© Med Sci Monit, 2012; 18(3): CS17-25
PMID: 22367132

www.MedSciMonit.com
Case Study

CS

Received: 2011.08.18
Accepted: 2011.10.04
Published: 2012.03.01

Multidisciplinary treatment of intra-thoracic desmoid tumors: Case series and narrative review

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Zoltán Mátrai[1ABCDEF], László Tóth[1BC], Zoltán Szentirmay[2BC], János Papp[3C], Zoltán Langmár[4E], Miklós Kásler[5AD]

[1] Department of General and Thoracic Surgery, National Institute of Oncology, Budapest, Hungary
[2] Department of Surgical and Molecular Oncopathology, National Institute of Oncology, Budapest, Hungary
[3] Department of Molecular Genetics, National Institute of Oncology, Budapest, Hungary
[4] 2nd Department of Obstetrics and Gynecology, Semmelweis University and St. Stephen's Hospital, Budapest, Hungary
[5] Department of Head and Neck, Laser and Reconstructive Plastic Surgery, National Institute of Oncology, Budapest, Hungary

Source of support: Departmental sources

Summary

Background: Primary intra-thoracic desmoids are exceedingly rare borderline tumors, with 34 reported cases in the English-language literature. The characteristic localized infiltrative growth and the high rate of recurrence can result in life-threatening conditions. Radical surgical resection is considered to be the primary treatment. Achieving negative surgical margins is a challenge. Cases with positive surgical margins are associated with a high rate of local recurrence; therefore, other multimodal approaches play a large role in their therapy.

Case Reports: The authors reviewed the relevant literature and presented examples of long-term follow-up of 3 intra-thoracic desmoid tumour patients, multidisciplinarily treated between 2000 and 2008. All reports of intra-thoracic desmoid tumors that the authors could find on PubMed or in the reference sections of these PubMed located articles were included using the search terms: intra-thoracic, desmoid, aggressive fibromatoses.

Conclusions: Because of the rarity of the disease and the heterogeneity of the cases, it is difficult to assess the importance of the information for everyday clinical practice. It does however provide a useful guide for reference.

key words: **desmoid tumour • intra-thoracic • aggressive-fibromatoses • b chest**

Full-text PDF: http://www.medscimonit.com/fulltxt.php?ICID=882506
Word count: 3098
Tables: 2
Figures: 3
References: 48

Author's address: Zoltán Mátrai, Department of General and Thoracic Surgery, National Institute of Oncology, Ráth György u. 7-9, H-1122 Budapest, Hungary, e-mail: matraidoc@gmail.com

Background

Desmoids are rare, borderline tumors of the connective tissue, with an annual incidence of 2 to 4 cases per million population [1–3]. They sometimes arise from the musculoaponeurotic structures of the body, but most frequently from the abdominal wall, mesentery and extremities [2]. Aggressive fibromatoses can be classified as extra-abdominal (60% of the cases), abdominal (25%) and intra-abdominal (15%) [2,3]. Macroscopically, the tumour is firm and rubbery, with a relatively homogeneous incisional surface of white and greyish bundles [4]. A characteristic proliferation of thin, spindle-shaped fibroblasts arranged in bands, surrounded by varying amounts of collagen, is found on the microscopic image [2,3]. Desmoids do not metastasize, but are locally invasive, causing deformity, loss of function or even life-threatening compression of vital organs [5–7]. Desmoid tumors have high recurrence rates (24–65% in 10 years) [3,5].

Although the etiology of the tumour is still not understood, factors like genetic predisposition, physical traumas and hormonal effects are acknowledged to be strongly associated with their development [2,3,5,8]. An estimated 2% of all desmoid tumors are associated with familial adenomatous polyposis (FAP), an autosomal dominant disease [2,3,9]. Germ-line mutations of the APC (adenomatous polyposis coli) gene are responsible for the development of FAP-associated desmoids [2,3,9,10]. In contrast, sporadical desmoids are linked to somatic mutations in either β-catenin or APC, resulting in β-catenin protein stabilization [2,3,7]. In approximately 25% of all recorded cases, a trauma to the site of the tumors, often surgical in nature, has been detected [2,11,12]. Sex hormones may have an important role in the pathogenesis of desmoid tumors [2,3,13]. Clinical observations supporting this hypothesis are the 3: 1 female-to-male ratio, the regular occurrence in females of childbearing age, progression with the use of oral contraceptives, and regression in post-menopausal patients or past oophorectomy or anti-oestrogen therapy.

Intra-thoracic desmoid tumors have been reported in the English-language literature 34 times; however, the majority of these cases were seemingly tumors originating from the chest wall with major intra-thoracic extensions [7,12,14–35]. True primary intrapleural desmoid tumors are exceedingly rare, with only 12 reported cases in the English-language literature to the authors' knowledge [7]. As representatives of an oncological centre for soft-tissue sarcomas and thoracic surgery, we present the multidisciplinary treatment and long-term follow-up of 1 FAP-associated and 2 sporadical primary intra-thoracic desmoid tumour cases diagnosed and multidisciplinarily treated by the authors between 2000 and 2008. As a second aim of the article, the relevant literature was also reviewed. In order to draw conclusions, the authors summarized the characteristics and outcomes of the 37 cases (including the ones reported in the present paper) reported to date.

Case Reports

Case 1

A 27-year-old male patient was admitted to our thoracic surgical department in 2004 with a histologically confirmed, recurrent retro-sternal desmoid tumour measuring 50×20 mm.

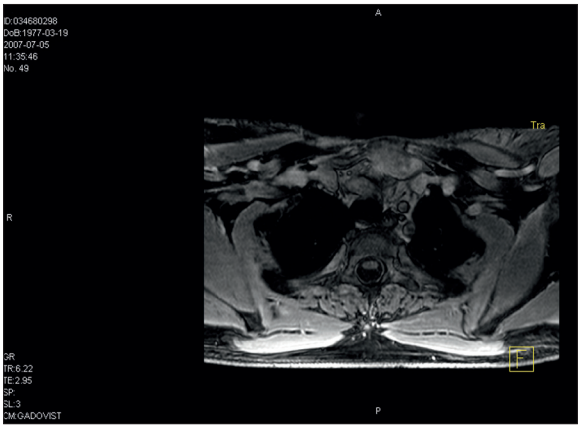

Figure 1. Recurrent tumour with the dimensions of 44×35×54 mm. The tumour was adherent to the left jugular and the left subclavian vein and in close relationship with the trachea.

The tumour was incompletely resected 3 times from the jugulum in another hospital within 16 months prior to admission to our unit. Even after the repeated diminutions, the tumour showed rapid progression toward the left subclavian vessel, the brachiocephalic trunk and the left sternocleidomastoideal muscle. The patient had a negative family history. After performing an MRI of the retro-sternal region and following a negative colonoscopy, radical tumour resection was performed through a clam-shell thoracotomy, with partial resection of the sternocleidomastoideal muscle. Histological investigation revealed microscopically positive resection margins. Adjuvant tamoxifen (20 mg/daily) and sulindac (150 mg/daily) treatment was administered for 12 months. The follow-up investigation at 24 months revealed an asymptomatic locally recurrent tumour with the dimensions of 44×35×54 mm (Figure 1). The tumour was adherent to the left jugular and the left subclavian vein and in close relationship with the trachea. The patient refused a re-operation. Radiotherapy was administered (3-dimensional conformal photon radiation therapy 30 Gy, 2 Gy/day). At the last follow-up at 34 months, the tumour showed no progression.

Case 2

A 17-year-old female patient presented with a primary extra-abdominal desmoid tumour in the lumbo-sacral region measuring 40×50 mm in 2002. The family history was negative. DNA samples retrieved from peripheral leukocytes were screened for all sequences encoding the APC gene using the SSCP/HD (single-strand conformation polymorphism/heteroduplex analysis) technique in order to exclude the possibility of Gardner's syndrome. Germ line mutation of the APC gene was confirmed by direct DNA sequencing (R1450X(4348C>T). Three 5–6 mm large polyps were excised from the large intestine via colonoscopy. The desmoid tumour of the trunk was radically excised. Despite the radical excision, a local recurrence occurred after a follow-up time of 16 months. The recurrent tumour was resected 9 times with microscopically involved surgical margins in the forthcoming 3 years. The desmoid tumour of the trunk was also treated with 3-dimensional conformal radiation therapy to the lumbo-sacral region (50 Gy, 1.8 Gy/day, 18 MV) and with tamoxifen (20 mg/day) and sulindac (2×150 mg/day) administered orally. At the time of the last follow-up, a locally

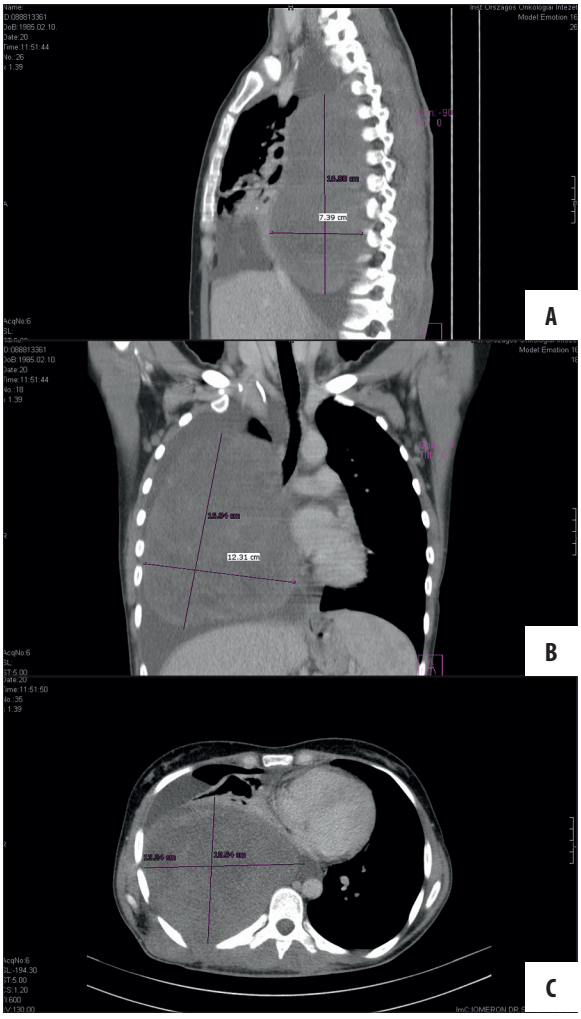

Figure 2A–C. Chest CT scans showed multicentric giant desmoids, a tumour measuring 13×21 cm in the right pleural cavity that almost totally compressed the left lung, another one measuring 3.5×7.8×10 cm in the right hemithorax originating from the basis of the diaphragm, and a lesion measuring 3.5×4×4.5 cm located in the right abdominal wall.

recurrent tumour with the dimensions of 100×120×50 mm was confirmed, showing slow progression.

The young patient was lost to follow-up for 2 years. She came back to our department in January 2009 with melena and weight loss of 20 kg. Colonoscopy revealed polyposis syndrome. A total colectomy with jejunostomy was performed. Histological examination verified adenocarcinoma (pT2 pN1 (1/18), Grade II) in the ascending colon. The patient refused chemotherapy. Three months after the abdominal surgery, the patient was admitted to our outpatient clinic with dyspnea and abdominal pain. Chest X-ray and chest and abdominal CT scans showed multicentric giant desmoids, a tumour measuring 13×21 cm in the right pleural cavity that almost totally compressed the left lung, confirmed by CT-guided percutaneous core biopsy, another measuring 3.5×7.8×10 cm in the right hemithorax originating from the basis of the diaphragm, and a lesion measuring 3.5×4×4.5 cm located in the right abdominal wall (Figure 2A–C). Palliative chemotherapy

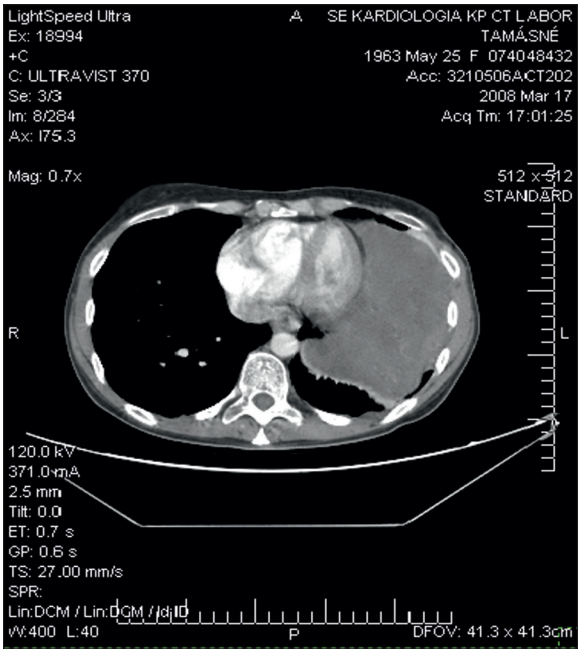

Figure 3. The chest CT revealed a giant tumour measuring 170×103×180 mm, protruding from the left pulmonary hilus with trans-phrenic extension to the level of the pancreas.

(doxorubicin 20 mg/m^2 and dacarbazine 150 mg/m^2) was performed, but the patient died 5 months later.

Case 3

A 45-year-old woman was admitted to our thoracic surgical department in 2007. A giant mass filling the left hemithorax was found on a routine chest X-ray. The patient complained of weak dyspnea after physical exercise. The chest CT revealed a giant tumour measuring 170×103×180 mm, protruding from the left pulmonary hilus with trans-phrenic extension to the level of the pancreas (Figure 3). The tumour infiltrated the posterior mediastinum, reaching the aorta and the oesophagus. A CT-guided core biopsy verified a desmoid tumour. Bronchoscopy, esophago-gastroscopy and colonoscopy were negative. An aggressive surgical strategy was undertaken by left-sided thoraco-phrenico-laparotomy. A wide radical resection of 10 cm^2 of the diaphragm was performed, with atypical resection of the eights segment of the lung and with a resection of the pericardium, 1.5 cm in diameter. The defect in the pericardium was closed with a direct suture, and the diaphragm was reconstructed with GoreTex Dual-Mesh®. Histology confirmed a desmoid tumour measuring 250×150×120 mm and weighing 2300 grams. The resection margin was microscopically free, thus the patient did not receive any adjuvant therapy. At the last checkup of the 27-month-long CT-guided follow-up, the patient was tumour-free. Genetic testing did not reveal any germ-line mutations of the APC gene.

Discussion

Literature search

A literature search was performed in Pubmed using the following keywords: intra-thoracic, aggressive fibromatoses, and desmoids tumors.

Clinical characteristics and demographics

Desmoids of the chest represent 20% of all extra-abdominal fibromatoses [5,7,8,10]. Desmoid tumors can originate at every site of the chest, most commonly in the shoulder girdle [5,8,10]. The intra-thoracic manifestation is extremely rare and probably arises from the pleura or the subpleural mesenchymal cells [5,7]. Shari defined intra-thoracic desmoids as those that originate from the pleura or mediastinum, with the bulk of the tumour within the thoracic skeleton, and minimal chest wall involvement [7]. Intra-thoracic desmoids described in the literature originated intrabronchially or from pulmonary vessels, the brachial plexus infiltrating the paravertebral muscles with interspinal extensions, the mediastinum, ribs of the chest wall, vertebral bodies with trans-diaphragmatic extensions, or subclavian vessels, causing compression of the lung and/or oesophagus [7,12,14–35].

The age distribution of the patients in the reported 37 cases (including the present ones) ranged from 2.5 to 73 years (mean 32.3 years) (Table 1). Twenty-two patients were men and 15 patients were women, which differs from the common female predominance of extra-abdominal desmoids. The preoperative diagnosis of desmoid tumors is based on clinical findings, imaging studies and morphological analysis.

Diagnosis

Intra-thoracic tumors are mainly asymptomatic [5,7,8,20]. True intra-thoracic desmoids are generally asymptomatic until the tumour becomes too large, with compression of the surrounding organs. Sixty percent of the reported intra-thoracic desmoids were greater than 10 cm at the time of diagnosis. Chest pain due to nerve involvement, dyspnea, cough due to compression of the airways and shortness of breath, tenderness, chest wall swelling and dysphagia are the major symptoms [7,12,20]. Limitation of shoulder motion, sweating, cyanosis, paresthesias and pain indicate the involvement of the brachial plexus. Symptoms are usually present for an average of 12–16 months before the discovery of the tumour [5]. According to the reports in the literature, the average tumour size ranged from 2.5 to 27 cm (mean 16.6 cm), and the tumour weights ranged from 680 to 5200 g (Table 1).

The primary diagnosis of intra-thoracic desmoids is often accidental and is made by imaging techniques; on plain chest roentgenograms, they appear mostly as abnormal shadows or minimal cortical erosions [5,8,10]. The size, site, extent and relationship of the tumour to adjacent structures can be best evaluated by CT and MR imaging [36]. The appearance of desmoids shows wide heterogeneity on CT or MR, and varies depending on their fibrous tissue content, cellularity and grade of myxomatous degeneration [36,37]. Desmoids may be hypo-, iso- or hyperintense to skeletal muscle. A definitive diagnosis of desmoid tumors based solely on imaging features is not possible.

FNA is fairly reliable for recognition of the benign nature of desmoids [4]. FNA could be a safer alternative to CNB (core needle biopsy) if tumors are located close to major vessels, nerves, pleura or the lungs, because of the higher rate of possible complications [4]. CNB in the preoperative diagnosis of desmoids is a simple and useful technique, yielding constant and abundant representative material for examination. The high degree of diagnostic accuracy suggests that CNB is the diagnostic method of choice [4]. Dalen et al found the diagnostic accuracy of FNA and CNB in 69 and 26 patients to be 50% and 92%, respectively [4]. Incisional biopsies are sometimes inevitable. Definitive histopathological diagnosis is mandatory if chest desmoids involve vital structures, or extensive surgical procedures or neoadjuvant nonsurgical treatments are required [5,8,10].

Surgical management

Aggressive surgical management is the treatment of first choice [5,7,8,10–12,20,38]. Wide local excision is generally recognized as the most effective treatment [5,8,10]. Radical resection is often a therapeutic challenge, due to the anatomy of the mediastinum, the high rate of recurrent tumors, or those involving vital structures [12,20].

Ninety-five percent of the reported intra-thoracic cases were treated with surgical resection [7,12,14–35] (Table 1). The radicality of the surgical resection is reported in only 23 cases: microscopically negative (R0) in 9 cases (39%) and microscopically positive (R1) in 6 cases (26%). Macroscopical residual tumour was left behind (R2) in 8 cases (35%).

Surgery is recommended to be carried out in specialized centers by experts. Surgical margins of 2 to 4 cm with en bloc removal are optimal where anatomic features make it possible [5,8,10,38]. Optimal resection by chest wall involvation includes 1 unaffected rib above and below the lesion, as well as intercostal muscles, pleura, and a wide clear margin of adjacent soft and osteal tissues [5]. Adequate marking of the specimen, intraoperative consultation with the pathologist, and frozen section analysis are essential to achieve complete resection. Radical excision may be difficult or impossible to perform if the process involves paravertebral structures, the spine, the brachial plexus, great vessels, or extends into the soft tissues of the neck [7,12,20]. Palliative surgical diminution might be life-saving when compression of vital organs is present [20]. Thorough examination and design of an individually planned treatment scheme should precede the surgical intervention, often requiring cooperation of more specialists (thoracic, vascular, neuro- and plastic surgeons).

Primary closure can generally be achieved after removal of extensive areas of the chest wall and contiguous structures, without significant cosmetic deformity or loss of function [5,8,10]. The overlying skin is usually uninvolved by the tumour, which facilitates wound closure [39]. In particular cases, adequate skeletal and soft-tissue reconstruction of the chest wall along with function, integrity, aesthetics and stability may be required following a radical en block resection [5,8,10]. The latissimus dorsi flap is considered to be the flap of choice in chest wall reconstruction [5]. Adequate stability can be achieved by the use of synthetic meshes. Chest wall resections are characterized by a high rate of complications, ranging from 21% to 46% of cases. With an occurrence of 20–24%, respiratory complications were most frequent [5,8,10,39,40]. Reviewing the records of 462 patients with chest wall resection and reconstruction by Mansour and Wayent, patient age, extent of pulmonary resection and defect size were found to significantly predict perioperative complications [39,40].

Non-surgical management

Since positive surgical margins are associated with a high risk of local recurrence, additional multimodal therapies are needed, including radiotherapy and medications to down-regulate signalling pathways resulting in tumour growth or to induce tumour regression [2,3,5,11,13,41–48] (Table 2).

Adjuvant therapy was not reported in 19 of the reported intra-thoracic cases [7,12,14–35] (Table 1). No further

Table 1. Characteristics of the 34 intra-thoracic desmoid tumour cases reported in the English-language literature.

	Reference	Gender	Age	Location	Size (cm)	Resection	Adjuvant therapy	Follow-up (months)
1.	Ibrahim [6] 2009	M	35	Left apicolateral chest wall near the brachial plexus	20×15×20	R2, small part was adherent to the brachial plexus, decortication of the left lung was done	Nr	Lost follow-up
2.	Murakawa [18] 2009	F	39	Right posterior wall 8–10 ribs, right lung compression, displacement of the mediastinum	27×17×7 (3232 g)	R1	anti-estrogen	Nr
3.	Bölke [17] 2009	F	17	Right upper thorax filled the complete hemithorax	nr (3580 g)	„Complete resection"	Nr	Nr
4.	Kim 2009	M	40	Left upper anterior chest wall protruded into the pleural cavity	2.5×2	R1„near total excision"	–	72 no recurrence
5.	Meyerson [19] 2008	F	42	In the right major fissure with extension into the hilum involving pulmonary vessels and the bronchus	11×8	R0 with pulmonectomy	Anti-estrogen	18 no recurrence
6.	Tajima [20] 2006	M	15	Left lower posterior chest wall including 7–12 ribs	18.5×10.5×10 (680 g)	R nr, „en bloc" reconstructed with nylon thread	–	36 no reurrence
7.	Borzellino [30] 2006	M	48	From the aortic arch into the mediastinum and into the right pleural cavity	15	„Radical excision of the mass"	–	36 no recurrence
8.	Andino [34] 2006	M	5	Pedunculated pleural based	5.6×4.3×1.8	R nr	nr	Nr
9.		M	43	Intrabronchial	7×3×2			
10.		F	67	Left parietal pleura	Nr			
11.		F	73	Right parietal pleura	Nr			
12.	de Jong [33] 2005	M	20	Right lower parietal pleura	19×17×6 (1700 g)	R1	nr	18 stable resid. tu.
13.	Cardoso [21] 2002	M	35	Right anterior-superior mediastinum	Nr	R1, „en-bloc" with cervical and paraspinal muscles, right vagus, phrenic nerves, SVC, left innominate vein, stellate ganglion	Radiotherapy 50Gy	72 no recurrence
14.	Shindle [22] 2002	F	12	Left hemithorax infiltrating T10 vertebral body compressing spinal cord	11	R2, with laminectomy from T7 to T10	Radiotherapy 50.4Gy	108 no recurrence
15.	Iqbal [23] 2001	F	60	Right apical parietal pleura	3.5	R nr	Nr	Nr
16.	Takeshima [11] 2001	F	46	Right chest wall protruded into the left pleural cavity	13×9×7	R1, „simple resection", surgical margin was not free from the tumor	–	32 no recurrence
17.	Kocak [24] 2000	M	40	Posterior mediastinum with transdiaphragmatic extension	20×6×5	R2 biopsy	Nr.	Nr

Table 1 continued. Characteristics of the 34 intra-thoracic desmoid tumour cases reported in the English-language literature.

	Reference	Gender	Age	Location	Size (cm)	Resection	Adjuvant therapy	Follow-up (months)
18.	Shah [25] 2000	M	40	Right chest wall with intra-thoracic extension with encasement of the subclavian vessels and brachial plexus	Nr	„Radical resection"	Nr	6 no recurrence
19.		M	35	Solitary pulmonary nodule contiguous with the anterior chest wall		„Declined surgery"		Nr
20.		M	25	Anterior chest wall with significant intrathoracic extension		„Radical excision"		12 Recurrence
21.	Kawashima [16] 2000	F	12	IIntrathoracic paraspinal tumor with intracanalicular extension	Nr	R, nr	Nr	Nr
22.	Wilson [26] 1999	F	16	Right and left posterior chest wall	16	R1	Radiotherapy and re-resection R0	Lost follow-up
23.		M	49	Right paravertebral parietal pleura	12	R0	–	96 no recurrence
24.		M	66	Right visceral pleura	5	R0	–	12 no recurrence
25.		F	45	Left apical parietal pleura	7	R2	Nr	12 stable resid. tu.
26.	Dosios [32] 1998	F	21	Left parietal pleura	5.5	R0	Re-resection, radiotherapy, anti-estrogen	9 (1st recurrence) 3 (2nd recurrence)
27.	Okamura [27] 1995	M	9	Left apical parietal pleura with rib destruction	Nr	„Subtotal resection"	Radiotherapy	Nr
28.	Winer-Muran [13] 1994	F	14	Intrathoracic with invasion of vertebral bodies and intraspinal extension	3	„Incomplete resection"	Nr	Nr
29.	Kaplan [31] 1986	M	19	Left hemithorax was filled, pushing spleen and stomach downwards	Nr (5200 g)	R, nr	–	6 no recurrence
30.		M	18	Mediastinal mass involving the right lung, with esophageal constriction	Nr	R, nr	Radiotherapy 20 Gy, indomethacin	2.25 Recurrence
31.	Krause [28] 1985	M	2.5	Right hemithorax compressing the airway and esophagus	Nr	R2„almost totally removed"	Nr	Nr
32.	Giustra [14] 1979	M	42	Extrapleural intrathoracic at the site of previous thoracotomy	9	R, nr	Nr	60 Recurrence
33.	Klein [29] 1977	M	21	Left intrathoracic mass	9×12	R nr„completely excised"	Nr	6 no recurrence*
34.	Ah-Tye [15] 1977	M	28	Intrathoracic tumour with transdiaphragmatic extension	Nr	Nr	Nr	Nr

F – female; M – male; Nr – not reported; R – resection; R0 – complete resection with no microscopic residual tumor; R1 – microscopic residual disease; R2 – macroscopic residual disease.

treatments were given to 7 patients after surgery. Adjuvant radiotherapy was administered in 6 cases, anti-oestrogen therapy in 4 cases, NSAID (non-steroidal anti-inflammatory drug) for 2 patients (indomethacin in 1 case and sulindac in another) and chemotherapy in 1 case.

Table 2. Multimodal (pharmacologic and radiotherapeutic) treatment of desmoid tumors.

Hormonal therapies	Tamoxifen, toremifene, raloxifene, progesterone, testolactone, glucocorticoids
NSAID	Sulindac, indomethacin, celecoxib
Chemotherapy	Doxorubicin-dacarbazine, vinblastin, carboplatin, vincristin, vinorelbine, cyclophosphamid, methotrexate
Radiotherapy	
Others	Interferon Imatinib-mesylate Goserelin acetate Letrozole Colchicines

Non-surgical care is the primary treatment of tumors that are found to be radically unresectable. Tumour size can be decreased by mono- or combination neoadjuvant therapy with anti-oestrogens, NSAIDs, and radio- and chemotherapy [2,3,5,11,13,41–48]. Evidence-based medical regimens and verified markers for monitoring the efficacy are not available yet [2]. The most substantiated results are reported in connection with selective oestrogen receptor modulators (SERMs) [3,11,13,44,45,48]. In a meta-analysis by Serpell et al., the response rate of 55 patients treated with anti-oestrogens was 51% [48]. Waddel reported a 70% response rate with SERMs in combination with NSAIDs [45]. It is notable that some authors found no evidence of the effectiveness of anti-oestrogens. The optimal dose and duration of tamoxifen therapy or other anti-oestrogens have not been determined (20–120 mg per os daily) [3]. Indomethacin and sulindac are the NSAIDs of choice in the pharmacologic treatment of desmoids [3,45]. Certain reports of cases registered a 50% regression rate when sulindac 150 mg twice daily was administered. Long-term follow-up data, however, are not available. The cardiovascular adverse effects of sulindac must be considered.

Radiotherapy

Although the role of radiotherapy in the adjuvant treatment of sarcomas has already been confirmed, its importance in the management of aggressive fibromatoses is less clearly described [2,11,42,47]. Combined treatment with surgery plus radiotherapy showed a significantly longer progression-free survival than surgical resection alone [42,47]. A study of 110 desmoid patients by Baumert confirmed that local control was significantly increased if radiotherapy was added to surgery, independent of tumour status and surgical margins [42]. Significantly better results are derived when post-operative adjuvant radiotherapy is added, compared to just radiotherapy at recurrence. Wide radiation field margins of at least 5 cm in the direction of possible infiltrative growth are recommended. To date, a dose-related effect has not been confirmed. Adjuvant radiation therapy should be considered for patients with irresectable or incompletely resected tumors or local recurrences [2,42,47].

Chemotherapy

The role and efficacy of chemotherapy in the treatment of desmoids is still a matter of controversy, with poor evidence [2,11,41,46]. Cytotoxic chemotherapeutic agents, single or in combination, have been used in unresectable tumors, progressive or recurrent disease, and in rare cases as neoadjuvant treatment to facilitate radical resection. The unsatisfactory outcome of chemotherapy was reported by a number of investigators, supposedly due to the hypocellular features of desmoids and the low mitotic index of the cells [46]. The outcome of chemotherapy seems to be better in FAP-associated tumors [41]. Combination chemotherapy is superior to single-agent use (doxorubicin) [46]. The overall response rates to combination chemotherapy in single-arm studies range between 17% and 100%, with a median response rate of 50%. Imatinib mesylate, an inhibitor of c-kit and PDGFR receptor tyrosine kinases, has been reported to be effective against advanced desmoid tumors [11,43].

Local control

Extra-abdominal desmoid tumors are associated with high local recurrence rates, depending on treatment duration and modalities applied, and range up to 68–85% if positive resection margins are present [2,5,8,38]. A localized control rate of 85% can be achieved with R0 excision. The overall local recurrence rate of chest desmoids was 30% in the investigation of 53 cases by Abbas [5]. The recurrence rate varied according to whether the desmoid had been previously resected, if the margins contained residual disease, or if radiation was administered post-operatively [5]. Eighty-nine percent of the patients with positive margins developed recurrences, compared with only 18% with negative margins [5]. Recurrences occurred in 50% of the patients who had a prior resection for desmoid and only 8% who did not have a previous resection. The absence of adjuvant radiotherapy in patients with negative margins resulted in a recurrence rate of 27% [5]. None of the patients who were given adjuvant radiation therapy with negative margins had recurrences. Factors found to be affecting recurrence were reoperation, positive margins, and post-operative radiation therapy [5].

Of the 21 patients who had been followed-up for a period of 3 to 103 months (mean 30.5 months), 13 patients (62%) survived with no evidence of disease and 8 (38%) had residual or recurrent tumors (Table 1). Three of them showed stable disease with lack of progression. One patient died of multicentric progressive giant desmoids in the thorax and retroperitoneum. Follow-up of 11 patients were not reported, and follow-up records of 2 patients were lost.

CONCLUSIONS

Intra-thoracic desmoid tumors are a difficult therapeutic challenge. The cases are variable and the information provided via summarizing the characteristics and outcomes of all reported cases to date is difficult to assess.

Following confirmation of diagnosis, radical resection is considered the mainstay of curative treatment for intra-thoracic desmoid tumors, yielding the best follow-up results. Disease progression may occur many years after treatment, so patients should be regularly monitored by physical examination, X-ray imaging and chest CT in symptomatic cases. The management of desmoids should be multidisciplinary from the start and not only when the tumors are irresectable, incompletely excised or recurrent.

REFERENCES:

1. Reitamo JJ, Hayry P, Nykyri E, Saxen E: The desmoids tumour. Incidence, sex, age and anatomical distribution in the Finnish population. Am J Clin Pathol, 1982; 77: 665–73
2. Shields CJ, Winter DC, Kirwan WO, Redmond HP: Desmoid tumors. EJSO, 2001; 27: 701–6
3. Hansmann A, Adolph C, Vogel T et al: High-dose tamoxifen and sulindac treatment for desmoid tumors. Cancer, 2004; 100: 612–20
4. Dalén BP, Meis-Kindblom JM, Sumathi VP et al: Fine-needle aspiration cytology and core needle biopsy in the preoperative diagnosis of desmoid tumors. Acta Orthop, 2006; 77: 926–31
5. Abbas AE, Deschamps C, Cassivi SD et al: Chest wall desmoid tumors: Results of surgical intervenion. Ann Thorac Surg, 2004; 78: 1219–23
6. Allen PJ, Shriver CD: Desmoid tumors of the chest wall. Semin Thorac Cardiovasc Surg, 1999; 11: 264–69
7. Ibrahim M, Sandogji H, Allam A: Huge intrathoracic desmoid tumor. Ann Thorac Med, 2009; 4(3): 146–48
8. Kabiri EH, Al Aziz S, El Maslout A, Benosman A: Desmoid tumors of the chest wall. Eur J Cardiothorac Surg, 2001; 19: 580–83
9. Deyrup AT, Tretakiova M, Montag AG: Estrogen receptor-β expression in extraabdominal fibromatoses. An analysis of 40 cases. Cancer, 2006; 106: 208–13
10. Dashiel TG, Payne WS, Hepper NGG, Soule EH: Desmoid tumors of the chest wall. Chest, 1978; 74: 157–62
11. Papagelopoulos PJ, Mavrogenis AF, Mitsiokapa EA et al: Current trends in the management of extra-abdominal desmoid tumors. World J Surg Oncol, 2006; 4: 21
12. Takeshima Y, Nakayori F, Nakano T et al: Extra-abdominal desmoid tumor presenting as an intrathoracic tumor: case report and literature review. Pathol Int, 2001; 51(10): 824–28
13. Janinis J, Patriki M, Vini L et al: The pharmacological treatment of aggressive fibromatosis: a systemic review. Ann Oncol, 2003; 14: 181–90
14. Winer-Muram HT, Bowman LC, Parham D: Intrathoracic desmoid tumor: CT and MRI appearance. South Med J, 1994; 87(10): 1007–9
15. Giustra PE, White HO, Killoran PJ: Intrathoracic desmoid at previous thoracotomy site. J Can Assoc Radiol, 1979; 30(2): 122–23
16. Ah-Tye P, Vieweg WV, Johnston WH et al: Intrathoracic desmoid tumor with transdiaphragmatic extension: roentgenographic presentation as a pericardial fat pad. Md State Med J, 1977; 26(6): 47–49
17. Kawashima A, Fishman EK, Hruban RH, Kuhlman JE: Intrathoracic paraspinal desmoid with intracanalicular extension: computed tomography and magnetic resonance imaging findings. Orthopedics, 2000; 23(4): 381–82
18. Bölke E, Krasniqi H, Lammering G et al: Chest wall and intrathoracic desmoid tumors: surgical experience and review of the literature. Eur J Med Res, 2009; 14(6): 240–43
19. Murakawa T, Fukami T, Nakajima J, Takamoto S: Chest wall desmoid tumor with life-threatening intrathoracic extension. Eur J Cardiothorac Surg, 2009; 35(3): 538
20. Meyerson SL, D'Amico TA: Intrathoracic desmoid tumor: brief report and review of literature. J Thorac Oncol, 2008; 3(6): 656–59
21. Tajima S, Hironaka M, Oshikawa K et al: Intrathoracic sporadic desmoid tumor with the beta-catenin gene mutation in exon 3 and activated cyclin D1. Respiration, 2006; 73(4): 558–61
22. Cardoso PF, da Silva LC, Bonamigo TP, Geyer G: Intrathoracic desmoid tumor with invasion of the great vessels. Eur J Cardiothorac Surg, 2002; 22(6): 1017–19
23. Shindle MK, Khanna AJ, McCarthy EF et al: Desmoid tumor of the spinal canal causing scoliosis and paralysis. Spine (Phila Pa 1976). 2002; 27(12): E304–7
24. Iqbal M, Rossoff LJ, Kahn L, Lackner RP: Intrathoracic desmoid tumor mimicking primary lung neoplasm. Ann Thorac Surg, 2001; 71(5): 1698–700
25. Kocak Z, Adli M, Erdir O et al: Intrathoracic desmoid tumor of the posterior mediastinum with transdiaphragmatic extension. Report of a case. Tumori, 2000; 86(6): 489–91
26. Shah J, Prasad S, Patkar D, Kothari S: Intrathoracic extension of aggressive fibromatoses. Br J Radiol, 2000; 73(865): 66–68
27. Wilson RW, Gallateau-Salle F, Moran CA: Desmoid tumors of the pleura: a clinicopathologic mimic of localized fibrous tumor. Mod Pathol, 1999; 12(1): 9–14
28. Okamura H, Murayama S, Murakami J et al: CT manifestations of pediatric intrathoracic desmoid tumors. Pediatr Radiol, 1995; 25(Suppl.1): S202–4
29. Krause LM, Schey WL, Bassuk A, Shrock P: Intrathoracic desmoid tumor in a child. Pediatr Radiol, 1985; 15(2): 131–33
30. Klein DL, Gamsu G, Gant TD: Intrathoracic desmoid tumor of the chest wall. AJR Am J Roentgenol, 1977; 129(3): 524–25
31. Borzellino G, Minicozzi AM, Giovinazzo F et al: Intra-thoracic desmoid tumour in a patient with a previous aortocoronary bypass. World J Surg Oncol, 2006; 4: 43
32. Kaplan J, Davidson T: Intrathoracic desmoids: report of two cases. Thorax, 1986; 41: 894–95
33. Dosios TJ, Angouras DC, Floros DG: Primary desmoid tumor of the posterior mediastinum. Ann Thorac Surg, 1998; 66: 2098–99
34. de Jong WK, van der Graaf WTA, van der Jagt EJ et al: A 20-year-old male with thoracic pain and a lower thoracic mass. Eur Respir J, 2005; 26: 740–42
35. Andino L, Cagle PT, Murer B et al: Pleuropulmonary desmoid tumors: immunohistochemical comparison with solitary fibrous tumors and assessment of beta-catenin and cyclin D1 expression. Arch Pathol Lab Med, 2006; 130(10): 1503–9
36. Vandevenne JE, De Schepper AM, De Bueckeleer L et al: New concepts in understanding volution of desmoid tumors: MR imaging of 30 lesions. Eur Radiol, 1997; 7: 1013–19
37. Brooks AP, Reznek RH, Nugent K et al: CT appearances of desmoid umors in familal adenomatous polyposis: further observations. Clin Radiol, 1994; 49: 601–7
38. Brodsky JT, Gordon MS, Hajdu SI, Burt M: Desmoid tumors of the chest wall. A locally recurrent problem. J Thorac Cardiovasc Surg, 1992; 104(4): 900–3
39. Mansour KA, Thourani VH, Losken A et al: Chest wall resections and reconstruction: A 25-year experience. Ann Thor Surg, 2002; 73: 1720–26
40. Weyant MJ, Bains MS, Venkatraman E et al: Results of chest wall resection and reconstruction with and without rigid prosthesis. Ann Thorac Surg, 2006; 81: 279–85
41. Azzarelli A, Gronchi A, Bertulli R et al: Low-dose chemotherapy with methotrexate and vinblastine for patients with advanced aggressive fibromatosis. Cancer, 2001; 92: 1259–64
42. Baumert BG, Spahr MO, Von Hochstetter A et al: The impact of radiotherapy in the treatment of desmoid tumors. An international survey of 110 patients. A study of the Rare Cancer Network. Radiat Oncol, 2007; 2: 12
43. Heinrich MC, McArthur GA, Demetri GD et al: Clinical and molecular studies of the effect of imatinib on advanced aggressive fibromatosis (desmoid tumor). J Clin Oncol, 2006; 24: 1195–203
44. Heidemann J, Ogawa H, Otterson MF et al: Antiangiogenic treatment of mesenteric desmoid tumors with toremifene and interferon alfa-2b. Report of two cases. Dis Colon Rectum, 2004; 47: 118–22
45. Waddel WR, Gerner RE, Reich MP: Nonsteroid anti-inflammatory drugs and tamoxifen for desmoid tumors and carcinoma of the stomach. J Surg Oncol, 1983; 22: 197–211
46. Okuno Sh, Edmondson JH: Combination chemotherapy for desmoid tumors. Cancer, 2003; 97: 1134–35

47. Nuyttens JJ, Rust PF, Thomas ChR, Turrisi AT III: Surgery versus radiation therapy for patients with aggressive fibromatosis or desmoid tumors. Cancer, 2000; 88: 1517–23

48. Serpell JW, Paddle-Ledinek JE, Johnson WR: Modification of growth of desmoid tumors in tissue culture by anti-oestrogenic substances: a preliminary report. Aust NZJ Surg, 1996; 66(7): 457–63