Presentation of a rare, highly aggressive peritoneal disease: desmoplastic small round cell tumor and its therapeutic options

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Summary
Background Desmoplastic small round cell tumor is a rare highly aggressive peritoneal disease (sarcoma) with mortality rates up to 70% in the first 3 years after diagnosis. It mainly affects young men. Patients clinically complain about diffuse abdominal pain. Methods This case report describes the clinical course of a 69-year-old man who presented with recurrent abdominal pain. Physical examination, laboratory testing, imaging, and gastroscopy were performed. Intra-abdominal peritoneal biopsies were taken during diagnostic laparoscopy. Results Physical examination was unremarkable. Laboratory results showed elevated white blood cells, C-reactive protein, and negative tumor markers. Computed tomography and positron emission tomography scan revealed extensive peritoneal metastases with diffuse intra-abdominal signal intensities and ascites. Gastroscopy was unremarkable, whereas diagnostic laparoscopy confirmed imaging results with a peritoneal cancer index of 39. Extensive immunohistochemical and consecutive molecular investigations led to the diagnosis of an intraperitoneal desmoplastic small round cell tumor.

Introduction
Desmoplastic small round cell tumor (DSRCT) is a rare highly aggressive form of sarcoma [1]. The entity was first described by Gerald and Rosai in 1989 [2] and mainly affects young men. DSRCT is associated with a very poor prognosis with mortality rates up to 70% in the first 3 years after diagnosis [3]. It mostly originates and spreads on peritoneal...
Case report

We report the case of a 69-year-old man who presented to our emergency department with recurrent severe abdominal pain for 1 week (numeric rating scale [NRS] 7/10). Six months previously, the patient had suffered from a similar episode. A colonoscopy had not revealed any significant findings. The patient denied any fever, dysuria, change in bowel habit, or weight loss. His past medical and surgical history were unremarkable.

On physical examination, his abdomen was soft without any tenderness. Laboratory results showed elevated white blood cells $10.41 \times 10^9/l$ (reference $3.5-9.8 \times 10^9/l$) and C-reactive protein $4.3 \text{mg/dl}$ (reference $<0.6 \text{mg/dl}$). Abdominal X-ray was unremarkable. To rule out an acute abdominal process we performed a computed tomography (CT) scan. Extensive lobulated peritoneal soft tissue masses with a large amount of ascites were detected (Fig. 1a, b). Furthermore, a $25 \times 16 \text{mm}$ hypodense structure was found in the pancreas. Positron emission tomography (PET)-CT scan showed diffuse intra-abdominal signal intensities (Fig. 1c).

Next, we performed a gastroscopy without any significant findings. Serological tumor markers (carcinoembryonic antigen [CEA], carbohydrate antigen [CA] 19-9, and CA 72-4) were all negative. Ascites was drained and cytological analysis revealed reactive-inflammatory cells. As the diagnosis was still unclear, we performed a diagnostic laparoscopy. Here, we saw multiple tense and spherical tumors on the parietal and visceral peritoneum (size: $1-5 \text{cm}$; Fig. 2). The peritoneal cancer index (PCI) was 39.

Histopathological analysis of laparoscopic biopsies revealed solid nests of round cells surrounded by cellular desmoplastic stroma. In addition, pleomorphic nuclei (hematoxylin–eosin staining) without any clear cell differentiation were detected. The proliferation index Kiel (Ki)-67 was about 40–50%. Further immunohistochemical analysis showed slightly positive epithelial markers (pan-cytokeratin CAM 5.2, cytokeratin [CK] 7, CK 20, epithelial membrane antigen [EMA], and Ber-Ep4). In contrast, mesothelial markers (thrombomodulin, podoplanin, calretinin, and Wilms tumor protein 1 [WT1]), neuroendocrine

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**Fig. 1** Coronal (a) and sagittal (b) contrast-enhanced computed tomography (CT) scan of the abdomen and pelvis showing diffuse soft-tissue masses (arrows) and ascites (stars) in the peritoneal cavity. Color-fused coronal positron emission tomography (PET)-CT scan (c) showing diffuse peritoneal nodules with enhanced fluorodeoxyglucose (FDG) uptake.
Fig. 2  Diagnostic laparoscopy revealed diffuse 1–5 cm tense and spherical tumors in the mesentery (a and b), right paracolic gutter (c), and in the pelvis (d).

Fig. 3  Hematoxylin–eosin (HE) staining and exemplary immunohistochemical (IHC) stainings (BerEp4, AE1/3, Wilms tumor protein 1 [WT1], podoplanin, thrombomodulin) of intraperitoneal biopsies. Scale bars are indicated.
markers (synaptophysin, chromogranin, and cluster of differentiation [CD]56), neurogen, and melanocytic markers (neuronspecific enolase [NSE], S-100, and Melan A), mesenchymal markers (myogenin-D1, desmin, and CD99), and lymphatic markers (among others CD34, CD45, CD68, CD117) were all negative (Fig. 3). Finally, fluorescence in-situ hybridization (FISH) revealed a translocation in the Ewing sarcoma breakpoint region 1 gene (EWSR1), which led to the diagnosis of an intraperitoneal desmoplastic small round cell tumor (DSRCT).

After laparoscopy, the patient became more and more immobile and suffered from diffuse abdominal pain with irregular bowel habits. In the interdisciplinary tumor board, palliative chemotherapy with doxorubicin, cyclophosphamide, and vincristine was scheduled. Cytoreductive surgery and heated intraperitoneal chemotherapy (HIPEC) were rejected because of multiple comorbidities (Eastern Cooperative Oncology Group [ECOG] 3). A few weeks after the primary diagnosis, the patient died during the palliative chemotherapy due to tumor toxic cardiovascular failure.

Discussion

DSRCT is a rare, aggressive form of sarcoma causing diffuse abdominal pain in mainly young men. Different preoperative imaging modalities are used for diagnosis to evaluate locoregional and extra-abdominal disease extent. Imaging studies show multiple soft tissue masses throughout the abdomen without clear disease extent. Further imaging modalities (among others CD34, CD45, CD68, CD117) were all negative (Fig. 3). Finally, fluorescence in-situ hybridization (FISH) revealed a translocation in the Ewing sarcoma breakpoint region 1 gene (EWSR1), which led to the diagnosis of an intraperitoneal desmoplastic small round cell tumor (DSRCT).

We present a very rare cause of recurrent abdominal pain caused by DSRCT. Especially in men presenting with unspesific abdominal pain and massive intra-abdominal tumor masses without any clear origin, DSRCT should be included in the differential diagnosis. All other possible malignancies with peritoneal masses (rhabdomyosarcoma, lymphoma, neuroblastoma, neuroectodermal tumor, mesothelioma, and tumors of gastrointestinal or ovarian origin) have to be included in the differential diagnosis and should be excluded with extensive immunohistochemical and consecutive molecular investigations [5]. Because only rare cases have been described so far, clear therapeutic guidelines are lacking. Therapeutic approaches include chemotherapy, radiotherapy, cytoreductive surgery, and/or hyperthermic intraperitoneal chemotherapy (HIPEC).

Conclusion

We present a very rare cause of recurrent abdominal pain caused by DSRCT. Especially in men presenting with unspesific abdominal pain and massive intra-abdominal tumor masses without any clear origin, DSRCT should be included in the differential diagnosis. All other possible malignancies with peritoneal masses (rhabdomyosarcoma, lymphoma, neuroblastoma, neuroectodermal tumor, mesothelioma, and tumors of gastrointestinal or ovarian origin) have to be included in the differential diagnosis and should be excluded with extensive immunohistochemical and consecutive molecular investigations [5]. Because only rare cases have been described so far, clear therapeutic guidelines are lacking. Therapeutic approaches include chemotherapy, radiotherapy, cytoreductive surgery, and/or hyperthermic intraperitoneal chemotherapy (HIPEC).

Author Contribution All authors contributed to the conception, design, performed material preparation, and data collection. The manuscript was written by J. P. Ramspott. D. Neureiter performed the histological analysis. T. Jäger and P. Schredl supervised the project. All authors read and approved the final manuscript.

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Declarations

Conflict of interest J. P. Ramspott, T. Jäger, D. Neureiter, K. Emmanuel and P. Schredl declare that they have no competing interests.

Ethical standards All procedures performed in studies involving human participants or on human tissue were in accordance with the ethical standards of the institutional and/or national research committee and with the 1975 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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