Case Report: Rare case of desmoplastic small round cell tumour of the heart

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Introduction

Desmoplastic small round cell tumour (DSRCT) is a rare, malignant mesenchymal neoplasm of polyphenotypic differentiation. It usually occurs in children and young adults with a median age of 27 years and shows strong male predilection (male-to-female ratio of 3:1). The tumour usually occurs within the abdomen, with peritoneal spread and distant metastases to lymph nodes, liver and lungs. [1] Other rare reported locations include mediastinum, ethmoid sinuses, scalp soft tissues, [2] ovary and parotid gland. [3] Treatment is multimodal with aggressive surgical debulking, radiation and chemotherapy. This tumour has an overall poor prognosis as majority of patients develop significant disease recurrence or die within 3 years. [4]

Histologically, DSRCTs are composed of nests of small undifferentiated cells within characteristic abundant desmoplastic fibrous stroma. The cells are small, relatively monomorphic, with hyperchromatic nuclei, inconspicuous nucleoli and scant eosinophilic cytoplasm. Mitotic figures are often numerous. Rare epithelial differentiation as evidenced by rosette-like structures, tubule/ gland formation and papillary structures can be seen. [1]

The cells co-express epithelial, myogenic and neural markers. They show perinuclear dot-like desmin expression (81%), nuclear WT1 expression (91%), keratin (87%), neuron-specific enolase (84%) and CD99 (23%). [2] Almost all cases are positive for the characteristic recurrent chromosomal translocation t(11;22)(p13;q12) resulting in the fusion of the Ewing's sarcoma (EWSR1) amino-terminus to the Wilms' tumour (WT1) carboxy-terminus. [1-3] Therefore, immunoreactivity is seen with antibodies directly against only the WT1 carboxy-terminus, and antibodies directed against the WT1 amino-terminus are negative. [3] This is helpful diagnostically when typical clinicopathologic and immunohistochemical features of DSRCT are lacking.
In this report, we describe a rare case of DSCRT occurring in the heart. Literature search showed only one other reported case of a cardiac malignant small round cell tumour occurring in a young woman [5], which had a morphology and immunophenotype which was consistent with DSRCT, but was not confirmed by molecular methods.

Case Presentation

Clinical findings

A female patient in her forties presented with palpitations, dyspnoea and orthopnoea. Past medical history was unremarkable. Echocardiogram and CT scan showed an 8 cm right atrial mass with infiltration to the right ventricle and with pericardial effusion. The abdomen and pelvis were unremarkable. Debulking surgery was performed. However, she developed cardiogenic shock, subsequent multiorgan failure and eventually succumbed.

Microscopic Findings and Immunohistochemistry

Histological examination showed a tumour composed of small cells arranged in sheets and nests, separated by scanty stroma with dilated gaping vessels. The tumour cells had hyperchromatic ovoid nuclei, inconspicuous nuclei, mild nuclear pleomorphism and scanty eosinophilic cytoplasm. Mitotic figures were noted up to 5 per 10 high power fields. The stroma showed focal myxoid change. Abundant desmoplastic fibrous stroma characteristic of DSRCT was not seen. No features of epithelial differentiation such as rosettes or tubules were identified.
The tumour cells were immunohistochemically positive for desmin, SMA and NSE, focally positive for neuroendocrine markers (synaptophysin and CD56), and negative for AE1/3, EMA, caldesmon, myogenin, S100, CD99, FLI-1, CD34, TLE1, MDM2, CD31, ERG, TdT and LCA. WT1 showed cytoplasmic staining only, as the antibody directed against the carboxy-terminus was not available in our centre.

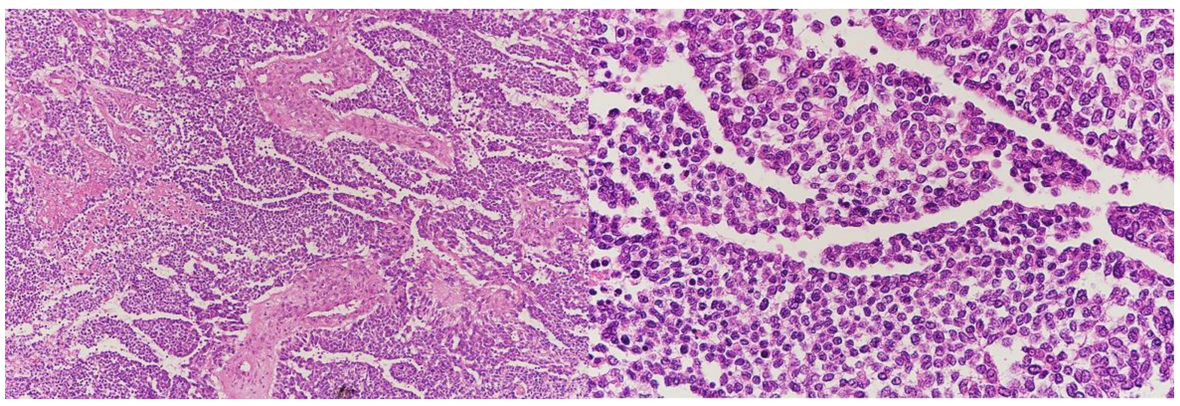


Figure 1. H&E sections of the tumour, low power 10x (left) and high power 40x (right).

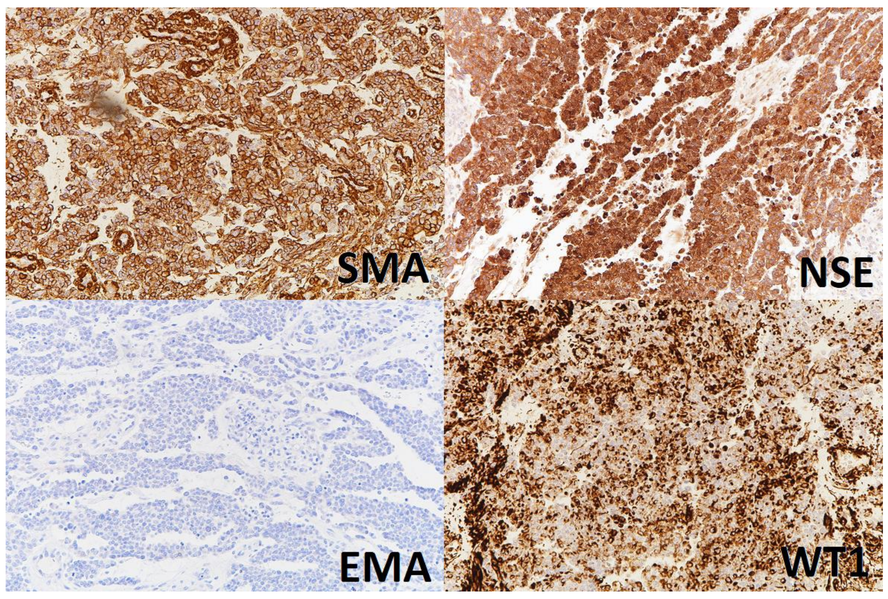
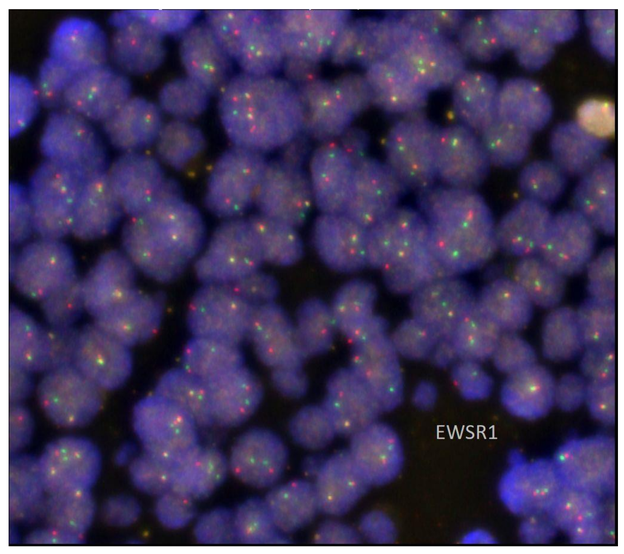


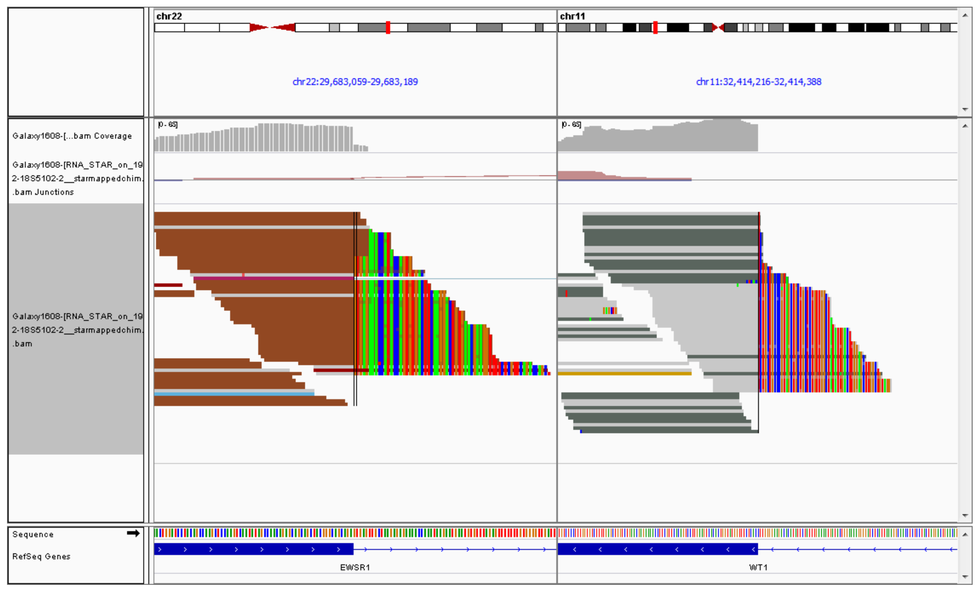
Figure 2. Immunohistochemistry showed positivity for SMA (top left) and NSE (top right). EMA was negative (bottom left). WT1 showed cytoplasmic staining only.

Molecular analysis

The tissue was subjected to FISH analysis by using LSI EWSR1 Dual Colour Break-apart Rearrangement Probe (Abbott). Only nuclei showing both green and orange signals were defined as informative nuclei. A total of 129 informative tumour cell nuclei from 3 different microscopic fields were examined. Split signal of EWSR1 was observed in 69.8% informative nuclei.



The tissue was also submitted for Illumina Pan-caner RNA sequencing analysis designed to detect fusion transcripts of 1385 cancer-related genes. Briefly, RNA was extracted from the formalin-fixed paraffin embedded tissue. The library prepared was sequenced by NextSeq500/550 mid output v.2 kit at 76bp pair-end on NextSeq500 sequencer (Illumina). The data was analyzed by RNA STAR Fusion pipeline. The raw reads were aligned to reference human genome (hg19) by RNA STAR v.2.4.0d. The fusion transcripts were determined by STAR Fusion software v.0.5.4. The chimeric transcript EWSR1-WT1 was detected. The fusion was created by joining the exon 7 of EWSR1 gene and exon 8 of WT1 gene. The fusion transcript was predicted to be in-frame.



IGV view of EWSR1-WT1 fusion. The fusion was joined by fusing exon 7 of EWSR1 to exon 8 of WT1. It is supported by 27 split reads and 29 spanning reads.

Discussion

DSRCTs primarily occur in the abdominal and pelvic cavity. The heart is an extremely rare location with only one other reported case found in literature search. [5]
The tumour cells in our case showed the typical "small round blue cell" morphology but lacked the classical abundant desmoplastic fibrous stroma. While the tumour was positive for smooth muscle markers SMA and desmin and neural marker NSE, it lacked staining for epithelial markers AE1/3 and EMA. Due to the "small round blue cell" appearance, our differential diagnoses included rhabdomyosarcoma, extraskeletal Ewing sarcoma, poorly-differentiated synovial sarcoma, neuroendocrine carcinoma and lymphoma. RNA sequencing showed EWSR1-WT1 fusion which is diagnostic of DSRCT. This is diagnostically helpful in cases showing atypical morphology. Cases with cord-like tumour cell structures embedded in predominantly fibrous stroma have been reported. In addition, the classical triad of EMA, desmin and NSE expression may not be present. [3]

In summary, we present a rare case of DSRCT occurring in the heart with lacking characteristic desmoplastic stroma and atypical immunoprofile. Our report draws attention to this diagnostic pitfall for when morphology and immunoprofile are atypical.

References

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