AMJ Australasian Medical Journal [AMJ 2017;10(1):11–17]

Our surgical experience in Desmoid Tumours

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RESEARCH

Please cite this paper as: Acar T, Acar N, Kar H, Tavusbay C, Kamer E, Atahan MK, Hacıyanlı M. Our Surgical Experience in Desmoid Tumours. AMJ 2017;10(1):11–17.
https://doi.org/10.21767/AMJ.2017.2704

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ABSTRACT

Background
Desmoid tumour (DT) is a locally aggressive soft tissue tumour which is histologically characterized by fibroblastic proliferation in collagen matrix. They may originate from almost any location, mainly from limbs, abdominal wall and abdominal cavity, and occur more frequently in women of childbearing age.

Aims
Radical resection is generally considered as the most appropriate treatment for patients with desmoid tumours. Alternative methods of treatment are available for patients with unresectable.

Methods
Nine patients who had DT pathology between January 2008 and January 2013 in İzmir Katip Çelebi University Atatürk Training and Research Hospital, General Surgery Clinic were included in the study.

Results
The mean age of the nine patients (three males and six females) was 40.1. Two patients (one male and one female) had been diagnosed with familial adenomatous polyposis (FAP), accompanied by Gardner's syndrome (GS). Among the desmoid tumours, five (55.6 per cent) were intra-abdominally located, two (22.2 per cent) were located in the anterior abdominal wall, one (11.1 per cent) in limbs, and one (11.1 per cent) in breast.

Conclusion
Surgical resection in which a sufficient amount of surrounding healthy tissue is removed together with the tumour provides an effective treatment. We believe that, for those tumours which cannot be resected or incompletely resected, addition of Tamoxifen to the therapy will provide favourable results for regression.

Key Words
Desmoid tumours, gardner's syndrome, familial adenomatous polyposis, tamoxifen

What this study adds:

1. What is known about this subject?
Removal of desmoid tumours which have a high local recurrence rate with the sufficient surrounding healthy tissue provides an effective treatment.

2. What new information is offered in this study?
Tamoxifen has a positive effect on the regression in patients whose tumour could not be resected or was resected inadequately.

3. What are the implications for research, policy, or practice?
Effectiveness of tamoxifen should be tested on more patients.

Background

Desmoid tumour (DT), also known as aggressive fibromatosis, is a locally aggressive soft tissue tumour which is histologically characterized by fibroblastic proliferation in collagen matrix.[1] They originate from musculoaponeurotic

tissue. They may develop sporadically or in patients with familial adenomatous polyposis (FAP), Gardner's syndrome (GS). They account for 3 per cent of all soft tissue tumours and 0.03 per cent of all neoplasias.[2] They may originate from almost any location, mainly from limbs, abdominal wall and abdominal cavity, and occur more frequently in women of childbearing age.[3,4] Local trauma, history of abdominal surgery and oestrogen are thought to play a role in their etiology.[5,6] They have a low metastatic potential, but high rates of recurrence and associated morbidity and mortality. They may cause obstruction in adjacent organs as a result of local invasion. Radical resection is generally considered as the most appropriate treatment for patients with desmoid tumours. In our study, we retrospectively reviewed the files of our nine patients diagnosed with DT to present the clinicopathological characteristics of the patients and our diagnosis and treatment approach along with the literature.

Method

Nine patients who had DT pathology between January 2008 and January 2013 in İzmir Katip Çelebi University Atatürk Training and Research Hospital, General Surgery Clinic were included in the study. Their files were retrospectively reviewed. Their clinicopathological and demographic characteristics such as age and gender were evaluated. Additional information was obtained on their history of pregnancy as well as familial history. The locations, sizes and histological characteristics of the tumours were examined. The methods used for diagnosis and treatment were reviewed. Data on operative morbidity, recurrence and mortality were collected.

Results

The clinicopathological characteristics of the nine patients included in the study are detailed in Table 1. The mean age of the nine patients (three males and six females) was 40.1 (20-65). The main complaints at admission were abdominal pain, nausea and vomiting in patients with intra-abdominally located tumours, and palpable mass in patients with tumours located in the limbs. Preoperative whole abdominal or superficial tissue ultrasonography (US) and whole abdominal computed tomography (CT) were performed in the patients. Four of the six female patients had a recent history of childbirth, and two patients (one female and one male) had a history of surgical intervention at the DT location. One male patient had been operated upon due to colon cancer and received chemotherapy.

Two patients (one male and one female) had been diagnosed with FAP accompanied by GS. In the patients with the diagnosis of FAP, total colectomy had been performed and intra-abdominal desmoid tumours were detected during their follow-up. Among the desmoid tumours, five (55.6 per cent) were intra-abdominally located, two (22.2 per cent) were located in the anterior abdominal wall, one (11.1 per cent) in limbs, and one (11.1 per cent) in breast. The mean size was 10.1 cm (0.8–25 cm). All patients received surgery as the primary intervention (Table 2). In the patient with Gardner's syndrome, who had received total colectomy due to FAP, exploration was performed due to an intra-abdominal mass. The mass was considered unresectable after seeing that it originated from the retroperitoneum and invaded the surrounding structures and it was impossible to completely resect it (Figure 1). Then the patient received adjuvant chemotherapy (CT), radiotherapy (RT) and Tamoxifen. During the follow-up, a significant regression was observed in the tumour associated with Tamoxifen (Figure 2). Postoperative routine RT was given to the patients with tumours located in the limbs and in the anterior abdominal wall.

The synchronous risk factors of the patients are described in Table 3. After a median follow-up of 34.6 months (17–83), local recurrence was detected in two patients, one in the rectus muscle and one intra-abdominal. The patient with recurrence in the rectus muscle had developed recurrence despite receiving postoperative RT. Re-excision had been performed in this patient. However, the mass could not be excised due to vascular invasion (Figure 3). One patient, in whom excision could not be performed, had died while seven patients are currently alive and disease-free and one patient is alive and continues Tamoxifen therapy due to an unresectable mass.

Discussion

Desmoid tumours are rare tumours which first entered in the medical literature at the beginning of the 19th century. It is derived from the Greek word "desmos", *w*hich means "tendon". They are benign tumours with aggressive behaviour originating from aponeuroses of fascia and muscle. They account for 3 per cent of all soft tissue tumours and 0.03 per cent of all neoplasias. The incidence is 2-4/1 million per year. They may be histologically benign but clinically aggressive. Koh et al. divided these tumours into five groups according to their clinical course: spontaneous regression, stable, variable growth, progressive growth and aggressive growth.

Although most of them are asymptomatic, they may show non-specific symptoms such as abdominal mass, abdominal pain, malaise or vomiting. They can also cause important

complications such as infiltration to adjacent organs, intestinal obstruction, ischemia, perforation, hydronephrosis, urethra fistulisation, and even aortic rupture.[7,8] GIST, lymphoma, carcinoid tumour, fibrosarcoma and inflammatory fibroid polyps should be considered in the differential diagnosis.[9] Although the aetiology of the disease is unknown, injury, previous operations, genetic and hormonal factors are thought to play a role.[5] The disease is more frequently seen mainly in women of childbearing age, aged between 25 and 40 years, while it is rare in men.[10] There are many articles reporting shrinking of existing tumours in menopausal women and in those receiving tamoxifen, and development of tumours in those receiving oral contraceptives and indicating the role of oestrogen in multifactorial pathogenesis.[11] In our study the number of female patients was greater and the mean ages were 41 and 38 for females and males respectively. Four of our six female patients had a recent history of childbirth, and two had a history of use of oral contraceptives. Tamoxifen was initiated in a patient with an unresectable mass and a significant regression was observed in the tumour. Desmoid tumours can be extra-abdominal (the shoulder girdle, trunk and lower limbs) or intra-abdominal (mainly in the rectus and fascial area of the anterior abdominal wall, mesentery or retroperitoneum) located, or a part of FAP or Gardner's syndrome. Those that are abdominally located are the most common group and rates as high as 37–50 per cent was reported in different publications. Such tumours do not involve the skin, and association with FAP is more common. Retroperitoneal tumours, on the other hand, are more frequently seen with Gardner's syndrome, especially after abdominal surgery. Those that are extra-abdominally located are seen mainly in the limbs. In our patients, the main locations of the tumours were the rectus muscle and mesentery. The tumour in one of the patients with Gardner's syndrome was located in the retroperitoneum and could not be resected.

Ultrasonography (US), computed tomography (CT scan)) and magnetic resonance imaging (MRI) can be used to diagnose desmoid tumors.[12] However, it is impossible to make a definitive diagnosis using laboratory and imaging methods. Diagnosis can be made using histological and immunohistochemical findings.[13] Imaging methods have generally provided information about the location and size of the mass and whether it has intra-abdominal association. While ultrasonography reveals a smooth-bordered, hypoechogenic mass with well-defined margins and variable echogenicity, CT scan reveals a sharp-bordered, homogeneous mass which is isodense-hyperdense compared to the muscle tissue.[14] Magnetic resonance reveals a mass that shows, compared to the muscle, shows low signal density in T1-weighted examination and variable signal density in T2-weighted examination.[10,15] Computed tomography and MRI can also be used to identify recurrences in postoperative screening and follow-up. Histologically, DT consists of long fibroblasts and myofibroblasts.[16] Fibrous tissues are present that are of hypocellular structure and invade adjacent muscles. In patients with spontaneous soft tissue masses and suspected DT, biopsy should first be performed. We requested US and CT scan in our patients for diagnosis, screening and differential diagnosis during the preoperative period and for follow-up during the postoperative period. In preoperative evaluation, especially CT scan served as a guideline in terms of the tumour's location and association with the surrounding structures. In patients with extra-abdominally located tumours, the definitive diagnosis was made using tru-cut needle biopsy and then excision was performed.

Close monitoring is an acceptable strategy for asymptomatic DT.[15] The French and Italian sarcoma group published an algorithm in this matter. They recommend that, in asymptomatic patients, if the patient consents, a "wait and see" approach be used as a first-line management, and if progression is seen, resection be performed.[17] However, in symptomatic patients, the main treatment is to perform wide local excision including a solid border of 1–2cm to remove the entire mass.[18,19] All effort should be made to completely eradicate the disease in the first operation. If possible, the peritoneum, abdominal organs or bone structures associated with the tumour should be removed. However, complete resection may not always be technically possible depending on the diameter or location of the tumour. Incomplete resection or positive surgical margin cause high local recurrence rates (20–77 per cent depending on the width and completeness of the initial resection).[10,15] Local recurrence rates following surgical resection are quite high especially in those with associated FAP or Gardner's syndrome.[20] Mendenhall et al. reported very high recurrence rates during their 10-year follow-up period after excision of tumours with positive surgical margin.[21] This rate is slightly lower in tumours located in the abdominal wall (20–30 per cent). The factors affecting disease-free survival include the size of tumour being >5cm, the location of the tumour, R1 resection status and history of recurrence.[22–24] Despite this aggressive course, they do not show metastasis or invade the skin.[10,16]

Alternative treatments include chemotherapy (CT), radiotherapy (RT), hyperthermia, hormonal therapy (Tamoxifen) and NSAIDs (non-steroidal anti-inflammatory

drugs).[25] Failure rates are higher in recurrent patients, young patients aged under 30 years, those with inadequate resection in the initial resection and those who did not receive RT despite macroscopic residual disease.[26,27] Therefore, RT is recommended in patients with DT or with positive surgical margins following resection. At least 55 Gy is required. However, it should be remembered that RT can cause complications such as fibrosis, paresis, oedema, enteritis or development of secondary cancer. Desmoid tumours show variable responses to CT. The most commonly used current CT protocol includes Vincristine, Actinomycin D and Cyclophosphamide. Most patients do not respond. In their retrospective study, Baliski et al. reported that 13 patients diagnosed with DT received 30mg/day Adriamycin during the preoperative period and 3,000 cCy RT during the postoperative period.[28] During the 71-week follow-up period, recurrence was seen in only two patients and the success rate was 85 per cent. The authors stated that therefore it will be better to use a preoperative CT and then a combination of surgery and RT than to use traditional treatment. It is thought that the effect of steroids used as an alternative in the treatment is secondary to inhibition of prostaglandin synthesis which is required for tumour growth. We gave CT, RT and then Tamoxifen to a patient with an unresectable mass originating from the retroperitoneum. A significant reduction was observed in the size of the tumour. Recurrence was observed in one of the other patients who received RT. When compared with the patients who did not receive postoperative treatment, no significant difference is seen in terms of disease-free and overall survival. A group of drugs such as indomethacins were used along with polynucleotides and theophylline, high-dose ascorbic acid have been used in the treatment of desmoid tumours. It was reported that desmoid tumours regress when Sulindak and other NSAID drugs are used concomitantly with Coumadin.[29] However there are publications reporting the contrary.[30]

A study with 179 patients[31] showed that patients with primary sporadic desmoid tumours who had received complete surgical resection but who had the S45F mutation had a greater tendency for local recurrence than those without it. With increasing use of “wait and see” for DT management, it will be important to determine whether mutation type predicts outcome for these patients.

Conclusion

Although rarely seen, desmoid tumours should be considered especially in women of childbearing potential, who have masses in the anterior abdominal wall or masses of which borders with intra-abdominal organs cannot be clearly defined.

Treatment of desmoid tumours remains controversial. Based on the findings we detected in our patients and the review of the other studies in the literature, these uncommon tumours have high local recurrence rates.

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PEER REVIEW

Not commissioned. Externally peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

FUNDING

No funding to declare.

ETHICS COMMITTEE APPROVAL

Ethic committee approval number: 30.2.IKC.0.05.06.00/37 Date: 25.02.2016.

Figure 1: The mass originating from the retroperitoneum (Axial and coronal CT image)

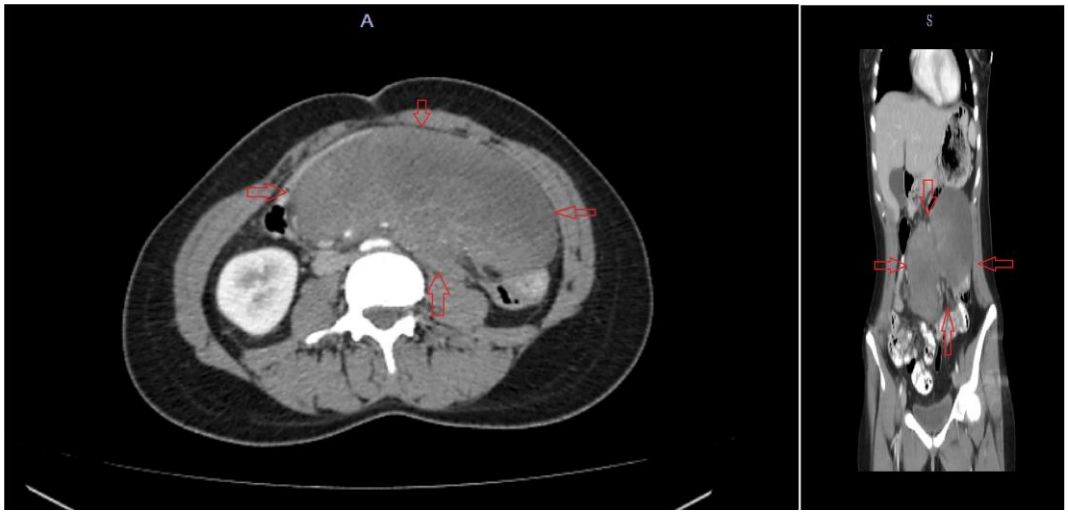

Figure 2: The regression after tamoxifen therapy (Axial and coronal CT image)

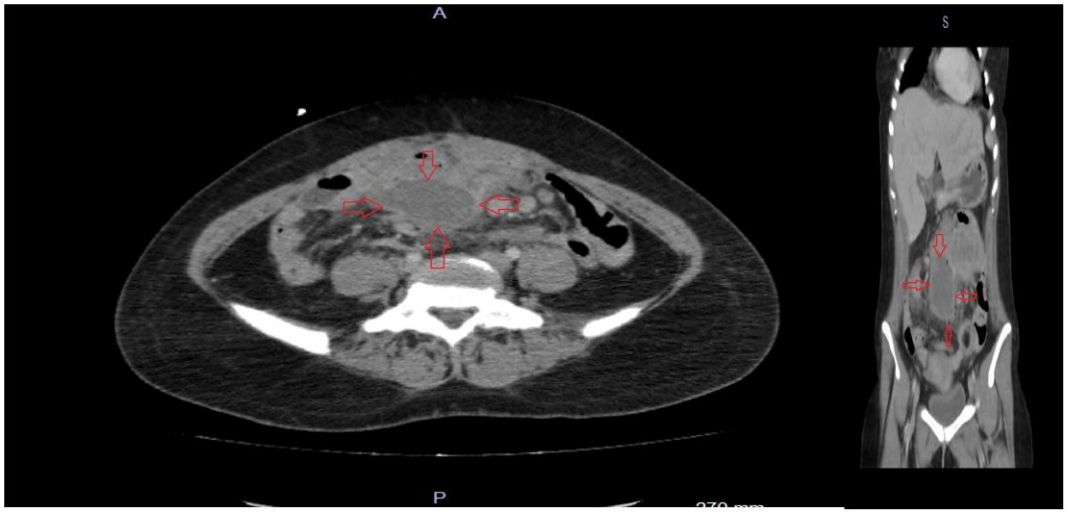

Figure 3: Recurrent mass in the rectus muscle and follow-up CT scan after excision

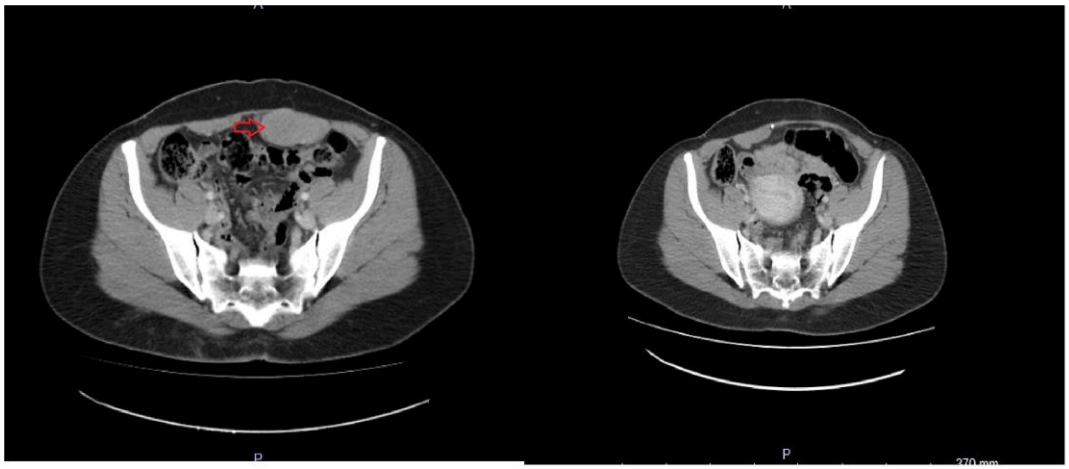

Table 1: Characteristics of the patients (n:9)

Patients	Age	Gender	Localization	Size (cm)	Pregnancy (Yakın dönem)	Type of the surgery	Recurrence	Follow-up (month)
1	41	M	Mesentery of the sigmoid colon	10	-	Colectomy	-	39
2	28	F	Left iliac fossa	9	+	Wide excision	-	28
3	20	M	Mesentery of the small intestine	17	-	Small bowel resection	-	31
4	34	F	Left rectus muscle	9	+	Wide excision	-	22
5	24	F	İntraabdominal	25	+	Exploration	+	19
6	45	F	Left breast	7.5	+	Mastectomy	-	17
7	53	M	Mesentery of the small intestine	0.8	-	Small bowel resection	-	50
8	51	F	Left rectus muscle	3	-	Wide excision	-	83
9	65	F	İntraabdominal	10	-	Debulking surgery	+	22

Table 2: Characteristics of the treatment applied to patients (n:9)

Treatment Characteristics of Patients	M	F
Cerrahi		
Radical excision	2	5
Debulking	0	2
Chemotherapy (CT)	0	1
Radiotherapy (RT)	0	4
Morbidity	1	1
Mortality	0	1

Table 3: Presence of risk factors or family history

Presence of risk factors or family history	Male	Female
Family history	1	1
FAP	1	1
Gardner syndrome	1	1
Colon cancer	1	