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EJSO
the Journal of Cancer Surgery
ELSEVIER
EJSO 35 (2009) 129–134
www.ejso.com

A critical analysis of treatment strategies in desmoid tumours: a review of a series of 106 cases

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Accepted 17 June 2008
Available online 29 August 2008

Abstract

Background: The management of desmoid tumours, previously based on strategies employed for sarcomas, should be reassessed, given the morbidity of interventions used in their treatment.
Methods: Long-term follow-up (median 123 months) of a series of 106 treated patients with 69 primary and 37 recurrent desmoids, in order to study natural history and outcome.
Results: Desmoids typically evolved actively over a median period of 3 years, and stabilised thereafter. Recurrences or progression most commonly occurred between 14 and 17 months. Risk factors for recurrence were presentation (primary vs. recurrent), gender, tumour location and resection margins. However, survival was independent from these factors, with equivalent survival whether resection had been performed or not. Tumour control and functional outcome depended on location and presentation. Functional impairment was proportional to number of operations and whether patients had received radiotherapy. Recurrences were observed in 12/23 patients after radiotherapy.
Conclusion: Desmoids are relatively indolent tumours needing different approaches than sarcomas. Direct surgery is advisable only in primary lower trunk wall/girdle locations. Wait-and-see and medical treatment is preferable in other types of presentations.

Keywords: Desmoid tumours; Aggressive fibromatosis; Treatment; Surgery; Radiotherapy; Benign disease; Functional impairment; Medical treatment

Introduction

Treatment for desmoid tumours (deep fibromatoses) has been modelled on that for low-grade soft tissue sarcomas, with which desmoids have been grouped.[1,2] Therapeutic options include surgery, the mainstay of treatment, radiotherapy, non-cytotoxic therapies,[3] and more traditional systemic chemotherapy. Treatment efficacy is difficult to evaluate because of the unpredictable behaviour of desmoids.[4–7] Despite local aggressiveness, desmoids are usually not life-threatening. Therefore, arguably, treatment should be different from that for sarcomas and other cancers. For example, quality of margins, which is of utmost importance in sarcoma,[8] gives somewhat paradoxical results in desmoids.[9–15] Owing to their infiltrative pattern, clear margins are difficult to obtain, leading to repeated operations and significant morbidity, functional impairment and disabling sequelae.[6,7,16] These complications can be compounded by radiotherapy.[17,18] Moreover, surgery may promote recurrences via the cicatrisation process.[19] The role of surgery in treating desmoids has therefore been questioned.[20] Some authors now suggest a wait-and-see policy in selected cases.[6,11,12,15,16] Desmoids form a heterogeneous group of tumours with regard to clinical variables (age of occurrence, gender distribution, location, symptoms, primary vs. recurrent presentation, growth patterns)[11,14,15] or with association to familial adenomatous polyposis (FAP).[21] Here we analyse the natural history of

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doi:10.1016/j.ejso.2008.06.1495

a series of desmoid tumours in order to identify clinical variables for establishing the prognostic factors that could lead to better treatment outcomes.

Patients and methods

Selection of patients, surveillance, definitions and follow-up

Patients treated or followed-up at our centre for desmoid tumours from 1976 to 2007 were included. For those operated outside the centre, a systematic pathological review was performed at referral. Primary and recurrent desmoids were included. For patients referred for recurrence, their initial medical history (date and type of treatments, surgical reports) was retraced. Age was determined at diagnosis. The Union Internationale Contre le Cancer (UICC) residual disease classification (*R*) was used to assess quality of surgery. Functional impairment was classified as absent, moderate (compensated by treatment) or major (disability or pain not compensated by treatment). Tumour growth patterns were analysed by calculating the intervals between the date of first event or treatment and date of first recurrence or progression (=time to first recurrence); the intervals between the first and the last tumoural events before stabilisation or regression (=time to progression); and the intervals between last progression and final follow-up (=stable period). Functional impairment was retrospectively determined on the patients' charts. Because of the long-running follow-up, two distinctive categories only were established, comprising none/minor and moderate/major functional impairment.

Survival analysis was not done because there was only a single specific death. Last follow-up was December 2007.

Patient characteristics

One hundred and six patient charts were analysed. Their characteristics are shown in Table 1. The female/male ratio was 2/1. Sixty-nine tumours were primary and 37 recurrent. Mean tumour size was 7 cm. With the exception of four teenagers, all other patients were over 16 years old. Median age was 41 years (range: 11–78 years) with a three-modal distribution of ages comprising a first peak around 20 years, a second around 35 years and a third around 60 years (figure not shown). There was a prior history of trauma at the future tumour zone in 13 patients and development of tumour within a wound scar in 23 patients. Six patients had superficial fibromatosis associated and 3 had an identified Gardner's syndrome. Seven patients had a personal history of intestinal polyps or cancer associated with a familial history of intestinal polyps or cancer or desmoids, highly suspicious of FAP. Three of them had a negative APC mutation analysis. In 8 patients there was either a personal or a familial history of intestinal polyps or cancer that could be linked to FAP.

Table 1
Patients and treatment characteristics

	Primary	Recurrent	Total
Number of patients	69	37	106
Gender (female/male)	51/18	20/17	71/35
Median age at diagnosis (range)	42 years	39 years	41 (11–78) years
Mean tumour size (range)	6	9	7 (1–22) cm
Surgery			
Excision	63	29	92
No excision/biopsy only	6	8	14
Radiotherapy	7	16	23
Chemotherapy	5	6	11
Other treatments (SERMs/NSAIDS/anti Cox2/imatinib/…)	20	22	44
Median follow-up in months (range)	85 (3–377)	170 (18–482)	123 (3–482)
Functional impairment			
Moderate	14	14	28
Major	8	11	19
Final patient status			
NED	51	20	71
AWD	12	12	24
DOC	6	4	10
DOD	–	1	1

NED: alive, no evidence of disease; AWD: alive with disease; DOC: dead of other causes; DOD: dead of disease (or treatment complications).

Treatment policy at our centre

During the 32-year period, various treatments were available. Surgery was advised for primary tumours without complementary treatment. When the tumours were deemed to be inoperable, a first-line medical treatment was delivered. This comprised endocrine treatments (SERMs, especially tamoxifen), non-steroidal anti-inflammatory drugs (NSAIDs), comprising also more specifically cyclooxygenase inhibitors (antiCox2) in the last decade, imatinib mesylate in the last 3 years, interferon and chemotherapy. Whenever possible, surgery was performed secondarily.

In recurrent tumours, re-excision followed by radiotherapy was proposed. During ultimate tumour re-progressions, the same medical treatments as for initial treatments were administered.

Treatments and outcome

Patients underwent a mean of 1.9 operations. Twenty-three patients underwent radiotherapy at a median dose of 50 Gy (range 20–60 Gy), 7 initially and 16 after recurrence. Eleven patients had chemotherapy and 44 received various medical treatments as detailed above. Treatment associations were used more recently. After all the delivered treatments, 47 patients remained with some functional impairment. At a median follow-up of 123 months (range: 3–482 months), one patient had died of treatment consequences (a postoperative vascular rupture after surgery for a recurrent mesenteric desmoid), 10 had died of other