumours that tend to be more aggressive than the superficial type. They may involve the musculature of the trunk and extremities, the abdominal wall, or the bowel wall and mesentery when associated with familial adenomatous polyposis.

Multifocal tumours have been reported involving the same anatomical site, and occasionally 2 anatomical sites,^{1,2} but desmoid tumours are not known to metastasise. Indeed, some cases have been reported to spontaneously cease growing or regress.³⁻⁵

Surgery is the recommended primary treatment, but there is a high risk of local recurrence, and achieving tumour-free resection may result in significant morbidity.^{3,6-11} Chemotherapy and radiotherapy have been used both preoperatively and postoperatively, although their roles and efficacy remain controversial.^{8,9,12-14}

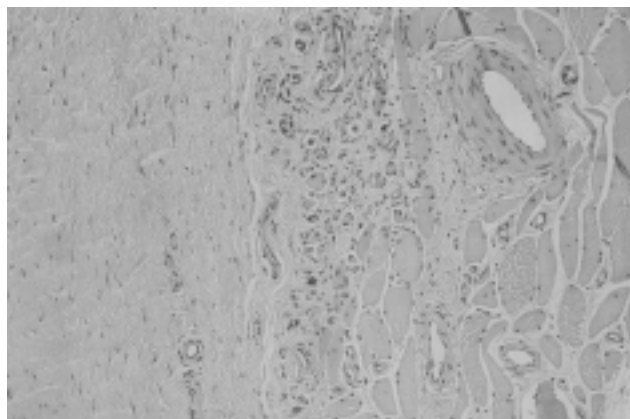


Figure 1 Photomicrograph showing margin of desmoid tumour (left) infiltrating skeletal muscle (right) [x200].

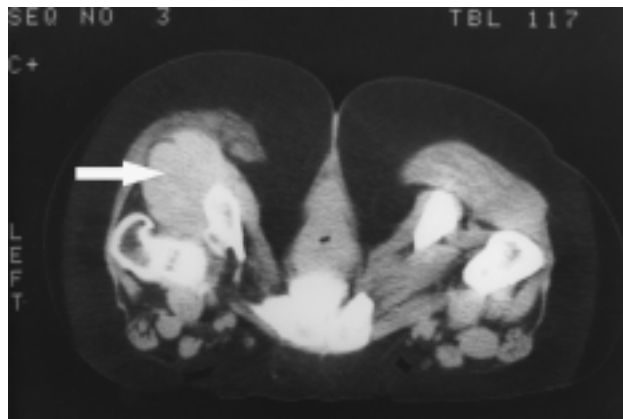


Figure 2 Computed tomographic scan of the patient taken at age 33 years showing desmoid tumour (arrow) posterior to left hip extending around ischium.

The frequent occurrence of desmoids in young, gravid, or parous women, and the occasional spontaneous remission following menopause, has suggested an endocrine influence in the pathogenesis of desmoid tumours.^{2,15} Anti-oestrogen therapy, such as tamoxifen, has been reported to induce regression of desmoid tumours,¹⁵⁻¹⁹ including one case of multifocal desmoid tumour,¹⁸ although oestrogen receptors have usually been negative.^{10,19}

CASE REPORT

A 26-year-old female school teacher presented to Dunedin Public Hospital in June 1982 with a lump behind the left knee that had gradually increased in size over the preceding 12 months. A computed tomographic (CT) scan identified a soft-tissue mass partially located in the medial head of the gastrocnemius. Surgical exploration revealed an ovoid mass of 60x40 mm arising from the fascia of the medial head of the gastrocnemius, with an extension passing towards the popliteal fossa.

Microscopic examination revealed a mild-to-moderate cellular desmoid tumour of bland spindle cells with minimal nuclear pleomorphism and minimal mitotic activity. Tumour tissue extended to resection margins (Fig. 1). Immunohistochemistry, using DAKO (DakoCytomation; Denmark) antibodies and standard labelled streptococcus avidin biotin (LSAB) technique, showed that the tumour cells were positive for vimentin and smooth muscle actin, but negative for CD34, desmin, and S100. Oestrogen

(clone 1D5) and progesterone receptor antibody immunohistochemistry was also negative.

Two years later, at age 28, a recurrence developed and extended proximally to the mid-thigh. The recurrent tumour surrounded the peroneal and tibial nerves in the popliteal fossa. A good clearance was achieved proximally, but further recurrence developed distally and required further excision shortly afterwards.

Pregnancy at age 30 years produced the patient's only child, at which time she appeared to be disease-free. However, by age 33 years, a grapefruit-sized tumour had recurred in the left gluteus maximus. The tumour was fixed to the posterior hip capsule and was eroding the ischium as it passed through the sciatic notch to encase the sciatic nerve (Fig. 2). Open biopsy confirmed the presence of desmoid tumour. As surgical clearance would have required hindquarter amputation, a trial of tamoxifen 20 mg daily was commenced instead. Serial CT and subsequent magnetic resonance imaging scans have shown no change in tumour size over 14 years (Fig. 3).

The patient developed menopausal symptoms at age 35 years, but hormone replacement therapy was not initiated. Pelvic ultrasound scans, cervical smears, and endometrial biopsies have revealed no side-effects from the tamoxifen therapy to date.

21 years after the initial resection of desmoid tumour in the popliteal fossa, and 14 years after starting tamoxifen therapy for the unresectable pelvic desmoid tumour, the patient remains healthy with a good quality of life. The operated left leg is mildly swollen, with some wasting of the gluteals

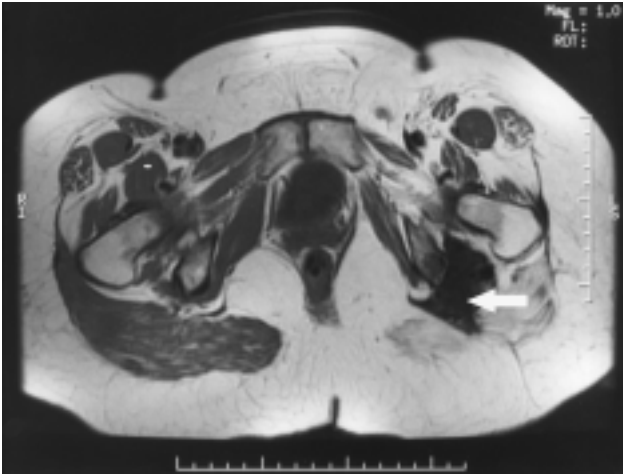


Figure 3 T1-weighted magnetic resonance imaging scan of the patient taken at age 47 years showing no change in desmoid tumour size (arrow) after 14 years of tamoxifen therapy.

and quadriceps, restriction of knee flexion to 100°, reduced flexion of the left hip to 80°, and some hamstring weakness. Her peripheral leg pulses are equal. An episode of cellulitis in the affected limb was treated in 2004.

DISCUSSION

The infiltrative growth pattern of desmoid tumours is implicated in their tendency to recur; therefore, surgical resection with clear margins is the goal for treatment. Recurrence rates vary considerably in the literature, ranging from 23% to 68% in extremity desmoids.^{3,6,8-11} The risk of local recurrence appears most closely related to the extent of surgical excision, with fewer recurrences in margin-negative patients than margin-positive patients.^{3,10,12} However, Merchant et al.⁸ and Gronchi et al.¹¹ found that positive margins were not prognostically significant. Microscopic examination of surgical margins, especially in recurrences, may be difficult to interpret because of the similarity of scar tissue and desmoid tumour.

Surgery is also recommended for recurrences, with good results reported after second resection. For example, recurrence-free survival was reported in 19 (86%) of 22 cases at 67 months,⁸ and 85% at 70 months.²⁰ Recurrence-free survivals are similar

for second and subsequent resections.³ However, Gronchi et al.¹¹ found only 59% disease-free survival 10 years after surgery for recurrence. Recurrence may also occur in a multifocal pattern, as seen in this case, suggesting a regional field defect.²

The rationale for hormonal treatment of desmoid tumours comes from observations summarised by Fong et al.² and Serpell et al.¹⁵ Wilcken and Tattersall¹⁹ reviewed a number of anecdotal reports and found a response in 28 (51%) of 55 cases, with follow-up ranging from 10 months to 8 years. The mechanism of action of these hormonal agents is not clear. Oestrogen receptors have been identified in 22% to 33% of desmoid tumours.^{15,21} However, Sorenson et al.¹⁰ found no oestrogen receptors in 72 patients and suggested that the effect may be due to an alternative mechanism via the induction of transforming growth factor beta.²²

An unusual feature of desmoid tumours is their ability to regress or cease growing. Rock et al.³ reported 68 patients who had no further treatment with tumour recurrence. During a mean follow-up period of 6.3 years, 6 of the tumours had regressed and 60 were stable in size. Lewis et al.⁴ reported a subgroup of 15 patients with unresectable recurrent desmoid tumours in the extremities who had a variety of adjuvant treatments rather than an amputation. At follow-ups of 25 to 92 months, no patients had required surgery, no metastases were detected, and no patient had died from the disease. In the 5 patients who received no treatment, the results were similar to the whole series.

Failure to completely resect a desmoid tumour may be associated with recurrence, but tumour progression rarely causes death. Therefore, it appears reasonable to closely observe a recurrent unresectable tumour, with or without adjuvant therapy.^{3,4,8,9}

It is not certain whether the pelvic tumour in this case would have regressed or stabilised spontaneously, but there was a compelling history of local and multifocal recurrence resulting in an inoperable tumour 7 years following initial presentation. This inoperable tumour has remained unchanged for 14 years with tamoxifen treatment, and we believe this is the longest follow-up of the disease without progression to date. Although there are no prospective randomised studies, tamoxifen should still be considered in the management of unresectable desmoid tumours.

REFERENCES

1. Reitamo JJ, Scheinin TM, Hayry P. The desmoid syndrome. New aspects in the cause, pathogenesis and treatment of the desmoid tumor. *Am J Surg* 1986;151:230-7.
2. Fong Y, Rosen PP, Brennan MF. Multifocal desmoids. *Surgery* 1993;114:902-6.
3. Rock MG, Pritchard DJ, Reiman HM, Soule EH, Brewster RC. Extra-abdominal desmoid tumors. *J Bone Joint Surg Am* 1984; 66:1369-74.
4. Lewis JJ, Boland PJ, Leung DH, Woodruff JM, Brennan MF. The enigma of desmoid tumors. *Ann Surg* 1999;229:866-73.
5. Dalen BP, Bergh PM, Gunterberg BU. Desmoid tumors: a clinical review of 30 patients with more than 20 years' follow-up. *Acta Orthop Scand* 2003;74:455-9.
6. Easter DW, Halasz NA. Recent trends in the management of desmoid tumors. Summary of 19 cases and review of the literature. *Ann Surg* 1989;210:765-9.
7. Pritchard DJ, Nascimento AG, Petersen IA. Local control of extra-abdominal desmoid tumors. *J Bone Joint Surg Am* 1996; 78:848-54.
8. Merchant NB, Lewis JJ, Woodruff JM, Leung DH, Brennan MF. Extremity and trunk desmoid tumours: a multifactorial analysis of outcome. *Cancer* 1999;86:2045-52.
9. Pignatti G, Barbanti-Brodano G, Ferrari D, Gherlinzoni F, Bertoni F, Bacchini P, et al. Extraabdominal desmoid tumor. A study of 83 cases. *Clin Orthop* 2000;375:207-13.
10. Sorensen A, Keller J, Nielsen OS, Jensen OM. Treatment of aggressive fibromatosis: a retrospective study of 72 patients followed for 1-27 years. *Acta Orthop Scand* 2002;73:213-9.
11. Gronchi A, Casali PG, Mariani L, Lo Vullo S, Colecchia M, Lozza L, et al. Quality of surgery and outcome in extra-abdominal aggressive fibromatosis: a series of patients surgically treated at a single institution. *J Clin Oncol* 2003;21:1390-7.
12. Ballo MT, Zagars GK, Pollack A, Pisters PW, Pollock RA. Desmoid tumor: prognostic factors and outcome after surgery, radiation therapy, or combined surgery and radiation therapy. *J Clin Oncol* 1999;17:158-67.
13. Nuyttens JJ, Rust PF, Thomas CR Jr, Turrisi AT 3rd. Surgery versus radiation therapy for patients with aggressive fibromatosis or desmoid tumors: A comparative review of 22 articles. *Cancer* 2000;88:1517-23.
14. Baliski CR, Temple WJ, Arthur K, Schachar NS. Desmoid tumors: a novel approach for local control. *J Surg Oncol* 2002; 80:96-9.
15. Serpell JW, Paddle-Ledinek JE, Johnson WR. Modification of growth of desmoid tumours in tissue culture by anti-oestrogenic substances: a preliminary report. *Aust N Z J Surg* 1996;66:457-63.
16. Kinzbrunner B, Ritter S, Domingo J, Rosenthal CJ. Remission of rapidly growing desmoid tumours after tamoxifen therapy. *Cancer* 1983;52:2201-4.
17. Thomas S, Datta-Gupta S, Kapur BM. Treatment of recurrent desmoid tumour with tamoxifen. *Aust N Z J Surg* 1990;60: 919-21.
18. Procter H, Singh L, Baum M, Brinkley D. Response of multicentric desmoid tumours to tamoxifen. *Br J Surg* 1987;74:401.
19. Wilcken N, Tattersall MH. Endocrine therapy for desmoid tumors. *Cancer* 1991;68:1384-8.
20. Posner MC, Shiu MH, Newsome JL, Hajdu SI, Gaynor JJ, Brennan MF. The desmoid tumor. *Arch Surg* 1989;124:191-6.
21. Lim CL, Walker MJ, Mehta RR, Das Gupta TK. Estrogen and antiestrogen binding sites in desmoid tumors. *Eur J Cancer Clin Oncol* 1986;22:583-7.
22. Colletta AA, Wakefield LM, Howell FV, van Roozendaal KE, Danielpour D, Ebbs SR, et al. Anti-oestrogens induce the secretion of active transforming growth factor beta from human fetal fibroblasts. *Br J Cancer* 1990;62:405-9.