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CASE REPORT

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Desmoplastic Small Round Cell Tumor in a Pregnant Woman: A Case Report and Literature Review

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Background: Desmoplastic small round cell tumor (DSRCT) is an aggressive malignant tumor commonly found in young men; most occurs in the abdominal cavity. Here we conducted an in-depth analysis of a pregnant patient in our hospital and explored all the case information in the literature on small round cell carcinoma of women. **Case presentation**: A 27-year-old pregnant woman underwent tumor resection in our hospital at 29 weeks gestational age for a large progressive shoulder lump. The postoperative pathology showed that the mass was a DSRCT. Genetic testing found no fusion gene. At 36 weeks gestation, a painful mass was found in the breast and proved to be a metastatic focus of the desmoplastic small round cell tumor. Twenty days after a successful cesarean section at 40 weeks gestation, she received the VAC-IE chemotherapy regimen, successfully completed the first course, but when awaiting the next chemotherapy, unfortunately, the patient died during follow-up due to tumor recurrence and metastasis. **Conclusion**: The treatment of DSRCT in pregnant women requires a multidisciplinary consultation, and the treatment and examination during pregnancy are subject to many constraints, which may have a negative impact on the patient's prognosis. Also, a review of the literature found that there is still no standard treatment protocol for DSRCT, and its prognosis in female patients is independent of age and tissue origin.

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Abbreviations: DSRCT, Desmoplastic small round cell tumor; HE, hematoxylin and eosin; MRI, Magnetic Resonance Imaging; HB, hemoglobin; AFP, alpha-fetoprotein; CRP, C-reactive protein; T1WI, T1-weighted image; T2WI, T2-weighted image; VAC-IE, vincristine, adriamycin, cyclophosphamide, with irinotecan and etoposide.

Keywords: Desmoplastic small round cell tumor, pregnant women, diagnosis, treatment, prognosis

Author Contributions: HL designed the study. AA,VGK, and YZD performed data collection. QRS, ZWW, and MHAHA analyzed the results, and HYZ (ORCID iD: 0000-0003-4068-9394) and SHAE drafted the manuscript.

[1]These authors contributed equally to this work.

BACKGROUND

Desmoplastic small round cell tumor (DSRCT) is a rare aggressive malignant neoplasm in the small round cell tumor family. Histologically, stained by hematoxylin and eosin (HE), it is characterized by nests of "small round blue cells" surrounded by dense proliferative matrix [1]. It is commonly seen in young males, and the abdominal cavity is the most frequent site it occurs, while extraserosal DSRCTs are extremely rare. Given its rarity, treatment recommendations regarding DSRCT are limited and there is still no consensus on the optimum treatment options [2,3]. Even with aggressive surgical excision and postoperative adjuvant high-dose chemotherapy and radiotherapy, or with incorporation of other treatment modalities, the clinical prognosis of patients with DSRCT remains highly unsatisfactory, as its mortality rate is 100% and the median survival remains at only 17.8 months [4,5]. Not to mention that the experience of treating special populations, such as pregnant women, has also been rarely reported or discussed, which we know from just two cases [6,7]. Like most of the malignancies, the cell of origin and mechanism of origin of DSRCT remains elusive, and the signature molecular features are under constant exploration to inspire more targeted gene therapy treatment, even though the reciprocal t (11; 22) (p13; q12) translocation of the *EWSR1* and *WT1* gene was identified in 1994 [8,9]. Immunohistochemical analysis also suggests multilineage differentiation, including epithelial, mesenchymal, and neuronal markers, leaving their origin hidden in a fog [10].

In this article, we report a case of a young woman with a rapidly progressing shoulder mass found in mid-pregnancy, and her final pathologic diagnosis is DSRCT. Meanwhile, we share our experience and lessons learned from the multidisciplinary management of this patient, review the incidence and treatment history of DSRCT in female patients in recent years, and discuss their clinical features, molecular characteristics, and existing prognostic factors that influence this aggressive tumor.

CASE PRESENTATION

A 27-year-old woman who was 29-weeks pregnant presented to our hospital due to a large mass in her right shoulder. The patient had inadvertently noticed a soybean sized bump on her right shoulder 6 months previous and was not experiencing any discomfort. To be on the safe side, she went to the local clinic where the mass was diagnosed as a "sebaceous cyst" and was left untreated in view of its benign clinical behavior. Three months later, she noticed that the mass gradually increased to the size of a ping-pong ball, and severely affected the movement of her shoulder, so she went to the local hospital for associated examinations. The local hospital performed a Magnetic Resonance Imaging (MRI) which revealed a large lump with malignant tendency. Local biopsy of the mass indicated a malignant skin tumor. She then came to our hospital in order to get better medical support. Throughout this period of time, her obstetric examinations were regularly performed and had gained satisfactory results. She denied any family history of malignant tumors.

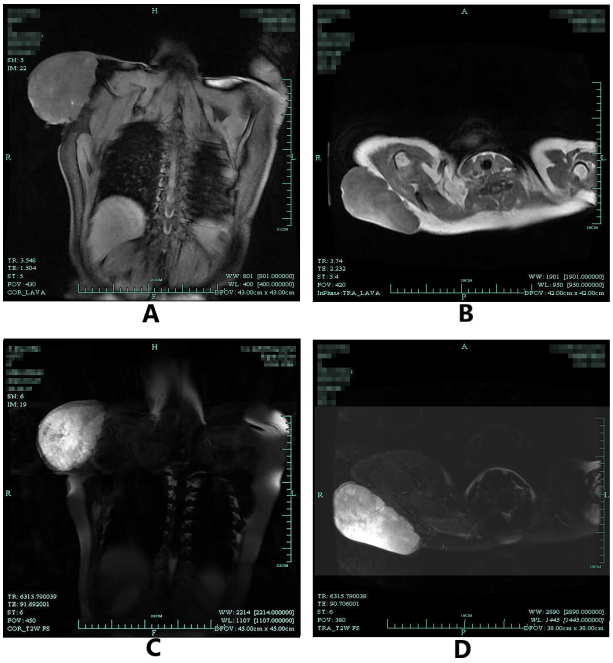

Figure 1. MRI results for patient. It suggested a largely clumpy signal foci in the skin and subcutis of the right shoulder-backside. Compared to the muscle, it was isosignal on T1WI with patchy slightly higher signal within (**A**,**B**), and was a high signal focus on T2WI (**C**,**D**). The size of the mass was about 12.6 x 11.3 x 6.6cm, with some long T2 signal in the adjacent muscles.

On the initial visit, we found a hard and immobile mass, approximately 9 x 10 cm in size, with unclear border and a small tumor ulcerated opening on the surface with oozing blood (Appendix A: Figure S1).

In addition to the shoulder lump, the patient was found to have a significantly increased level of alpha-fetoprotein (AFP) in the blood (334.9 ng/ml), whereas other oncological parameters such as CA125, CA199 were within the normal range. Besides the elevated leukocytes ($11.2x10^9$), high percentage of neutrophils (83.5%) and high C-reactive protein (CRP) (38.1 mg/L) showed signs of infection. Her coagulation function had also been adversely affected, as D-dimer was 1628ug/L. And just like many pregnant women, the patient also presented with mild hypoalbuminemia and moderate anemia. Fortunately, the liver function and kidney function were undamaged. And multiple bedside non-stimulatory fetal heart

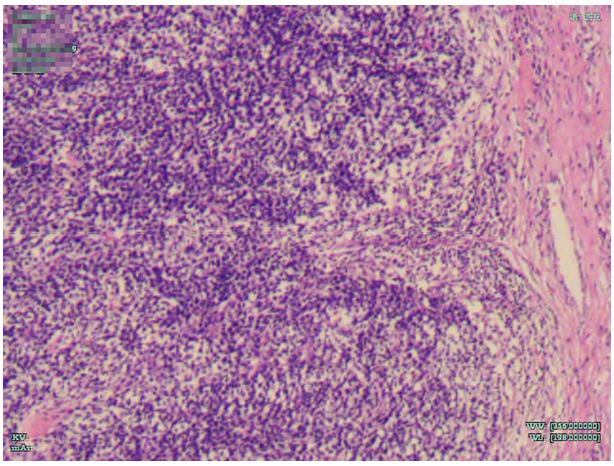

Figure 2. Pathological image of the lesion. The tumor cells were arranged in a prominent nesting pattern, had obvious cellular atypia, visible mitotic figures. The cells grew infiltrated with more small vessels between them.

monitoring revealed normal fetal heart rate of 130-150 beats/min.

Following laboratory examination, she underwent imaging consultation. MRI of the shoulder showed a large mass of iso-signal on T1-weighted image (T1WI) and high-signal on T2-weighted image (T2WI) and had clear borders but unsmooth edges (Figure 1). Simultaneously, the ultrasound of the lower abdomen suggested multiple high signal echoes in the liver, the nature of which was to be determined. The good news was that the fetal ultrasound findings and the patient's echocardiogram were normal. PET-CT is a diagnostic imaging modality for evaluating the whole body conditions in patients with malignant tumors for early detection of metastases, however, the patient did not undergo this test since the second trimester of pregnancy is an important period of fetal organ development and a large amount of radionuclides have teratogenic effects.

Due to the patient's and her relatives' strong desire to keep the baby, preoperative chemotherapy to reduce tumor volume was not administered. And after conferring with the obstetricians, the patient underwent extensive lumpectomy at 29w+5d gestation in view of the large progressing mass and persistent ulcerative trauma. A 10 x 10 cm mass was removed during surgery. The mass had borders that were poorly demarcated. About 2 cm of surrounding tissue from the outer edge of the mass was removed to achieve a negative tumor cut margin that was confirmed by the intraoperative frozen section of the tumor. Due to the large skin defect and the wait for the final diagnosis of pathology (Appendix A: Figure S2), we did not close the wound, instead, continuous negative pressure suction caused by vacuum sealing drainage (VSD) was applied and cefuroxime was used to fight infection. Postoperative pathology showed that the mass was first diagnosed as a highly malignant small round cell tumor, whereas Ewing sarcoma or low-grade synovial sarcoma could not be completely excluded (Figure 2). The immunohistochemical results were MyoD1(-), Myogenin(-), CK(pan)(-), CD31(-), CD34(-), CD99(+), INI-1(+), EMA(-), Desmin(-), SMA(-), WT1(+), Vimentin(+), Ki-67(+60%), S-100(-), HMB45(-), β-Catenin (membrane+), CgA(-), Syn(-), TFE3(-), ERG(-), STAT6(-), which indicated that the diagnosis of small round cell undifferentiated sarcoma, such as CIC-DUX4 or BCOR-CCNB3 sarcoma, was first considered, and if necessary, genetic testing was recommended to clarify the pathological type.

Based on the dynamic monitoring of the patient's laboratory parameters during hospitalization (Appendix A: Figure S3), a staged wound repairing operation was performed. On the 6th day after the first surgery, when the patient's condition was stable, we partially closed the wound. After another 6 days, the leftover skin defect was covered with skin graft from her thigh (Appendix A: Figure S4).

In the meantime, multidisciplinary discussions were held to determine the best way to manage this case. Throughout the case, the obstetrician examined the patient and determined appropriate progress of the pregnancy. And multiple times of labor examination showed safe results. Given to the subsequent treatment of the tumor, Chemotherapy and radiology were considered to treat the tumor, but were rejected due to the potential cytotoxic effects and uncertain efficacy of chemotherapy and the minimal effect of radiation therapy on small round cell tumors. The radiologists recommended that it was better to perform an appropriate chemotherapy regimen according to the genetic testing, which may lead to a better prognosis. However, the following genetic testing of the patient's tumor failed to find the related fusion gene for DSRCT.

Soon after, a painful hardness mass, about 6 x 6 cm in size, was found on the lateral quadrant of the left breast at around 36 weeks gestation. Due to the proximity of delivery, the patient did not want to experience any additional problems, so further consultation of the mass was abandoned. She underwent an uneventful cesarean section at 40w+6 and delivered a healthy baby boy. The patient then came to our hospital for examination of the breast mass, and it was classified as BI-RADS IV, a highly malignant imaging grading of breast mass diagnosed by ultrasound. Additionally, multiple hypoechoic foci in the right axilla, which was considered an enlarged lymph node, were found by ultrasound (Figure 3). Further needle biopsy of the left breast mass confirmed that it was a small round cell malignancy with immune results of CK5/6 (myoepithelial+), ER (-) (Appendix A: Figure S5). Enhanced

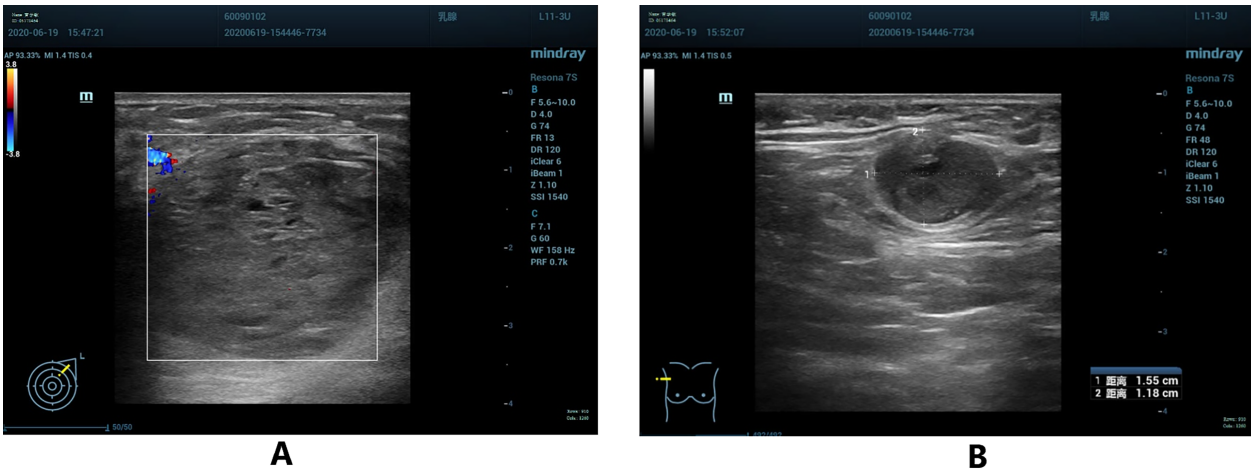

Figure 3. (**A**) **A mixed echogenic mass was detected in the upper quadrant of the left breast, the size was about 3.3 x 2.6 x 3.6 cm, the border was clear, and the morphology was irregular**. There was a cord-like strong echogenic interval and a small amount of signal inside. The color Doppler did not detect any abnormal blood flow signal. (**B**) A hypoechoic foci was detected in the right axilla with a size of about 1.6 x 1.2 cm, clear border, uneven internal echogenicity, and a fluid dark area.

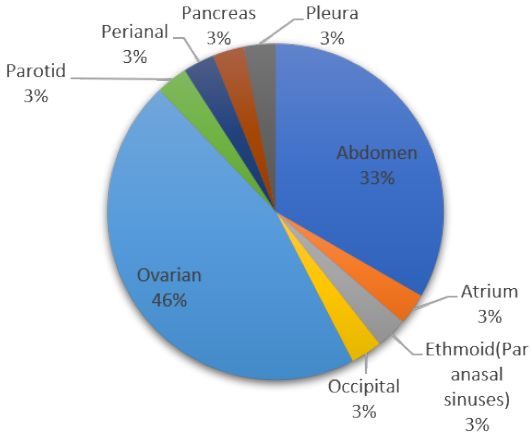

Figure 4. Distribution of DSRCT in different parts of human body.

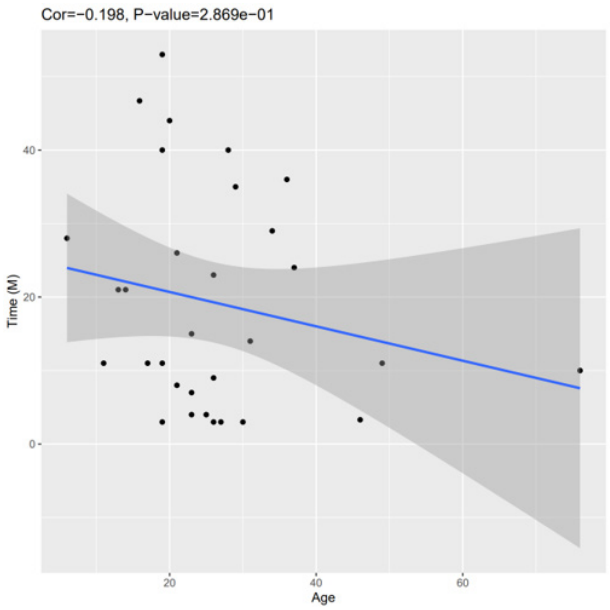

Figure 5. Age and survival time of all patients.

CT findings in the lungs revealed multiple nodules and enlarged axillary lymph nodes on both sides, and a breast mass on the left side, they were multiple metastases considered; meanwhile, a small amount of pleural effusion was found in the left lung. There were multiple slightly low-density foci with metastases considered in the liver. However, all tumor markers including AFP were normal values in this laboratory test.

In consideration of the patient's undetermined tumor subtype and the distant metastases that had already occurred, she was hospitalized to initiate on a complex vincristine, adriamycin, cyclophosphamide, with irinotecan and etoposide (VAC-IE) alternating chemotherapy regimen. During the first course of chemotherapy, the patient experienced severe nausea and vomiting, along with low back pain, which resolved with no recurrence after twice administration of 5 mg morphine tablets orally. Additionally, after chemotherapy, 6 mg thiopental was given to prevent the common side effect of chemotherapy drugs, a decrease in white blood cell count. The patient was eventually discharged from our hospital in stable condition and awaited the second course of chemotherapy. We followed up with the patient by phone after discharge, and the patient died 11 months after the initial discovery of

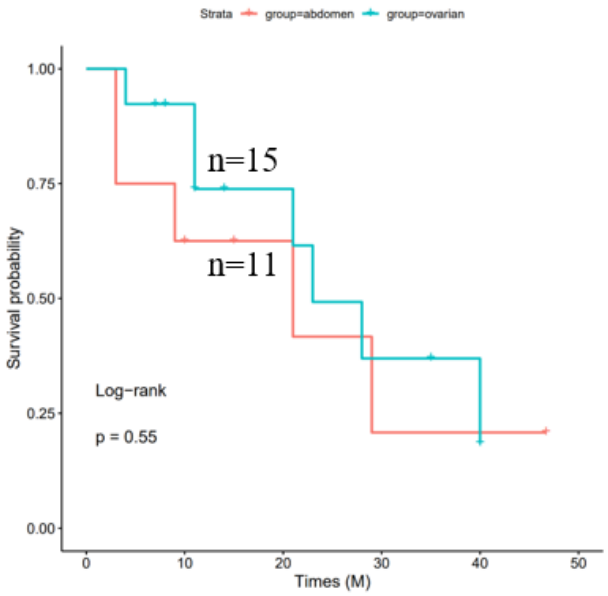

Figure 6. The survival probability curve of DSRCT originated from abdomen and ovarian groups.

the mass with uncontrolled metastasis of multiple tumors throughout the body.

DISCUSSION AND CONCLUSIONS

We present a case of the DSRCT in a pregnant woman who survived for only 5 months with complete surgical resection and chemotherapy support. The short survival period confirms the rapid progression and poor prognosis of DRSCTs, and the localized oversized mass is one of the predictors of poor prognosis. However, delayed diagnosis, delayed chemotherapy, and lack of standard treatment protocols also contributed to the patient's poor prognosis. To a great extent, some adverse factors greatly attributed to the unique physiologic period of the patient—pregnancy, which makes the decision-makers, both the physicians and the patient, more concerned when formulating a treatment plan and selecting an option, and suggests the need for multidisciplinary consultation and further scientific research to provide better treatment options.

In this case, we can easily find out that the patient's initial misdiagnosis delayed the optimal treatment opportunity, not only related to the patient's non-specific clinical presentation, but also to the rarity of DSRCT and the specific location of the patient's mass. We searched the PubMed database using the keywords "DRSCT" and "women." Eventually, we found 27 research articles from 1991 to 2020. According to an integration of all studies, we located 32 cases of DSRCT in women. In these 32 cases, all had a shorter overall survival time, mainly shorter than 10 months, and frequently originated from the abdomen and ovaries, which is similar to its overall characteristics [2,4,11] (Figures 4 and 5). Meanwhile, the great variability of tumor markers during pregnancy also greatly reduces the utility of this early diagnostic tool [12,13]. Our patient was not only a pregnant woman, but her DSRCT was also found in the shoulder, which to our knowledge has not been reported in publications, thus greatly reducing the chance of an early diagnosis. In light of this, we hope that this case will serve as a wake-up call for clinicians to pay attention to masses encountered in clinical practice and to perform imaging and necessary biopsies early enough for in-time diagnosis and treatment. We must keep in mind that early surgical treatment can be of great benefit for most tumor patients.

A needle biopsy of the mass confirmed a skin malignancy, and an MRI revealed the large shoulder mass was well-defined, making surgery the first choice for a skin tumor at the extremity [14-16]. A complete surgical resection is undoubtedly necessary, but the formulation of the surgical scheme for such a patient requires not only the participation of the attending physician, but also the evaluation of the patient's intrauterine viable fetus by the obstetrician, and the anesthesia protocol administered by the anesthesiologist based on the patient's unique physical condition.

In addition to the complexity of the patient's treatment plan, the inadequate examination of the patient also contributes to the tragedy of the patient's treatment. As we all know, DSRCT is a highly malignant tumor, which can easily metastasize to the lungs and many other parts of the body through hematologic spread [17,18], and the rapid increase in the size of the mass since the discovery of the tumor also indicates that the tumor was highly malignant [19,20]; so a comprehensive imaging examination is very important, especially PET-CT, which is very sensitive to tumor imaging. However, it cannot be ignored that the high radiation dose of PET-CT is highly likely to cause adverse obstetric outcomes such as miscarriage, lower intelligence, and teratogenesis [21-23]. With these in mind, along with the patient's progressively increasing maternal nature during the fetal maturation, it was not surprising to see her refusal of further radioactive imaging examination, which may have deprived us of the possibility of early detection of metastatic lesions.

Furthermore, adjuvant chemotherapy or radiation therapy before or after surgery for high-grade or large soft tissue sarcomas has shown to be beneficial for overall patient survival [20,24]. There has also been considerable research demonstrating that intrauterine chemotherapy does not cause significant birth defects, and some specific chemotherapy regimens are safe to use during mid- and late pregnancy, meanwhile, the incidence of nausea, vomiting, fatigue, hair loss, and neutropenia is even higher with postpartum chemotherapy than with gesta-

tional chemotherapy [25-27]. However, it has possible complications such as preterm labor, miscarriage, low birth weight, and other adverse outcomes, as well as the unknown optimal regimen of chemotherapeutic agents or radiation therapy, including dosage, dose intensity, and assessment of curative efficacy, that was caused by the vastly altered human physiology during pregnancy, make the early postoperative chemotherapy on this patient unformative [28,29].

The lack of specific targeted genes is also an unfortunate finding. Although in all likelihood, patients will refuse targeted therapy during pregnancy due to its proven detrimental effects on the fetus [27]. However, a number of retrospective data tell us that genome-directed therapy may be associated with substantial clinical benefit in patients with sarcoma in advanced disease, and some subtypes are highly sensitive to targeted therapy while relatively insensitive to chemotherapy [30,31]. At the same time, despite the rise of genomics, driver gene variants representative of therapeutic targets have only been identified in a few sarcoma subtypes, such as gastrointestinal stromal tumors, and the specificity of the genes associated with soft tissue tumors needs to be improved [30,32,33]. This indicates that our genetic analysis of soft tissue sarcomas is still incomplete, and we believe with more in-depth scientific research, there will be more targeted genes discovered for early diagnosis and treatment of patients.

There was also a factor that contributed to the final outcome of the patient's death, the delay in the check. We can see that the patient did not undergo further examination of the breast lump found in the third trimester until after delivery and did not receive follow-up chemotherapy until the month after delivery. There are several possibilities for this process, firstly, the patient was protective of her baby and did not want to raise obstacles to childbirth; secondly, the patient's understanding of the degree of malignancy of the tumor may have been skewed; in addition, a gap in the physician's close relationship with the patient may have emerged with her discharge, resulting in the loss of more detailed examination and attention. This reminds us of the importance of educating patients about malignant tumor and the need for regular follow-up, and we hope to improve these issues in the future clinical practice.

Further study of the literature revealed that, unlike the overall patient population, which exhibits characteristics where site is a major determinant of outcome and recurrence patterns [19], in women, the overall survival curves of DRSCTs found different body sites did not differ significantly (Figure 6), which may indicate that the malignancy of the tumor has no tissue specificity.

Overall, we report a rare case of shoulder-located DSRCT in a pregnant woman with a 5-month survival time after initiated diagnosis that may be attributed to the high degree of malignancy of the tumor or to a delay in diagnosis and treatment. And from our review of the literature, we conclude that the prognosis of DSRCT was not tissue specific and there was no correlation between survival times and age. It suggests that the early diagnosis of the DSRCT patients can refer to patients with different tissue sources, in women of different ages.

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Availability of data and materials: The dataset supporting the conclusions of this article is included with the article.

Ethics approval and consent to participate: The study protocols were approved by the Medical Ethics Committee of the First Affiliated Hospital of the College of Medicine, Zhejiang University.

Consent for publication: Written informed consent was obtained from the patient for publication of clinical details and clinical images. Upon request, a copy of the consent form is available for review by the Editor of this journal.

REFERENCE

1. Gerald WL, Rosai J. Case 2. Desmoplastic small cell tumor with divergent differentiation. Pediatr Pathol. 1989;9(2):177–83.
2. Xiang T, Zhang SY, Wang SS, Fei RS, Li H. A nationwide analysis of desmoplastic small round cell tumor. Medicine (Baltimore). 2020 Jul;99(30):e21337.
3. Ota S, Ushijima K, Fujiyoshi N, Fujimoto T, Hayashi R, Murakami F, et al. Desmoplastic small round cell tumor in the ovary: report of two cases and literature review. J Obstet Gynaecol Res. 2010 Apr;36(2):430–4.
4. Schwarz RE, Gerald WL, Kushner BH, Coit DG, Brennan MF, La Quaglia MP. Desmoplastic small round cell tumors: prognostic indicators and results of surgical management. Ann Surg Oncol. 1998 Jul-Aug;5(5):416–22.
5. Jayakrishnan T, Moll R, Sandhu A, Sanguino A, Kaur G, Mao S. Desmoplastic Small Round-cell Tumor: Retrospective Review of Institutional Data and Literature Review. Anticancer Res. 2021 Aug;41(8):3859–66.
6. Xie YP, Shen YM. Ovarian involvement of a desmoplastic small round cell tumor of unknown primary origin with lymph node and lung metastases: A case report. Oncol Lett. 2016 Feb;11(2):1125–9.
7. Neff RT, Kellert B, Isley M, Backes F. Management of a rapidly enlarging new adnexal mass: a rare case of desmoplastic small round cell tumor of the ovary arising in pregnancy. Gynecol Oncol Rep. 2016 May;17:23–5.
8. Hingorani P, Dinu V, Zhang X, Lei H, Shern JF, Park J, et al. Transcriptome analysis of desmoplastic small round cell tumors identifies actionable therapeutic targets: a report from the Children's Oncology Group. Sci Rep. 2020

Jul;10(1):12318.
9. Sawyer JR, Tryka AF, Lewis JM. A novel reciprocal chromosome translocation t(11;22)(p13;q12) in an intraabdominal desmoplastic small round-cell tumor. Am J Surg Pathol. 1992 Apr;16(4):411–6.
10. Ordóñez NG. Desmoplastic small round cell tumor: II: an ultrastructural and immunohistochemical study with emphasis on new immunohistochemical markers. Am J Surg Pathol. 1998 Nov;22(11):1314–27.
11. de Alava E, Marcilla D. Birth and evolution of the desmoplastic small round-cell tumor. Semin Diagn Pathol. 2016 Sep;33(5):254–61.
12. de Haan J, Vandecaveye V, Han SN, Van de Vijver KK, Amant F. Difficulties with diagnosis of malignancies in pregnancy. Best Pract Res Clin Obstet Gynaecol. 2016 May;33:19–32.
13. Sarandakou A, Protonotariou E, Rizos D. Tumor markers in biological fluids associated with pregnancy. Crit Rev Clin Lab Sci. 2007;44(2):151–78.
14. Tanabe KK, Pollock RE, Ellis LM, Murphy A, Sherman N, Romsdahl MM. Influence of surgical margins on outcome in patients with preoperatively irradiated extremity soft tissue sarcomas. Cancer. 1994 Mar;73(6):1652–9.
15. Bogumill GP, Sullivan DJ, Baker GI. Tumors of the hand. Clin Orthop Relat Res. 1975 May;108:214–22.
16. Chao AH, Mayerson JL, Chandawarkar R, Scharschmidt TJ. Surgical management of soft tissue sarcomas: extremity sarcomas. J Surg Oncol. 2015 Apr;111(5):540–5.
17. Meyer M, Seetharam M. First-Line Therapy for Metastatic Soft Tissue Sarcoma. Curr Treat Options Oncol. 2019 Jan;20(1):6.
18. Vezeridis MP, Moore R, Karakousis CP. Metastatic patterns in soft-tissue sarcomas. Arch Surg. 1983 Aug;118(8):915–8. doi: 10.1001/archsurg.1983.01390080023007.
19. Brennan MF, Antonescu CR, Moraco N, Singer S. Lessons learned from the study of 10,000 patients with soft tissue sarcoma. Ann Surg. 2014 Sep;260(3):416–21.
20. Mahmoud O, Tunceroglu A, Chokshi R, Benevenia J, Beebe K, Patterson F, et al. Overall survival advantage of chemotherapy and radiotherapy in the perioperative management of large extremity and trunk soft tissue sarcoma; a large database analysis. Radiother Oncol. 2017 Aug;124(2):277–84.
21. Dauer LT, Thornton RH, Miller DL, Damilakis J, Dixon RG, Marx MV, et al.; Society of Interventional Radiology Safety and Health Committee; Cardiovascular and Interventional Radiology Society of Europe Standards of Practice Committee. Radiation management for interventions using fluoroscopic or computed tomographic guidance during pregnancy: a joint guideline of the Society of Interventional Radiology and the Cardiovascular and Interventional Radiological Society of Europe with Endorsement by the Canadian Interventional Radiology Association. J Vasc Interv Radiol. 2012 Jan;23(1):19–32.
22. De Santis M, Di Gianantonio E, Straface G, Cavaliere AF, Caruso A, Schiavon F, et al. Ionizing radiations in pregnancy and teratogenesis: a review of literature. Reprod Toxicol. 2005 Sep-Oct;20(3):323–9.
23. Xie T, Zaidi H. Fetal and maternal absorbed dose estimates for positron-emitting molecular imaging probes. J Nucl Med. 2014 Sep;55(9):1459–66. doi: 10.2967/jnumed.114.141309.
24. Pasquali S, Pizzamiglio S, Touati N, Litiere S, Marreaud S, Kasper B, Gelderblom H, Stacchiotti S, Judson I, Dei Tos AP, Verderio P, Casali PG, Woll PJ, Gronchi A; EORTC – Soft Tissue and Bone Sarcoma Group. The impact of chemotherapy on survival of patients with extremity and trunk wall soft tissue sarcoma: revisiting the results of the EORTC-STBSG 62931 randomised trial. Eur J Cancer. 2019 Mar;109:51–60. doi: 10.1016/j.ejca.2018.12.009.
25. Cardonick E, Iacobucci A. Use of chemotherapy during human pregnancy. Lancet Oncol. 2004 May;5(5):283–91.
26. Blatt J, Mulvihill JJ, Ziegler JL, Young RC, Poplack DG. Pregnancy outcome following cancer chemotherapy. Am J Med. 1980 Dec;69(6):828–32.
27. Dekrem J, Van Calsteren K, Amant F. Effects of fetal exposure to maternal chemotherapy. Paediatr Drugs. 2013 Oct;15(5):329–34.
28. Mir O, Berveiller P. Increased evidence for use of chemotherapy in pregnancy. Lancet Oncol. 2012 Sep;13(9):852–4.
29. Anderson GD. Pregnancy-induced changes in pharmacokinetics: a mechanistic-based approach. Clin Pharmacokinet. 2005;44(10):989–1008.
30. Italiano A. Is There Value in Molecular Profiling of Soft-Tissue Sarcoma? Curr Treat Options Oncol. 2018 Dec;19(12):78.
31. Bui NQ, Wang DS, Hiniker SM. Contemporary management of metastatic soft tissue sarcoma. Curr Probl Cancer. 2019 Aug;43(4):289–99.
32. Nakano K, Takahashi S. Current Molecular Targeted Therapies for Bone and Soft Tissue Sarcomas. Int J Mol Sci. 2018 Mar;19(3):E739.
33. Ratan R, Patel SR. Chemotherapy for soft tissue sarcoma. Cancer. 2016 Oct;122(19):2952–60.

Appendix A

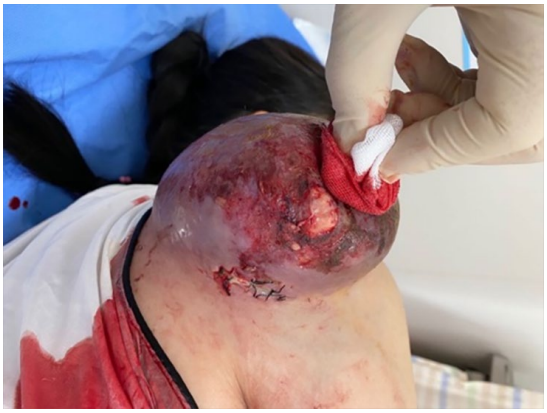

Figure S1. Large lump with oozing wound.

Figure S2. Large skin defect after tumor resection.

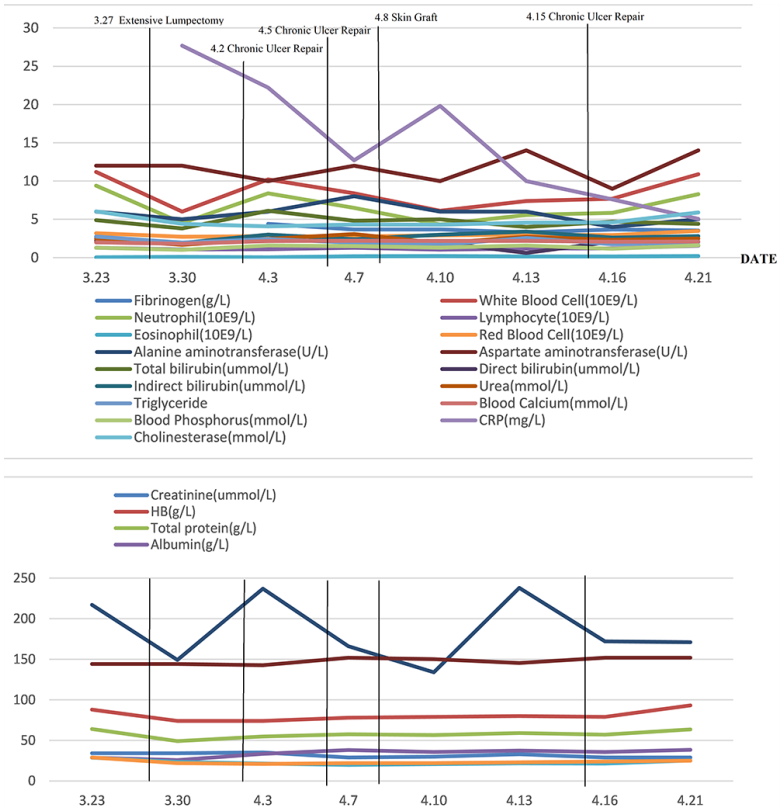

Figure S3. Changes in abnormal test parameters in patients during hospitalization.

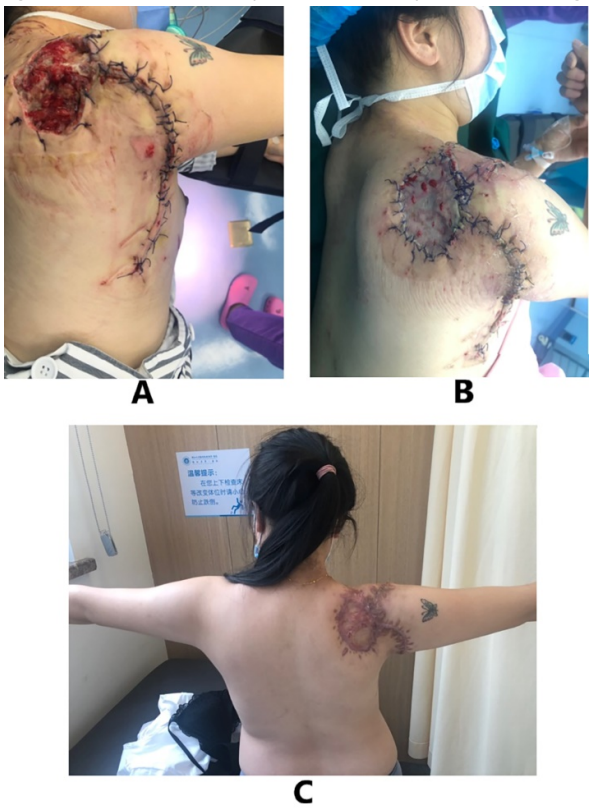

Figure S4. The appearance of wound. (A) Wound surface after initial suture. (B) Wound

surface after skin graft. (C) One month after operation, the patient regained full shoulder function.

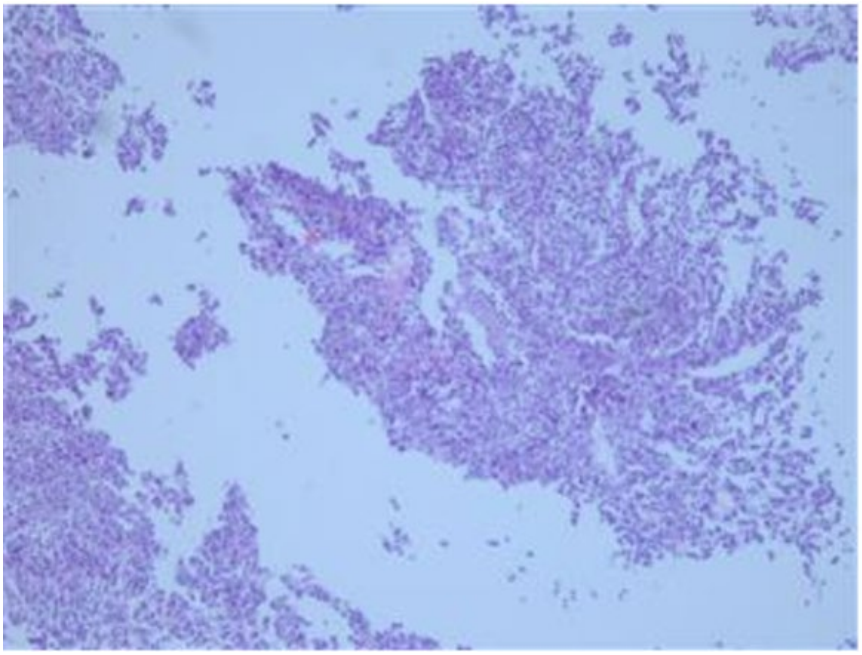

Figure S5. Pathological picture of left breast enlargement.