EUROMEDITERRANEAN BIOMEDICAL JOURNAL

for young doctors

Case Report

INTRAABDOMINAL DESMOPLASTIC SMALL ROUND CELL TUMOR: CASE REPORT WITH LITERATURE REVIEW

Joseph Kreiker [1], Iskandar Daou [2], Georges Nawfal [3], Tarek Bou Assi [4], Giovanni Tomasello [5], Abdo Jurjus [6]

Summary

Intra-abdominal desmoplastic small round cell tumors are rare aggressive neoplasms, with a very poor prognosis, observed in young adults with a male predominance. Their etiology is unknown and the diagnosis is based on histopathology, immunohistochemistry and cytogenetics. Histological analysis shows typically clusters of round cells separated by abundant desmoplastic stroma. These tumors exhibit a multi-marker immunohistochemistry profile expressing the three embryonic lineages: epithelial, neural and mesenchymal. They are positive for desmin and cytokeratin and are characterized by a specific recurring translocation t (11: 22) (q12 - p13), which involves EWSR1 WT1 gene. They are usually fatal despite an aggressive multidisciplinary therapeutic approach. Hereby we report the case of a 39 year old man who presented with an intra-abdominal desmoplastic small round cell tumor. The diagnosis was made by radiological, histological and immunohistochemistry profile analyses of a CT scanguided biopsy. This article also includes a mini review of the literature.

Introduction

Intra-abdominal desmoplastic small round cell tumors (DSRCT) were described first by Gerald and Rosai in 1989, and since then, around 200 cases have been reported in

Address of the authors:

[1] Department of Gastro-Enterology, Hôpital St Joseph des Sœurs de la Croix - Centre Médical Raymond et Aida Najjar, Faculty of Medicine, Saint Joseph University Beirut, Lebanon

[2] Department of Radiology, Hôpital Saint Joseph des Sœurs de la Croix- Centre Raymond et Aida Najjar, Beirut, Lebanon

[3] Department of Interventional Radiology, Hôpital Saint Joseph des Sœurs de la Croix-Centre Raymond et Aida Najjar, Beirut, Lebanon

[4] Department of Laboratory Medicine, Hôpital Psychiatrique de la Croix, Jal el Dib, Lebanon

[5] Università de gli Studi di Palermo — Dipartimento Universitario BIONEC - Sezione di Anatomia Umana

[6] Department of Anatomy, Cell Biology & Physiology, Faculty of Medicine, American University of Beirut, Beirut, Lebanon

Send correspondence to: *Joseph Kreiker, josephkreiker@gmail.com; Abdo Jurjus, aj00@aub.edu.lb*

Received: *1st December, 2015 — **Revised:** 6th December, 2015 — **Accepted:** 10th December, 2015*

the literature [1-3]. Desmoplastic tumors affect 'with a strong male predominance' children, adolescents and young adults [4-5]. The male to female ratio is around 4: 1 [6]. The median age at diagnosis is 22 years with a range between 6 and 49 years [7]. Three years old pediatric cases have been reported [8]. Some studies showed that the average age at diagnosis is 28 with a maximum of 46 years [9]. The same study reported a male to female ratio of 5: 1, which further confirms that desmoplastic small round cell tumors affect males predominantly [9]. These tumors are classified as soft tissue sarcomas without any known risk factor. They are extremely rare, highly malignant, and have poor survival [8].

They remain asymptomatic for many years and usually appear in 75% of cases as an abdominal mass. Other associated clinical manifestations that may reveal these tumors include abdominal pain (50%), deterioration of the general condition (15%), sweating (5%), nausea, vomiting, back pain (5%), lethargy (5%), ascites and pleural effusion. Rarely, they can be discovered incidentally during laparotomy for appendectomy or Caesarean section [9]. These tumors typically develop in the abdominal cavity, invading the omentum, and can reach the diaphragm, the splenic hilum, the mesentery, and the pelvic area. Metastases are frequent and usually involve the liver, lungs, pleura, bones, spleen and lymph nodes [5]. A delayed extra-peritoneal metastasis can occur [5, 10]. However, extraperitoneal primary tumors have been reported in various organs including paratesticular regions, ovaries, pleura, pancreas, liver, head and neck and salivary glands [5-11].

The diagnosis of desmoplastic small round cell tumors is histological, showing clusters of small round cells suspended in a dense desmoplastic stroma. Immunohistochemistry studies are positive for epithelial markers (keratin, epithelial membrane antigen), neural (neuron-specific enolase), and muscle (desmin) [2, 7]. Diagnosis is confirmed by cytogenetic studies that reveal a specific single translocation t (11: 22) (p13; q12) that leads to the fusion of two genes and the expression of (EWSR1 - WT1),an oncogenic chimeric protein. This latter protein functions as an aberrant transcription factor that fails to suppress tumor growth [7, 12]. The rarity and the lack of early clinical manifestations make it difficult to detect these tumors before they reach a large volume [7]. These tumors can be confused with other intra-abdominal tumors and lymphomas; they are a subgroup of the pediatric small round cells tumors and should be distinguished from rhabdomyosarcoma, neuroblastoma, neuroectodermal primary tumors, small round cell mesothelioma, Ewing's sarcoma and Wilm's tumor [1, 7].

CT scan and Magnetic Resonance Imaging (MRI) reveal heterogeneous solid masses in 70 to 100% of cases. These masses are usually multiple (90%) and rarely single (10%); they sometimes have a cystic component secondary to the hemorrhagic and necrotic foci. The size of these tumors varies typically between 5 and 10 cm. However, their sizes can vary according to various studies from a few millimeters to 20 cm. The most common site is peritoneal (90%); and in the vast majority of cases the initial mass is located in the abdomen (63%) followed by the pelvic area (6%). The CT scan also may reveal intratumoral calcifications (20%), ascites (30%), or pleural effusion (25%). Lymph nodes may be involved in several locations including peritumoral (80%), para-aortic (71%), aortocaval (50%), portocaval (13%), and mediastinal (20%). Imaging studies detect earlier liver (20%), lung (5%) and bone metastases (5%) [9-13].

The objective of this study is to report a patient with a desmoplastic small round cell tumor and clarify, through a brief literature review, the different epidemiological, clinical, diagnostic and therapeutic aspects of these rare tumors.

Case Report

We report the case of a 39 year old man of Armenian origin, previously healthy when he started complaining from fatigue, anorexia, minimal deterioration of his general condition, bloating and an upper left quadrant abdominal pain described as deep and vague pain. He presented to the emergency department

with acute onset abdominal pain, distension and inability to pass stools and gaz. Physical exam revealed a left upper quadrant abdominal mass, bloating and a diffuse pain, more severe in the left periumbilical area. Complete Blood Count showed leukocytosis (14,900 /mm^3), polynucleosis (83%) and mild anemia. Liver function, pancreatic, renal, lipid and cardiac blood tests were within the normal limits. The patient personal and family history were not remarkable.

Abdominal X-ray showed intestinal distension located mainly in the jejunum with some air-fluid levels (Figure 1). Chest X-ray was normal. Abdomino-pelvic CT scan revealed a heterogeneous mass located in the left upper quadrant with irregular borders measuring around 5.5 cm x 8.5 cm. This mass was adhering

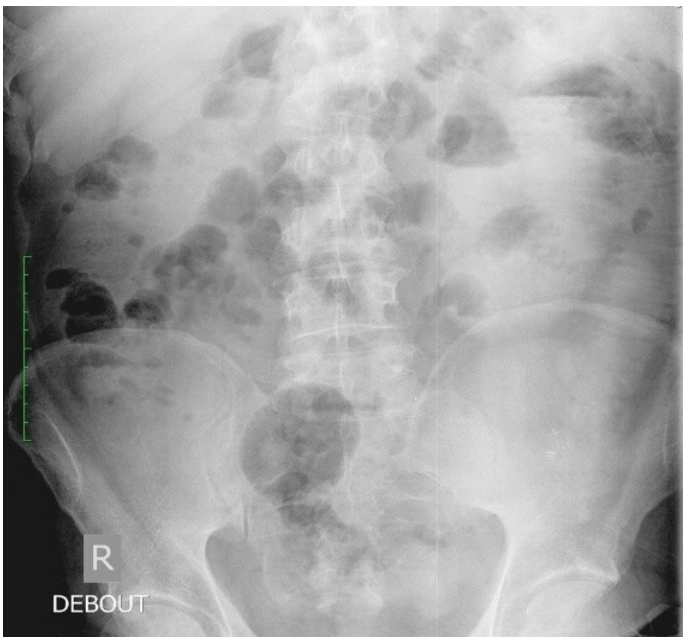

Figure 1. Abdomen X-Ray: Air-fluid levels

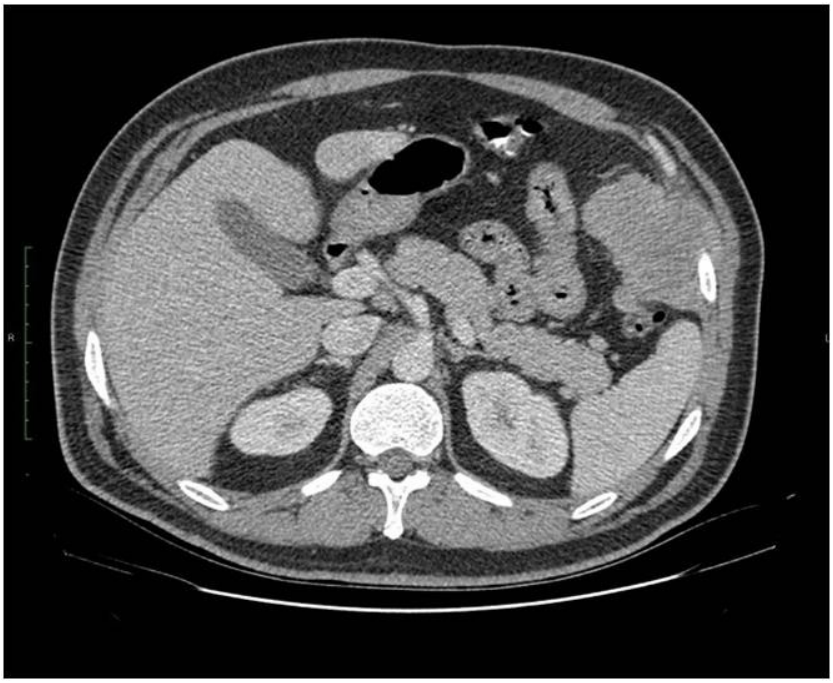

Figure 2. CT scan showing a solid mass

to the diaphragm and the intercostals muscles and doesn't seem to refer to one intra-abdominal organ (Figure 2).In addition, an extrinsic compression of the left colonic angle was observed without intraluminal invasion. Three metastatic lymph nodes with a discrete peri-tumoral costal infiltration were noted. A CT-guided needle biopsy was taken, from the mass for histological and immunohistochemical examination (Figure 3).

Histological studies were performed using several stains: hematoxylin and Eosin, Periodic acid–Schiff, Diastase, Alcian Blue and reticulin. Immunohistochemistry studies included: CK (AE1-AE3), desmin, S100, AML, WT1, calretinin, MIB1, vimentin and EMA. Microscopic examination showed dense reticulin matrix infiltrated by clusters of epithelioid small round cells having round nuclei and light anisonucleosis. These clusters were invasive and dense in some areas. Their cytoplasm was usually scant but sometimes vacuolar with intranuclear vacuoles. Immunohistochemistry profile analysis showed that these tumor cells were positive for pancytokératine, WT1, vimentin, EMA and focally weak for desmin. The proliferation index was low to moderate.

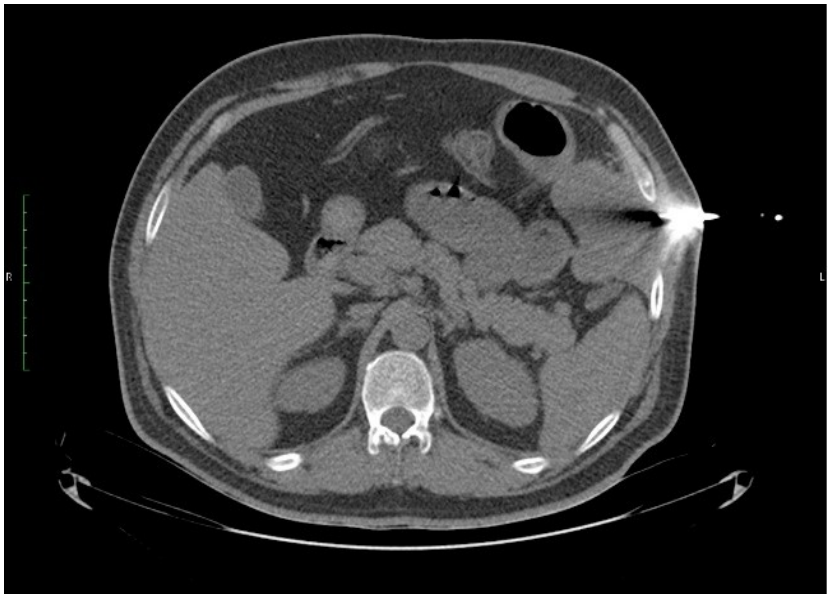

Figure 3. CT-guided needle biospy of the mass

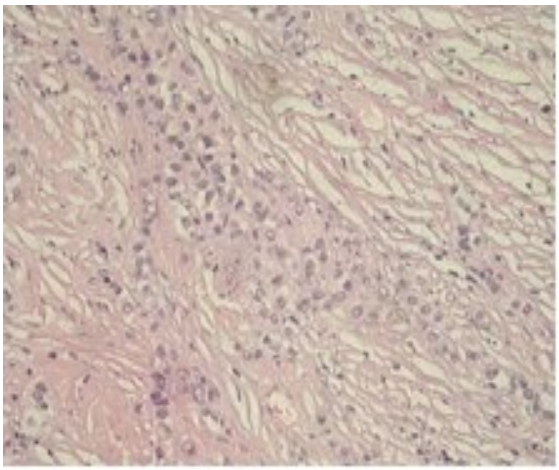

Figure 4. Microscopic features of neoplastic cells (magnification x200)

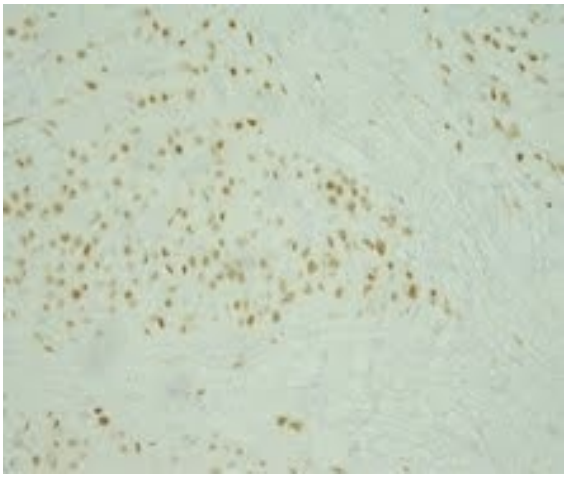

Figure 5. Immunohistochemistry: Expression of Desmin (magnification x200)

Following these histological and immunohistochemical studies, the diagnosis of desmoplastic small round cell tumor was made (Figures 4 and 5).

Discussion

Desmoplastic small round cell tumors are rare soft tissue sarcomas; they are rapidly fatal and affect predominantly young males. Similarly with other sarcomas they are relatively common in children and young adults [14]. For this sarcomas, the mean age at diagnosis varies between 22 and 28 years; with extreme ages of 3 and 49 years. No known risk factors specific for the disease have been identified [1]. This article reports the case of a young adult male (39 years old), of Armenian origin. The patient had a single abdominal mass, while the majority of the reported cases manifested as multiple abdominal or more rarely pelvic masses. In our patient, the clinical picture consisted of a nonspecific intestinal occlusion without any particularity and that corresponds to the typical clinical presentation of such tumors. The abdominal mass volume (5.5 cm x 8.5 cm) was quite significant; it demonstrates that their early diagnosis remains difficult because of the lack of early warning signs. The patient remained healthy for many years as the tumors grew and spread uninhibited within the abdominal cavity with frequent metastasis mostly involving the liver, lungs, and bones [1]. The presence of peri-tumoral metastatic lymph nodes and costal bone involvement, in our case, denotes the frequent and early dissemination of the disease at diagnosis. Imaging studies did not reveal any extra-peritoneal mesothelial lesions in our case such as the pleura and the tunica vaginalis of testis or solid organs such as the pancreas, liver, kidneys and ovaries (9). However, it is important to note that some cases have been reported in women simulating ovarian tumors with elevated CA 125 levels [15].

Abdomen CT is considered by all specialists as the initial test of choice; it helps to diagnose and classify desmoplastic tumors, and allows performing CT-guided needle biopsies (Figure 3). Histological and immunohistochemistry examination of biopsies confirm the diagnosis. Abdomen CT allowed identifying the dominant solid mass measuring more than 5 cm in diameter in 69% of cases [9, 16]. These masses do not originate from any abdominal organ and is at least twice as large as other peritoneal lesions in 80% of cases [9-16]. These masses occur in the abdomen (62%), the pelvis (36%), and the para-vertebral region adjacent to the diaphragm pillar (6%) [9, 13, 17]. The diagnosis of our case was made based on the radiological characteristics shown on CT scan and the results of the immunohistochemistry profile. Our patient had a large heterogeneous peritoneal mass, around 8.5 cm in diameter, located in the left upper quadrant not originated from any abdominal organ. This mass was compressing the splenic angle without invading the intestinal lumen. Furthermore, we detected metastatic lymph nodes with a discrete peritumoral costal involvement but without any pulmonary or liver metastasis.

Endoscopic ultrasound is of limited value; it reveals heterogeneous lobulated and hypoechoic lesions and allows performing guided biopsies in cases of superficial tumors [18]. Magnetic resonance imaging (MRI) shows the masses and defines the hemorrhagic and necrotic intra-tumoral characteristics that are not specific for such tumors [13]. Also, MRI does not allow performing differential diagnosis with other abdominal tumors [9].

[18F] fluorodeoxyglucose-positron emission tomography FDG -PET / CT reveals occult lesions not detectable by CT or MRI. In addition, it allows to evaluate the response to chemo-radiotherapy and detects early relapses before any other conventional imaging studies [19]. Tumor metastasis are early and frequent (63% to 100%); they affect mainly the liver (20%) followed by the lungs (5%) and the bones (5%). Metastatic lymph nodes involvement is noted in more than half of cases at diagnosis. These lymph nodes are usually intra-abdominal in 80% of cases and affect the para-aortic (71%),-aorto-caval (50%), and mesenteric porto -caval area (13%) [2-5].

Typical histological criteria consist of small round cells nests suspended in a

dense desmoplastic stroma [2-5]. This aspect corresponds to the histopathological findings observed in our patient. However, these tumors may exhibit unusual morphological aspects in almost one third of cases [8, 20]. Predominant components include: spindle cells, pseudo-rosettes, Homer-Wright rosette and island forms. Several patterns may be seen including glandular, basaloid, solid area with little stroma, rhabdoid, clear cells, pleomorphism, fusiform and papillary (2). These various atypical histological presentations should be well known to avoid diagnostic errors and confusion with other tumors [21].

Immunohistochemistry analysis of desmoplastic tumors displays a triple co-expression that includes the epithelial markers (keratin and EMA), the mesenchymal markers (desmin and vimentin) and occasionally the neuronal marker (neuron specific enolase). However it is pertinent to note that Primitive neuroectodermal tumors and Ewing's sarcoma are negative for desmin; Neuroblastoma is vimentin and desmin negative while small cell mesotheliomas are desmin, CD15 and CD57 negative [1]. Interestingly, Calretinin which is a protein highly expressed in normal mesothelium and mesothelioma, is negative in desmoplastic small round cell tumors [20]. Gerald et al. suggested that desmoplastic tumors are related to the mesothelium because their tumor growth model is similar to mesothelioma and they occur in serous cavities. WT1 gene is frequently expressed in mesothelioma and fetal mesothelioma is positive for keratin and desmin [2]. The histological and immunohistochemistry results seen in our patient were similar to the literature and typical for desmoplastic tumor. In fact, we described small round cells suspended in a dense desmoplastic stroma and positive for pancytokératine, WT1, vimentin, EMA and focally weak for desmin which strongly supported the diagnosis of desmoplastic small round cell tumors.

These tumors are genetically characterized by the translocation (11: 22) (p13; q12). This translocation leads to the expression of an oncogenic fusion protein EWSR1 - WT1 that acts as an aberrant transcription factor promoting uncontrolled tumor growth [7, 12]. According to numerous studies, genetic abnormalities are highly specific and can confirm the diagnosis of these tumors. However, some reservations have been issued by Alaggio and Wang concerning the expression of this fusion protein in some pediatric cases of leiomyosarcomas and kidney tumors. This observation suggests that EWSR1-WT1 fusion may not be entirely specific for desmoplastic tumors [22, 23].

Therapeutic options

A multidisciplinary therapeutic approach is the best way that may improve the prognosis with a 3-year survival of 58%. Surgery is often complex and the complete resection of these tumors is rarely possible. Surgery is usually associated with heavy chemotherapy while radiotherapy may yield better results compared to chemotherapy or radiotherapy alone [9]. The resection of liver metastases may be performed by radio frequency, cryotherapy, or Radio-embolization by Yttrium microspheres [24]. Hyperthermic intra-peritoneal therapy used in peritoneal carcinomatosis of ovarian origin, was also tested in the treatment of desmoplastic tumors with unclear results. This new procedure should be further investigated by prospective randomized trials [7].

Conclusion

Desmoplastic small round cell tumors are rare and aggressive tumors. The majority of patients are usually seen at a late stage. The diagnosis should be considered in a young adolescent male who is presenting with:

1 . multiple diffuse peritoneal masses,or

2 . a dominant mass measuring at least 5 cm or a single mass not originated from any abdominal organ.

3 . Abdominal CT scan is considered the initial gold standard imaging study.

4 . Diagnosis is made by histology, immunohistochemistry and cytogenetics studies. FDG-PET / CT are useful in the monitoring and may detect early relapses.

A multidisciplinary therapeutic management including aggressive debulking surgery combined with intensive chemotherapy and radiotherapy remain the only hope for improving the survival of these patients.

References

1. Koniari K, Mahera H, Nikolaou M, Chatzis O, Glezakou O, Magiasis V, Kiratzis G. Intraabdominal desmoplastic small round cell tumor: Report of a case and literature review. Int. J. Surg. Case Rep. 2011; 2(8): 293-296

2. Gerald WL, Miller HK, Battifora H, Miettinen M, Silva EG, Rosai J. Intraabdominal desmoplastic small round cell tumor: report of 19 cases of a distinctive type of high-grade polyphenotypic malignancy affecting young individuals. American Journal of Surgical Pathology. 1991; 15(6): 499-513.

3. Ladanyi M, Gerald W. Fusion of the EWS and WT1 genes in desmoplastic small round cell tumor. Cancer Research. 1994; 54(11):2837-2840.

4. Rodriguez E, Sreekantaiah C, Gerald W, Reuter VE, Motzer RJ, Chaganti RSK. A recurring translocation, t (11; 22) (p13; q11.2), characterizes intraabdominal desmoplastic small round cell tumors. Cancer Genetics and Cytogenetics. 1993; 69(1): 17-21.

5. Vincent PM Cliteur, KarolySzuhai, Hans J Baelde, Jurriaan van Dam, Hans Gelderblom, Pancras CW Hogendoom. Paratesticular desmoplastic small round cell tumor: an unusual tumor with an unusual fusion; cytogenetic and molecular genetic analysis combining RT-PCR and COBRA-FISH. Clin Sarcoma Res 2012; 2:3

6. Gerald WL, Rosai J. Desmoplastic small cell tumor with divergent differentiation. Pediatric Pathology.1989; 9 (2):177–183.

7. Dufresne A, Cassier P, Couraud L, Marec-Bérard P, Meeus P, Alberti L, Blay JY. Desmoplastic Small Round Cell Tumor: Current Management and Recent Findings. Sarcoma 2012; 2012:714986.

8. Angunawela P, Khalafallah A, Wolfswinkel K, Seaton D, Brain T. An Unusual Presentation of Desmoplastic Small Round Cell Tumor of the Abdomen: Morphological, Immunohistochemical, Ultrastructural and Molecular Studies. Case Reports in Oncological Medicine. 2011; 2011: 183938.

9. Thomas R, Rajeswaran G, Thway K, Benson C, Shahabuddin K, Moskovic E. Desmoplastic small round cell tumour: the radiological, pathological and clinical f eatures. Insights Imaging. 2013 Feb; 4 (1):111-118.

10. Hayes-Jordan A, Anderson PM. The diagnosis and management of desmoplastic small round cell tumor: a review. Current Opinion in Oncology. 2011; 23 (4): 385-389.

11. Yin WH, Guo SP, Yang HY, Chan JK. Desmoplastic small round cell tumor of the submandibular gland: a rare but distinctive primary salivary gland neoplasm. Hum Pathol. 2010; 41(3): 438-42.

12. Murphy AJ, Bishop K, Pereira C, et al. A new molecular variant of desmoplastic small round cell tumor: significance of WT1 immunostaining in this entity. Human Pathology. 2008; 39 (12): 1763-1770.

13. Zhang WD, Li CX, Liu QY, Hu YY, Cao Y, Huang JH. Ct, MRI, And FDG-PET/CT imaging findings of abdominopelvic desmoplastic small round cell tumors: Correlation with histopathologic findings. Eur J radiol. 2011; 80(2): 269-273.

14. Ratto N, De Cian F, Ratto GB. New therapeutic options in the treatment of metastatic limb sarcomas: A case series. Euromediterranean Biomedical Journal 2013, 8(9):46-53.

15. Ordonnez NG, Sahin AA. CA 125 production in desmoplastic small round cell tumor: report of a case with elevated serum levels and prominent signet ring morphology. Hum Pathol. 1998; 29 (3):294-9

16. Chouli M, Viala J, Dromain C, Fizari K, Duvillard P, Vanel D. Intra-abdominal desmoplastic small round cell tumors : CT findings and clinicopathological correlations in 13 cases. Euro J Radiol. 2005; 54(3):438-442.

17. Outwater E, Schiebler ML, Brooks JJ. Intraabdominal desmoplastic small cell tumor: CT and MR findings. J Comput Assist Tomogr. 1992; 16(3): 429-432.

18. Bellah R, Suzuki-Bordalo L, Brecher

E, Ginsberg JP, Maris J, Pawel BR. Desmoplastic small round cell tumor in the abdomen and pelvis: report of CT findings in 11 affected children and young adults. AJR Am J Roentgenol. 2005; 184 (6): 1910-1914.
19. Ben-Sellem D, Liu K, Cimarelli S, Constantinesco A, Imperial A. Desmoplastic small round celltumot: Impact of 18f-FDG PET induced treatment strategy in a patient with long-term outcome. Rare Tumors. 2009; 1:31-33.
20. Ordonez NG. Desmoplastic small round cell tumor: I. A histopathologic study of 39cases with emphasis on unusual histological patterns. American Journal of Surgical Pathology. 1998; 22 (11): 1303-1313.
21. Zhang PJ, Goldblum JR, Pawel BR, Fisher C, Pasha TL, Barr FG.Immunophenotype of desmoplastic small round cell tumors as detected in cases with EWS-WT1 gene fusion product. ModPathol. 2003; 16(3):229-35.
22. Alaggio R, Rosolen A, Sartori F, Leszl A, d'Amore ES, Bisogno G. et al. Spindle cell tumor with EWS-WT1 transcript and a favorable clinical course: a variant of DSCT, a variant of leiomyosarcoma, or a new entity? Report of 2 pediatric cases.Am J Surg Pathol. 2007; 31(3): 454-9.
23. Wang LL, Perlman EJ, Vujanic GM, Zuppan C, Brundler MA, Cheung CR. Et al. Desmoplastic small round cell tumor of the kidney in childhood. Am J SurgPathol. 2007; 31(4):576-84.
24. Subbiah V, Myurth R, Anderson PM. Yttrium microsphere radioembolotherapy in desmoplastic small round cell tumor hepatic metastases. J Clin Oncol. 2011 ; (11):292-294.