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# Desmoid tumor of lung with pleural involvement — the case of unique location of aggressive fibromatosis

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**Abstract:** Desmoid tumors (DTs) are rare mesenchymal neoplasms with unpredictable natural history. There is a high risk of recurrence despite adequate surgical resection, however DTs do not have the capacity to metastasize. The estimated incidence in general population is 2–4 cases/million/year. They may occur at any age but most commonly in the third and fourth decades. Both sexes may be affected, but there is a slight female predominance. DTs can occur at any body site. The exact etiology remains unclear, but trauma, hormonal disturbances, pregnancy, genetic and hereditary factors are postulated to be in association with its' development. Potential to attain large size, infiltration and destruction of adjacent vital structures and tendency to recur are main management problems and important causes of morbidity and mortality. Wide excision is standard first-line treatment of primary or recurrent symptomatic desmoids. We present case of 33-years-old Caucasian female patient admitted to hospital with 2 months history of squeezing pain in right upper quadrant which appeared after meals. The patient was in general good condition. There were no abnormalities on basic laboratory tests on admission. CT of chest revealed hydrothorax to the level of the apex of the right lung and tumor sized 7 × 13 × 13 cm located in the lower lobe of right lung. Histopathological diagnosis of desmoid tumor of right lung was formulated. We report, to our knowledge for the first time in Poland, case of aggressive fibromatosis of lung with invasion of pleura.

**Key words:** desmoid, fibromatosis, pleura, lung.

## Introduction

Desmoid tumors (DTs), also called deep or aggressive fibromatosis, are rare mesenchymal neoplasms with unpredictable natural history. DTs arise from fascial and muscle-aponeurotic structures and are composed of proliferating spindle cells arranged in long fascicles. DTs have

high risk of recurrence (25–65%) [1], despite adequate surgical resection, but do not have the capacity to metastasize. They account for 0.03% of all neoplasms[2]. The estimated incidence in general population is 2–4 cases per million per year, there is no significant racial or ethnic predilection [2]. DTs may occur at any age but the most commonly in the third and fourth decades [3]. Both sexes may be affected, but there is a slight female predominance [3]. DTs can occur at any body site, but the abdominal wall, soft tissue of the extremities, shoulder, neck and chest wall are the most frequent location [2]. Symptoms are depending on location. Patient usually presents with a slow growing firm mass greater than 5cm without associated pain or discomfort, unless there is nerve involvement. The exact etiology of DTs remains unclear, but trauma, hormonal disturbances, pregnancy, genetic and hereditary factors are postulated to be in association with DTs development [3, 4].

## Case report

33-years-old Caucasian female patient was admitted to the Sokolowski Pulmonary Hospital in Zakopane with 2 months history of squeezing pain in right upper quadrant which appeared after meals. She was in good general condition, suffered of hypothyreosis but had no other chronic diseases. Her body weight was stable in the last few months. The patient underwent 2 birth, last period was 2 years before symptoms of the current disease began. She was permanently on letrox and oral contaception (depot medroxyprogesterone acetate). Family history was not contributory. There were no abnormalities on basic laboratory tests on admission. CT revealed hydrothorax to the level of the apex of the right lung and tumor sized 7 × 13 × 13 cm located in the lower lobe of right lung (Fig. 1). Invasion of the 9$^{th}$ right

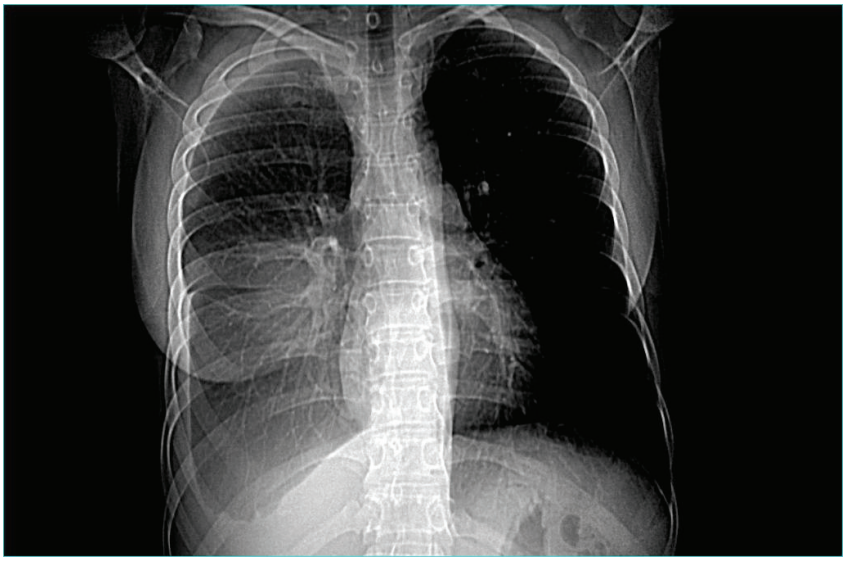

**Fig. 1.** CT scan of thorax (frontal section). Hydrothorax to the level of the apex of the right lung and tumor in size of 7 × 13 × 13 cm in lower lobe of right lung, atelectasis of lower lobe of right lung.

rib, thoracic vertebra 8th–9th and atelectasis of lower lobe of right lung were observed. Fine needle aspiration biopsy performed during bronchoscopy revealed no diagnostic material. An exploratory right thoracotomy showed large tumor of lung deriving from lower posterior mediastinum. Incision biopsy was performed. Intraoperative histologic consultation confirmed involvement of pleura by a tumor. Due to size of the tumor, involvement of pleura, infiltration of corpse of 8th–9th thoracic vertebra and 9th right rib and technical difficulty of surgery combined with expected poor postoperative outcome the resection of the tumor was not performed. Obtained samples were evaluated, in correspondence with clinical presentation, histopathological diagnosis of desmoid tumor of right lung with involvement of the pleura was formulated. Postoperative course was uneventful. The patient was discharged from hospital in good general conditions instructed of further treatment but failed to present herself to next appointment and was lost from follow up.

## Material and methods

Clinical data was obtained from the archive files of Sokolowski Pulmonary Hospital in Zakopane. The original samples had been fixed in the formaldehyde solution, routinely processed and embedded in paraffin and stained with haematoxylin and eosin. Immunohistochemistry was performed using a standard protocol.

## Pathological examination

Histologically the tumor was composed of spindle cells, arranged in short, partially irregular fascicles (Fig. 2, Fig 3). The stroma contained myxoid foci, collagen clusters and

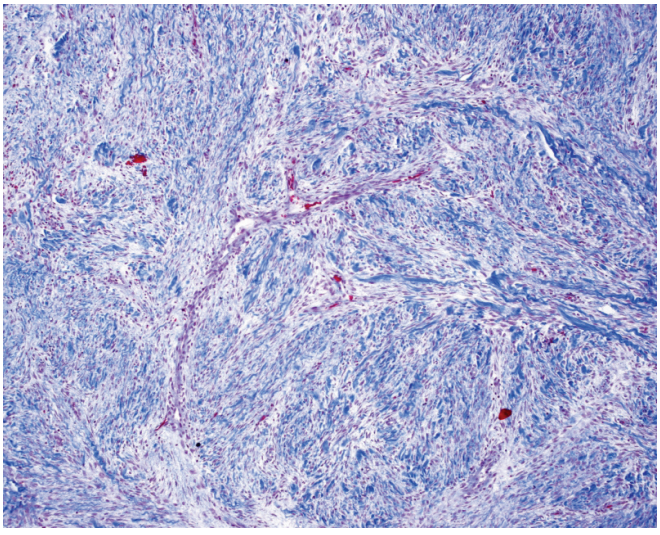

**Fig. 2.** Spindle-shaped cells with fascicular architecturem thick collagen fibres, dense collagen in area (Gomori trichrome stain, original magnification × 40)

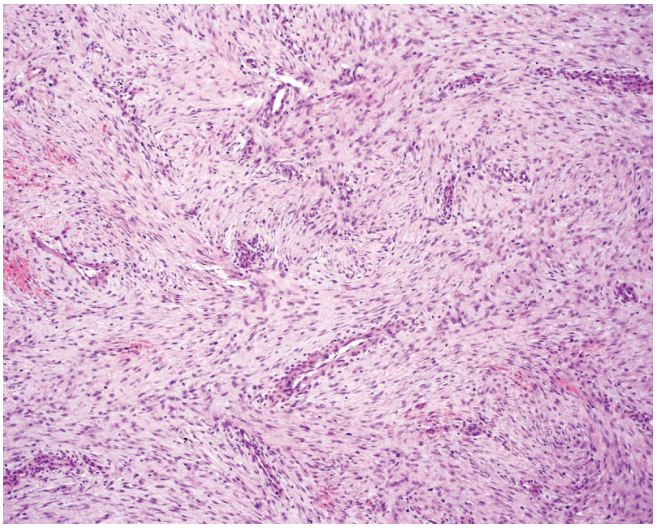

**Fig. 3.** Spindle-shaped neoplasm arranged in short, partially irregular fascicles (HE, original magnification × 40)

hemorrhagic areas. Vessels were surrounded by distinct myopericit cuff. The cells showed neither polymorphism nor mitotic activity. Some plasma cells, mast cells and lymphocytes were seen within the tumor. Tumor cells showed expression of smooth muscle actin (SMA) and beta-catenin, the later both in cytoplasmatic and nuclear location, but was negative for CD34, desmin, S-100, ALK1, HHV8, calretinin, pan-cytokeratin (pan-CK), CK5/6, EMA and HMB45. Proliferation activity of neoplastic cells as measured by expression of antigen Ki 67 was low (<2%). These findings were consistent with the diagnosis of desmoid tumor.

## Discussion

Aggressive fibromatoses can be classified as extra-abdominal (60%), abdominal (25%) and intra-abdominal (15%) [5]. DTs of the chest represent 20% of all extra-abdominal fibromatoses [5]. Only 37 cases of intra-thoracic DTs have been reported in the English-language literature [5]. The majority were apparently originating from the chest wall with major intra-thoracic extensions [5]. True primary intrapleural desmoid tumors are extremely rare, with only 12 reported cases [5]. The age of the patients in the reported intra-thoracic DTs cases ranged from 2.5 to 73 years (mean 32.3 years) [5]. Twenty-two patients were men and 15 patients were women, which differs from the common female predominance of extra-abdominal desmoids [5]. Most of intra-thoracic DTs (60%) were greater than 10 cm at the time of diagnosis [5]. True intra-thoracic DTs are generally asymptomatic until the tumour becomes to large, with compression of the surrounding organs [5]. Most of the reported (95%) intra-thoracic cases were treated with surgical resection. 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%) [5]. Adjuvant therapy was not reported in 19 of the reported intra-thoracic cases [5]. Radical resection may be difficult or impossible to perform if the tumor infiltrate paravertebral structures, the spine, the brachial plexus, great vessels, or extends into the soft tissues of the neck. Chest wall resections are characterized by a high rate of complications, ranging from 21% to 46% of cases [5]. Desmoid tumors may occur sporadically, in association with familial adenomatous polyposis (FAP; such association is referred as Gardner's syndrome) or as hereditary desmoid disease [2]. DTs affects 10–15% of patients with FAP, and these patients have an over 800-fold increased risk of developing deep fibromatosis in comparison with general population [2]. Risk of DTs development in patients with FAP is associated with positive family history, female gender, an adenomatosis polyposis coli (APC) gene mutation 3' to codon 1399 and abdominal surgery in the past. Sporadic DTs are also associated with somatic mutations in either beta-catenin or APC genes [2]. 98% patients with sporadic DT were shown to have mutations of codons 41, 45 of exon 3 of beta-catenin gene (CTNNB1) [2]. Patients with mutations of codon 45 of exon 3 of beta-catenin gene (45F) are at particularly high risk for the recurrence [4]. Only 23% of patients with 45F mutations were free from progression at 5 years, while 59% of patients with a 41A mutations and 65% with no APC mutation had stable disease [2]. Both CTNNB1 and APC gene products are part of Wnt signaling pathway and mutations in either genes result in stabilization of beta-catenin protein leading to a constant activation of the T-cell factor/lymphoid enhancer factor (TCF/Lef) family of transcription factors [4]. This signaling pathway may be a target for future therapies. Most studies have shown that DTs are negative for estrogen receptor (ER) alpha, progesteron receptor and c-kit, but positive for ER beta [2]. In fact, DTs grow is probably under hormonal control[2]. Length of telomers was found to be inversely related to the size of DTs [2]. Grossly, DT presents as a firm mass with poorly defined margins and adhering to adjacent structures. On histologic examination the lesion usually show infiltrative margins and consists of spindle-shaped cells arranged in broad sweeping fascicles separated by abundant collagen-rich stroma [4]. Tumor cells do not show cytological atypia and the mitotic activity is low. DTs express vimentin and SMA and usually do not show reactivity to desmin or S-100 protein. Molecular studies of X chromosome inactivation proved that these tumors are monoclonal proliferation, consistent with a neoplastic character rather than reactive process as thought in the past4. Potential to attain large size, infiltration of adjacent structures and tendency to recurrence are main management problems and important causes of complications and mortality. A multidisciplinary approach tailored to the individual case is required for good outcome. Asymptomatic or non-progressive tumors may be monitored without definitive treatment [4]. Spontaneous resolution may occur in some cases. Primary and recurrent DTs which are symptomatic, do progress or are located in the proximity of vital organs should be treated with surgical resection when broad margins are obtainable and risk of functional impairment and disfigurement is low. Radical surgery is not always feasible because of location and technical difficulty. Furthermore, DTs may recur even after complete resection with seemingly negative margins. Further treatment may not be necessary even with positive resection margins. Recurrence is more frequent with extraabdominal (30–50%) than intraabdominal desmoids (15–30%) [3]. Positive surgical

margins are indications for adjuvant radiotherapy (RT) combined with surgery or definitive RT. Prominent or unacceptable function and cosmetic loss suggest to choose RT as first line treatment. The recommended dose of RT for definitive therapy is 50–60 Gy in 5-7 weeks at 1.8–2 Gy per fraction [2]. Local recurrence rates do not appear to be reduced by the use of higher doses [2]. Reasonable decision about using RT should balance between potential benefit and late side effects like secondary malignancies. Patients with unresectable DTs or multiple locoregional recurrences are candidates for systemic treatment. Possible options are: NSAIDs (e.g. sulindac, indomethacine), hormonal therapy (tamoxifen), interferon, cytotoxic agents (anthracyclines, liposomal pegylated doxorubicine), imatinib or new methods such as intralesional injections of irritating solutions and radiofrequency ablation. MRI allows to present exact relationship with adjacent structures therefore is the best option for imaging of desmoids. In addition MRI may have prognostic value because higher T2 signal is reportedly associated with more rapid growth [3]. After therapy it is recommended to perform imaging follow-up every 3–6 months and 6–12 weeks in patients undergoing chemoradiation3. Intervals between check-up depends on rate of growth and presence of symptoms. Recently, in a series of nine cases, FDG-PET was deemed reliable for the imaging of DTs and provided additional information in the response to imatinib, as exemplified by a decreased standardized uptake value of the tracer [2].

## Conclusions

Because of difficulty of diagnosis, possibility to occur in any body site, variable clinical presentation and behavior, many cases might remain misdiagnosed and inadequately treated. Wide excision is standard first-line treatment of primary or recurrent symptomatic desmoid. Radiological picture may be suggestive but an explicit confirmation of the diagnosis is based on histopathology. Intra-thoracic desmoids are exceedingly rare tumors, with 37 reported cases in the English-language literature [5]. Involvement of the pleura is extremely rare for this entity, only 12 cases have been described [5]. We report, to our knowledge for the first time in Poland, case of aggressive fibromatosis of lung with invasion of pleura.

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Contributions: the authors contributed equally.

## Conflict of interest

None declared.

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