



## Case report

## Desmoplastic small round cell tumor of the lung: A case report and literature review



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## ABSTRACT

Desmoplastic small round cell tumor (DSRCT) is a rare, aggressive and malignant tumor that is characterized by nests of small tumor cells surrounded by a cellular and vascular collagenous stroma and predominantly affects young adolescent males. This tumor most commonly originates in the abdomen; however, in rare cases, DSRCT can originate in other body regions. The main manifestations of DSRCT are chest pain and respiratory symptoms, and patients' average survival after diagnosis is less than two years. In this report, we describe a case involving DSRCT of the lung that proved to be difficult to diagnose, and we conduct a literature review.

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## 1. Introduction

Desmoplastic small round cell tumor (DSRCT) was first described by Gerald and Rosai in 1989<sup>1</sup> as a distinct tumor with specific histological and immunohistochemical patterns and chromosomal translocation [1–3]. DSRCT is a rare, aggressive, malignant tumor that predominantly affects young males, with a median patient age of 19 years and reported male-to-female ratios ranging from 5:1 to 10:1 [4,5]. No standard therapy is currently available for patients with DSRCT, and the prognosis for DSRCT remains extremely poor<sup>5</sup>. DSRCT is a member of the small round blue cell tumor family, which includes small-cell carcinoma, Merkel cell carcinoma, synovial sarcoma, Ewing's sarcoma/primitive neuroectodermal tumor, neuroblastoma, lymphoma, and rhabdomyosarcoma [6]. Due to the rarity of DSRCT and the absence of specific clinical manifestations of this tumor, clinicians may overlook the

diagnosis of this disease, particularly for cases in which DSRCT arises in the thorax. The main manifestations of DSRCT are chest pain and respiratory symptoms [7]. In this report, we present a case of a young female who was diagnosed with DSRCT of the lung that rapidly produced a fatal outcome, and we review relevant literature.

## 2. Case report

A 21-year-old female was admitted to our hospital after 3 weeks of marked general symptoms (asthenia, hyporexia and weight loss of 5 kg) accompanied by left chest pain, low-grade fever and shortness of breath on exertion. The patient had no known toxic habits and no significant medical or family history. On clinical examination, the patient was hemodynamically stable and afebrile, with an oxygen saturation of 93% while inspiring room air. Auscultation of the chest revealed inaudible breath sounds in the left thorax. The remaining findings from general physical and systemic examinations were essentially normal. Initial investigations revealed a hemoglobin level of 11.6 gm/dL, a white cell count of 13,680/μL with 80% neutrophils, and a normal platelet count. The patient's serum lactate dehydrogenase (LDH) was 420 U/L. The remaining biochemical parameters were essentially normal. An enzyme-linked immunosorbent assay (ELISA) for human immunodeficiency virus (HIV) was non-reactive. A chest X-ray (Fig. 1) revealed a large left pleural effusion.

A diagnostic thoracentesis was performed, and analysis of the pleural fluid revealed 620 cells, with a differential count of 85%

**Abbreviations:** Desmoplastic small round cell tumor, DSRCT; Lactate dehydrogenase, LDH; Enzyme-linked immunosorbent assay, ELISA; Human immunodeficiency virus, HIV; Adenosine deaminase, ADA; Computed tomography, CT; Transbronchial needle aspiration, TBNA; Leukocyte common antigen, LCA; Smooth muscle actin, SMA; Polymerase chain reaction, PCR; Magnetic resonance imaging, MRI; Fluorodeoxyglucose positron emission tomography/CT, FDG-PET/CT; Primitive neuroectodermal tumor, PNET.

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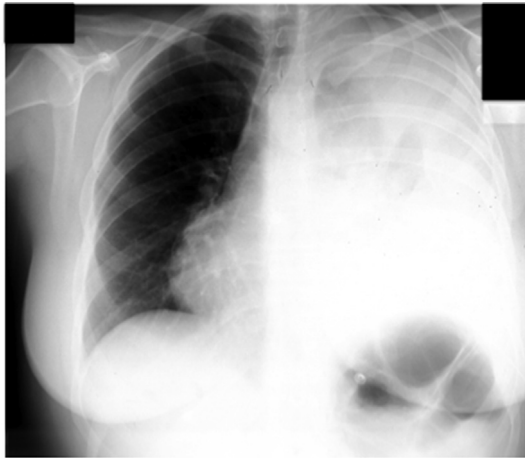


Fig. 1. Chest X-ray depicting a left pleural effusion.

lymphocytes and 15% polymorphs. The sugar and protein levels of the pleural fluid were 50 mg/dL and 3.4 gm/dL, respectively. Serum protein was 6.5 gm/dL. The adenosine deaminase (ADA) level in the pleural fluid was 32 U/L. Pleural fluid cytology was positive for malignant cells. A closed pleural biopsy revealed tumor infiltration by a small round monomorphous cell; however, we were unable to identify a clear lineage in the pathological anatomy. A computed tomography (CT) scan (Fig. 2) revealed a large left pulmonary mass that infiltrated the left pulmonary artery, left main bronchus and main carina as well as a severe pericardial effusion that was primarily localized around the left ventricle. A large subcarinal adenopathy was observed. No abdominal or pelvic abnormalities were found.

A bronchoscopy (Fig. 3) revealed a whitish exophytic lesion that almost completely obstructed the left main bronchus. Bronchial biopsies of the mass and transbronchial needle aspiration (TBNA) of the subcarinal adenopathy were performed. The results suggested a malignant low-grade tumor of possible mesenchymal origin with an uncertain immunohistochemical profile (with tumor cells negative for vimentin, desmin, neuron-specific enolase, epithelial membrane antigen, synaptophysin, S-100, CD117, CD31, CD5 and CD20 and positive only for CD34).

Tumor markers were within normal limits, with the exception of CA-125, which was elevated. On the 7th day after admission, the patient began to experience extremely intense, continuous left shoulder pain that exhibited neuropathic characteristics. Brachial plexus infiltration was suspected; however, due to the patient's intolerance of the supine position, an MRI could not be performed. Due to the absence of a definitive histological diagnosis, the patient was subjected to an open lung biopsy. During this procedure, she exhibited cardiac tamponade and was admitted to the ICU with acute respiratory failure and cardiogenic shock. Unfortunately, the patient died 24 h later.

The family agreed to an autopsy. At the macroscopic level (Fig. 4), the autopsy revealed a tumor mass with large dimensions that weighed 1750 g. The tumor was exclusively intrathoracic, it occupied the entire left hemithorax; surrounded and infiltrated the left main bronchus and left great vessels; was firmly adhered to the chest wall, diaphragm, pericardium, and left atrium wall; and had pushed the heart to the right side. Microscopically (Fig. 5), an intense infiltrate of undifferentiated tumor cells with extensive mitosis was observed. Immunohistochemical assessments indicated that tumor cells were negative for leukocyte common antigen (LCA), cytokeratin, neuron-specific enolase, synaptophysin, smooth muscle actin (SMA), CD1, S-100, CD15, chromogranin, CD57 and CD99 but strongly expressed CK7, 34B12, desmin and vimentin (Fig. 6). This pattern confirmed the diagnosis of DSRCT. Polymerase chain reaction (PCR) analysis to detect the t(11; 22) (p13; q12) translocation produced negative results.

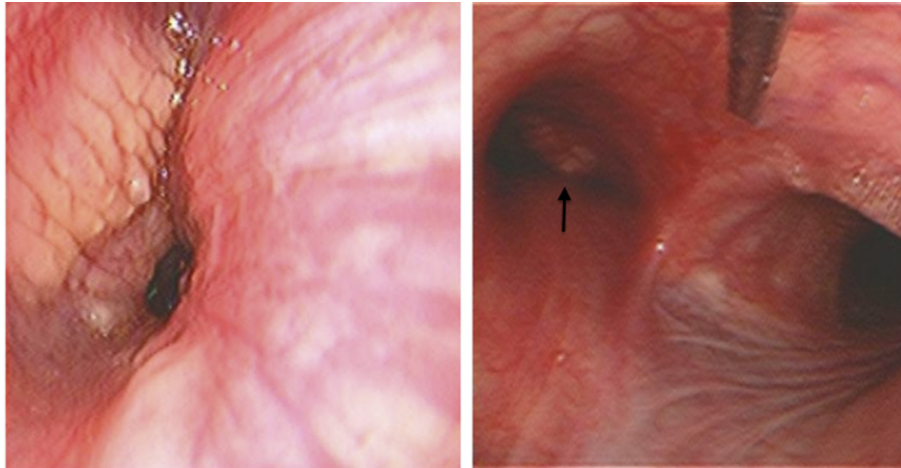
### 3. Discussion

DSRCT is a rare but aggressive tumor. DSRCT was first described in 1989 by Gerald and Rosai, who noticed a distinctive type of small cell tumor that predominantly involved the abdomen and affected young males [1]. The prognoses of patients with DSRCT have not substantially improved since this disease was first described. This tumor is known as a desmoplastic small round cell tumor because DSRCT is characterized by nests of small tumor cells surrounded by a cellular and vascular collagenous stroma. Although this stroma is always observed, its quantity varies with tumor progression [1,6]. More than 100 cases of DSRCT of the peritoneum have been reported in English-language publications [1,3,6]. Other reported sites of DSRCT include the tunica vaginalis testis, skull, parotid gland, hand, uterine serosal surface, ovarian surface, and urogenital region [7,8]. To date, 7 cases of DSRCT in the thoracic cavity have been described, although the tumor was confined to the thorax in only one of these cases [6,7,9]. The present paper describes the second case of DSRCT confined to the thorax that has been reported in the literature.

Pathologically, DSRCT consists of round, blue cells embedded in a desmoplastic stroma. Immunohistochemical markers are used to distinguish DSRCT from other small cell tumors. Ordóñez assessed a variety of epithelial, mesenchymal, and neuronal markers in 39 tumors and detected cytokeratin in 37/39 tumors, epithelial membrane antigen in 24/25 tumors, desmin in 39/39 tumors, vimentin in 22/27 tumors, neuron-specific enolase in 18/25 tumors, synaptophysin in 3/19 tumors, chromogranin in 1/22 tumors, WT1 protein in 8/9 tumors, muscle-specific actin in 3/19 tumors, and alpha-smooth muscle actin in 3/16 tumors [9]. Lee and Hsiao observed that all examined DSRCT cells are reactive to cytokeratin, desmin, vimentin, and WT-1. The EWS-WT1 fusion gene has been identified in three patients with DSRCT [10]. Thus, although DSRCT was initially thought to be of mesodermal origin, due to its sites of origin, this tumor is now thought to originate from a progenitor cell



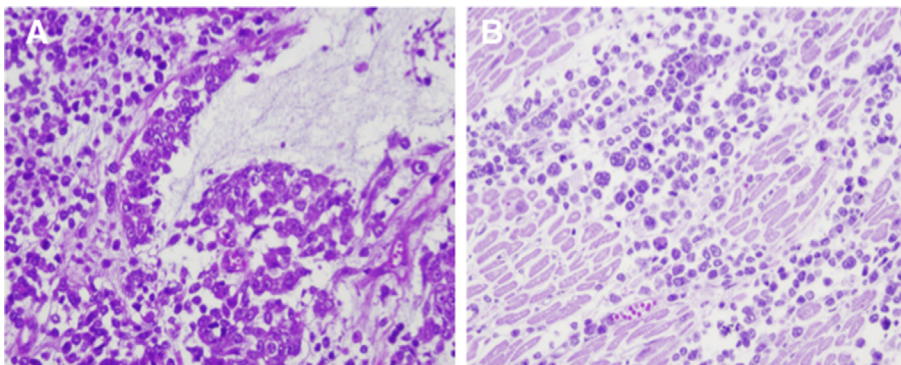
Fig. 2. CT scan depicting a large left pulmonary mass infiltrating the left pulmonary artery, left main bronchus and main carina as well as a severe pericardial effusion that is primarily localized around the left ventricle. An enlarged subcarinal lymph node is also visible.



**Fig. 3.** Bronchoscopy revealed a whitish exophytic lesion that almost completely obstructs the left main bronchus.



**Fig. 4.** Autopsy revealed a tumor mass with large dimensions that weighed 1750 g. The tumor occupied the entire left hemithorax; surrounded and infiltrated the left main bronchus and left great vessels; and was firmly adhered to the chest wall, diaphragm, pericardium and left atrium wall.



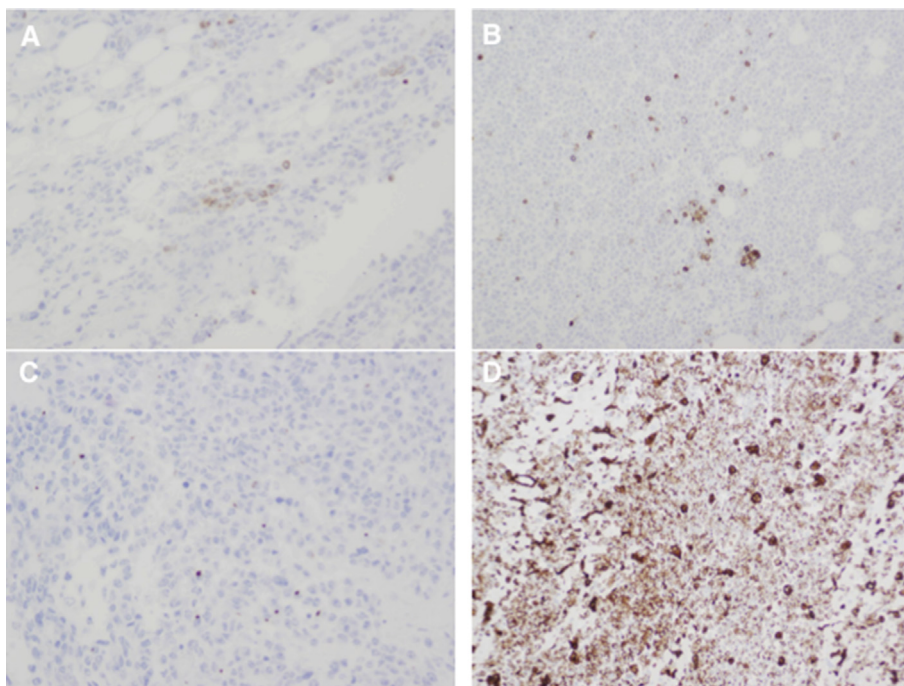
**Fig. 5.** (A,B) The biopsy revealed a cellular tumor comprising of nests and groups of polygonal to spindle shaped pleomorphic cells, separated by fibrous septa, having high nuclear to cytoplasmic ratio, high mitosis and some areas of necrosis.

with multiphenotypic differentiation [11].

A diagnosis of DSRCT is supported by the presence in electron microscopy images of perinuclear whorls of intermediate filaments, which correspond to dot-like immunostaining with desmin, in combination with the pertinent negative findings of an absence of specialized cell junctions, neurosecretory granules, and long microvilli [1,12]. Gerald et al. examined 19 patients with DSRCT and concluded that this tumor predominantly occurs in the abdomen, with a mean age of occurrence of 18.4 years and a predilection for adolescent males [4]. This tumor rarely occurs in females; in female patients, DSRCT can even be mistaken for ovarian cancer [13]. Our

examined case was particularly rare because it involved a young female patient. DSRCT exhibits a characteristic  $t(11; 22)(p13; q12)$  chromosomal translocation that brings the *EWS* gene on chromosome 22 to the *WT1* gene on chromosome 11 [3]. In a study by Lae et al., this translocation was present in 29/32 examined tumors [14]. Our patient was negative for this chromosomal translocation.

Common manifestations of DSRCT include abdominal pain; a palpable abdominal mass; abdominal distention due to a mass or ascites; hydronephrosis due to the obstruction of the urinary tract by the tumor; intra-abdominal lymphadenopathy; and liver metastasis [15]. As observed in our patient, who presented with



**Fig. 6.** Immunohistochemistry indicated that tumor cells were positive for CK7 (A), 34B12 (B), desmin (C) and vimentin (D), confirming the diagnosis of desmoplastic small round cell tumor.

respiratory symptoms, the clinical manifestations of DSRCT also depend on the site of the tumor. Contrast-enhanced CT and magnetic resonance imaging (MRI) of involved sites reveal that DSRCT is a mass of heterogeneous density and intensity. Fluorodeoxyglucose positron emission tomography/CT (FDG-PET/CT) can provide additional information regarding the stage of DSRCT [16]. The differential diagnosis of DSRCT includes small cell mesothelioma, primitive neuroectodermal tumor (PNET)/Ewing's sarcoma family tumors, malignant non-Hodgkin's lymphoma and small cell carcinoma [17].

With respect to the treatment of DSRCT, there have been efforts to establish treatments to control this disease. One such treatment combines aggressive surgery, radiation therapy applied to the tumor bed and myeloablative multiagent chemotherapy [18]. A recent report describing experiences with DSRCT at the Memorial Sloan-Kettering Cancer Center [5] revealed that overall survival rates for 66 patients were 44% and 15% at three and five years, respectively, after treatment with a combination of the P6 regimen, surgical debulking and 30 Gy of radiotherapy. However, more than half of these patients had no distant metastases. At present, there is no standard therapy for patients with DSRCT, particularly in cases involving inoperable/metastatic DSRCT, and few reports have addressed the treatment of metastatic DSRCT [5,6]. Multi-institutional randomized control trials involving DSRCT are not available due to the rarity of this disease.

In summary, DSRCT is a rare but aggressive malignancy with a poor outcome that should be considered in the differential diagnosis of undifferentiated small round cell tumors of the thorax. An aggressive treatment approach that involves multiple modalities can provide temporary survival benefits for patients with this disease.

#### Conflict of interest

The authors have no conflicts of interest to declare.  
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