A Rare Case of Extrauterine Leiomyosarcoma with Metastases to the Gut and Pancreas

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Introduction

The Soft tissue sarcomas (STS) are exceptionally rare mesenchymal derived tumors accounting for only 1% of all malignancies. Leiomyosarcoma (LMS) include 5-10% of STS cases that displays heterogeneous subtype of malignant mesenchymal tumor originated from smooth muscle tissues [1]. The LMS Commonly diagnosed in the fifth and sixth decades of life, and it can be detected every anatomic site, including the uterus, retroperitoneum, extremities, and vasculature [2]. The two primary categories of LMS contains uterine LMS (uLMS) and extrauterine (euLMS) types, the first is commonest subtype of uterine sarcoma, while metastatic euLMS are not well described in terms of treatment, outcomes and prognostic factors[3]. The treatment of this tumor is controversial. However, regardless the site of origin, surgical resection is cornerstone treatment for localized LMS [2,4]. The standard surgical procedure includes a complete excision with wide negative margins that gives the best chance of cure [2]. Pelvic external beam radiation therapy with or without brachytherapy are recommended for locally resected tumors, especially for advance metastatic disease, chemotherapy considered as an option[2,4]. In the euLMS is not clear that the choice of specific agent or sensitivity to first-line systemic therapy affects the response rate and clinical outcomes [5].

The molecular heterogeneity of leiomyosarcoma is uknown also targeted therapy not available now, detection of different molecular subtypes is urgent to weigh novel therapeutic options. Two diagnostic immunohistochemical markers newly detected in formalin-fixed, paraffin-embedded tissues; are LMOD1 (Leiomodin 1) in subtype I and ARL4C (ADP-ribosylation factor-like protein 4C) in subtype II leiomyosarcoma [6,7]. Acording leiomyosarcoma tissue microarray and considering clinical outcome, specified that subtype I leiomyosarcoma is associated with good outcome in extrauterine leiomyosarcoma nonetheless, subtype II is related to poor prognosis in uterine and extrauterine leiomyosarcoma [7].

Due to rarity and few confirmed cases reported in the literature, this case report presents a young female patient with euLMS, invading the ovary, uterus, small intestine, sigmoid colon, rectum, omentum and pancreas, which were treated with radical surgery and adjuvant chemotherapy.

Case history

A 34-year-old female that referred to a gynecologist in Mashhad, Iran in December 2022, with the chief complaint of hypogastric pain lasting more than 1 year which was firstly diagnosed as Pelvic inflammatory disease (PID). The initial trans-vaginal ultrasound revealed heterogeneous right adnexal mass with irregular margin measuring 3.1 × 6.3 cm in size and multi nodular small size mass on the right side of Culdesac. Abdominopelvic computed tomography (CT) scan in April 2023 illustrated solid masses in the pancreatic head (Figure 1A) and small intestine wall (Figure 1B) also solid cystic complex mass on the right side of pelvis, measuring 3 x 6 cm in size in the right parametrial space that extended and attached to right ovary (Figure 2A,B). Tumor marker CA125, CEA, CA19-9, βhCG and LDH were normal. Abdominopelvic sonography

revealed normal abdominal viscera with a fluid-filled folded and tubular liquid right adnexal lesion measuring 2.9 × 6.7 cm suggesting long term lasting pyosalpinx. The abdominal pain had progressively worsened and she was referred for colonoscopy and endoscopy evaluation that revealed normal results. The patient was a candidate for diagnostic laparascopy in December 2023 since persistent abdominal pain, multiple smooth muscle-like nodules suggesting diffuse peritoneal lyomayomatosis was seen during operation, biopsies from omental lesions were obtained and referred to pathology, and the microscopic pathology findings confirmed myoma.

Methods

Due to severe abdominal pain the patient referred to us as gynecologic oncology specialists, then in November 2023, she was subjected to open laparotomy. We detected multi nodular solid mass on laparotomy that involved intestinal wall, omentum (figure 3A), small intestine especially near the ileocecal junction, appendix, recto-sigmoid region and pancreas. The general surgeon excised omentom then sample was sent to frozen section and histological analysis. High grade metastatic sarcoma was reported. A total hysterectomy with bilateral salpingo-oophorectomy, pelvic tumor resection and appendectomy were performed; also the celiac plexus blocked, then samples referred to pathology assessments (Figure 3), tissues specimens included the uterus, fallopian tubes, the vermiform appendix, peritoneal fluid sample and multiple lesions on the bowel. Pathology report confirmed high grade sarcoma on surface of right ovary, appendix, and isolated mass from the gut, also abdominal fluid suggesting malignant peritoneal effusion. The Hematoxylin-Eosin (H&E) staining of samples revealed cell proliferation, strong intensity nuclear staining, and evident nuclear atypia (Figure 3B,C). In the histopathology report of the hysterectomy specimen, no obvious abnormalities of uterine wall and endometrium reported. Immunohistochemical analysis showed positive result for smooth muscle desmin (Figure 3D) but negative for CD117, CK7, CDX2 and Caldesmon. Weakly positive immune reaction for Actin and CK also reported.

Outcome and follow-up

Postoperatively, the patient was discharged 3 days after surgery with significant reduction in the abdominal pain. After 3 weeks, our patient received the first Docetaxel plus Gemcitabin chemotherapy cycle and continued for 4 cycles until now.

Discussion

Considering that the definitive treatment of metastatic euLMS, as a curative method, is still unknown and the rarity of these cases, there is urgent to provide such case reports [5]. The Surgical resection of primary tumors that performed in more than 80% of all metastatic euLMS doesn't seem to prolong their survival[2]. To reach the acceptable survival time, surgical resection of primary tumors and metastasectomy should be considered, based on the decision of multidisciplinary team during and after surgery, our case underwent surgical resection of metastatic tumors and adjuvant gemcitabine plus docetaxel chemotherapy started as soon as possible regarding the extent of the invasion.

Prognostic factors in metastatic extrauterine LMS (euLMS) are not completely explained, and it is not fully known that the choice of systemic therapy agent influence response rate [2,9]. A large-scale retrospective study evaluated the association of clinicopathologic factors, first-line systemic therapy agent, and objective response with overall survival since metastasis in patients with advanced euLMS, they reported that younger age, female sex, smaller primary tumor size (<10 cm), and less than two sites of metastasis at the onset of advanced disease were independent predictors associated with better outcome [5].

Various chemotherapy regimens used in metastatic euLMS, include: doxorubicin, doxorubicin plus ifosfamide, gemcitabine plus docetaxel, pazopanib, eribulin and trabectedin. in addition, the number of chemotherapy cycle in these patients was in the range of 1 to 5 [10]. We used docetaxel plus gemcitabin chemotherapy regimen and continued for 4 cycles.

The most common sites of uLMS metastasis include, lung (74%), peritoneum (41%), Bones (33%) and liver (27%), however pancreas and gut (less than 1%) are uncommon metastatic sites[11,12,13]. In the present

case, omentum, small intestine, recto-sigmoid colon, vermiform appendix and pancreas were under invasion. Based on a cohort study, patients with objective response to the first systemic treatment had better overall survival than cases with stable or primary progressive disease, therefore it is important to choose the best therapies which may be useful for patients with advanced euLMS[5]. A particular regimen cannot be found equally effective in all patients, the metastatic euLMS patients needs a multidisciplinary approach to select best therapies that may be beneficial for them.

more extensive investigations are needed to understand genetic and epigenetic factors influencing response rate of euLMS to chemotherapy regimen [14,15]. The heterogeneity in molecular and immunological properties of euLMS also impact on clinical outcomes, there is a need to personalize treatment strategies to help agent sensitivity and longevity of patients with advanced disease[5,16,17].

Conclusion

We reported a case of metastatic euLMS with uncommon metastatic sites, pancreas and gut. The metastatic tumors surgically resected then adjuvant gemcitabine plus docetaxel chemotherapy was applied for this patient, given the rarity of such patients and lack of guidelines for oncological therapy of such cases, we suggest that multimodal therapy, by a multidisciplinary team, is essential to achieve an optimal outcome.

Ethical Approval

This study has been performed according to the declaration of Mashhad University of Medical Sciences.

Consent

Written consent was obtained from the patient.

Author Contribution

Dr. Malihe HasanzadeMofrad: Patient care, methodology; valdation; review and editing. **Dr. Mojde Pajokh:**Validation**;** writing**-** original draft review and editing.**Dr. Elham Sharafkhani** : Methodology; Validation; review and editing.

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