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The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

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Shedding light on pancreatic metastasis of clear cell sarcoma: An exceptional journey

Preeti Kumari Chaudhary, Soochong Kim

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Abstract

This editorial comments on the study by Liu *et al* investigating pancreatic metastasis of clear cell sarcoma (CCS) published in the *World Journal of Clinical Cases*. CCS is a rare and aggressive melanocytic tumor, that typically arises from tendons and aponeuroses of the limbs, and metastasizes to the lungs, bones, and brain. However, pancreatic metastasis has rarely been reported, presenting unique diagnostic and therapeutic challenges. Elucidating the clinical characteristics, imaging features, prognostic factors, and treatment outcomes of patients with pancreatic CCS metastasis is crucial. Surgery remains an effective management strategy for CCS. However, the high recurrence rate and low effectiveness of traditional adjuvant treatments necessitate a shift towards more personalized and targeted treatment plans. Research is needed to investigate and validate novel therapeutic approaches specifically tailored to the distinct genetic and molecular characteristics of rare malignancies like CCS. Additionally, the development of late metastases after a long disease-free interval is common in CCS patients. Therefore, routine postoperative surveillance for metastasis using computed tomography, magnetic resonance imaging, bone scans, and positron emission tomography scans is crucial. Moving forward, enhanced collaboration, investigation, and creative thinking among scientists, medical professionals, and legislators are essential to gain a deeper understanding of these rare presentations.

Key Words: Clear cell sarcoma; Pancreas; Metastasis; Diagnosis; Treatment

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Core Tip: Due to the extreme rarity of pancreatic metastasis of clear cell sarcoma (CCS), drawing definitive conclusions about its clinical courses, diagnosis, prognostic factors, and optimal treatment is challenging. Nevertheless, for individuals with a history of CCS, routine postoperative follow-up using computed tomography, magnetic resonance imaging, bone scans, and possibly positron emission tomography scans remains crucial for effective treatment.

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INTRODUCTION

Clear cell sarcoma (CCS) is a rare and aggressive form of cancer that primarily affects deep soft tissues. It has also been referred to as CCS of the tendons and aponeuroses or malignant melanoma of the soft parts and has distinctive clinical, histological, molecular, and genetic characteristics from other soft tissue sarcomas and malignant melanomas[1-3]. Notably, metastasis to the pancreas is rarely reported in the medical literature, presenting unique diagnostic and therapeutic challenges[4].

The prevalence of soft tissue sarcomas is low across the globe. Young adults in their twenties to forties are the most common age group affected with no specific gender preference. These cancers typically affect the extremities, especially the hands and feet, and are frequently found in association with tendons, aponeuroses, and fasciae.

The distinct genetic marker that distinguishes the tumor is the translocation t(12; 22)(q13; q12) in the neural spine, which results in the fusion of the *ATF1* gene on chromosome 12 with the *EWSR1* gene on chromosome 22[5]. This fusion gene is thought to be a distinguishing feature of CCS and plays a critical role in the disease pathophysiology by promoting the transcription of cancer-causing genes. Despite exhibiting melanocytic development, as evidenced by the expression of melanoma-associated antigens and melanin synthesis in some cases, CCS is genetically distinct from cutaneous malignant melanoma.

Histologically, CCS is characterized by nests or fascicles of homogeneous, polygonal to spindle-shaped cells embedded within a fibrous stroma. These cells exhibit cytoplasm that ranges from clear to eosinophilic and have oval vesicular nuclei with characteristic prominent nucleoli. Patches of necrosis and multinucleated large cells are observed. The tumor cells' melanocytic origin is supported by immunohistochemical expression of the S-100 protein and melanoma-specific markers including HMB-45 and Melan-A. However, pathologists must pay particular attention to differentiating these tumors from melanoma through the correlation of clinical, histological, immunophenotypical, and molecular genetic studies, which could be a significant diagnostic challenge[6,7].

CCS typically has a poor prognosis due to its high rate of local recurrence and aggressive distant metastases, most frequently affecting the lungs, followed by the lymph nodes, bones, and brain. Preoperative assessments using imaging techniques such as computed tomography (CT), magnetic resonance imaging (MRI), or positron emission tomography (PET) scans in conjunction with the patient's medical history can aid in determining the location and extent of tumor invasion[8]. The preferred course of treatment for advanced CCS is wide surgical excision with negative margins, often combined with adjuvant chemotherapy or radiation therapy, followed by long-term follow-up[3,9-11]. While the effectiveness of chemotherapy remains controversial, further studies are required to provide tailored treatments based on the specific molecular traits of each CCS patients[12-17].

PANCREATIC METASTASIS OF CCS: AN EXCEPTIONAL JOURNEY

CCS rarely metastasizes to the gastrointestinal tract, with pancreatic involvement being even less frequent[4,18]. Gastrointestinal CCS is prevalent in the walls of the small intestine, stomach, colon, or peritoneum without any symptoms or may manifest symptoms like abdominal pain, intestinal obstruction, anemia, nausea, and vomiting[19,20].

In the recent issue of the *World Journal of Clinical Cases*, Liu *et al*[21] published an interesting paper on rare pancreatic metastatic CCS that sheds light on the imaging and histological features, and treatment outcomes of a 47-year-old man presenting with abdominal pain and diarrhea[21]. This case report skillfully handles the difficulties associated with pancreatic metastasis of CCS by utilizing cutting-edge imaging methods, CT and MRI, and meticulous histological analysis to successfully identify the true nature of the malignancy. The authors have provided details of the clinical manifestations, imaging features, and histopathological characteristics of a patient with metastatic CCS of the pancreas. This journey of diagnosis not only confirms the critical role of technology in contemporary medicine but also emphasizes the need for a multidisciplinary approach to unravel the mysteries of uncommon cancers. This case also highlights the need for tailored treatment strategies for atypical presentations or locations of CCS. The effectiveness of the surgical procedure, which included a distal pancreatectomy and splenectomy without any complications or discomfort until the six-month postoperative follow-up as described in this case, is evidence of the accuracy and creativity of modern surgical oncology. After the initial procedure, there was no regular follow-up or re-examination, which allowed the CCS to spread to the pancreas. The case of delayed diagnosis resulting from neglectful follow-up emphasizes the importance of close

monitoring for individuals with a history of CCS. Therefore, the most important takeaway from this example may be how crucial it is to have routine postoperative follow-up for metastasis by CT, MRI, bone scans, and possibly PET.

In addition to the research on pancreatic metastasis of CCS published by Liu *et al*[21] two additional cases of primary pancreatic CCS have been documented before[4,22]. Very recently, in a study by Xiang *et al*[4,22] a 54-year-old woman with epigastric pain also failed to reveal any discernible abnormalities by serum tumor markers. However, CT imaging revealed a heterogeneously enhanced mass with calcification, measuring 3.5 cm × 3.8 cm within the pancreatic body[22]. Equipped with the findings of a CT-guided biopsy, the diagnosis deviated into an unknown territory: The primary CCS of the pancreas. The patient received targeted therapy (anlotinib, liposomal doxorubicin, and cisplatin chemotherapy) to deliberately stop cancer progression. However, a dismal image of an enlarging pancreatic lesion and multiplying liver metastases was presented on a six-month follow-up CT scan, demonstrating the aggressive nature of primary pancreatic CCS. Likewise, a study by Huang *et al*[4] unfolded a case of a 36-year-old man who presented with jaundice, signaling the beginning of a journey through the difficulties associated with both identifying and treating pancreatic CCS[4]. Preoperative abdominal CT imaging showed an enlarged pancreatic duct and a low-density lesion within the pancreas. This ambiguous presentation resulted in ambiguity and diagnostic uncertainty. After surgery, a tumor that was histologically and immunohistochemically consistent with CCS was discovered, highlighting the pancreas as a new front in the fight against this cancer. The diagnosis is further solidified by the identification of the EWSR1 gene translocation by fluorescence in situ hybridization, which offers molecular validation for this atypical presentation.

The presence of CCS in the pancreas fosters a conversation that crosses the boundaries of molecular genetics, pathology, and oncology. The aggressive clinical course, propensity for metastasis, and rarity of gastrointestinal CCS present a dismal picture of the prognosis and emphasize the critical need for prompt, precise identification. Research on pancreatic metastatic CCS not only contributes to our understanding of the clinical and pathological spectrum of the disease but also serves as a wake-up call for the medical community. These findings call on scientists, medical professionals, and legislators to unite in support of more cooperation, investigation, and creativity in the field of uncommon malignancies. The authors emphasized the value of global rare cancer registries and databases in promoting cross-border knowledge and experience exchange. By working together, we can better comprehend these uncommon entities more quickly, which can lead to more creative treatments and eventually better patient results.

CLINICAL IMPLICATIONS

CCS metastases to the pancreas have important clinical implications that influence patient prognosis, therapeutic choices, possible complications, and patient management. Because CCSs seldom metastasize to the pancreas and its symptoms are ambiguous, they can confuse patients with primary pancreatic illnesses or other metastatic tumors, making the initial diagnosis more difficult. Although typical for CCS, the functions of radiation and chemotherapy must be customized according to the patient's state, the extent of metastasis, and the possible impact on quality of life. When CCS spreads to the pancreas, it indicates an advanced stage of the disease, which is typically linked to a worse prognosis and fewer treatment options, thus emphasizing the necessity for early detection, aggressive and focused treatment approaches, palliative care choices and psychosocial support due to the likelihood of additional metastasis or recurrence. Further advancements in CCS management and understanding of its metastatic patterns rely heavily on ongoing research and patient participation in clinical trials.

CONCLUSION

CCS presents as a deep-seated, slow-growing tumor often associated with tendons or aponeuroses. Because of its uncommon nature, intricate genetic makeup, and aggressive nature, CCS is still a difficult and mysterious disease. While many patients remain asymptomatic in the early stages, some may experience pain or discomfort. Therefore, a sufficient understanding of the molecular foundations of this disease and possible targets for treatment, overall disease burden, and operability are essential to improve patient outcomes and management. A multidisciplinary approach is crucial for accurate diagnosis, which calls for a high index of suspicion, thorough imaging examinations, and histological analysis of biopsy samples. Clinical trials investigating new therapeutic compounds or combinations may be appropriate for patients with uncommon metastatic presentations, such as CCS to the pancreas, potentially improving their prognosis. Additionally, it is important to have a proactive and ongoing relationship with survivors to ensure early detection of metastases or recurrences, which is essential for modifying the trajectory of this difficult disease.

To conclude, the rarity of CCS makes it difficult to draw conclusive statements regarding its clinical behavior, prognostic factors, and ideal treatment. This work not only contributes to the limited literature on pancreatic metastases of CCS, but also highlights how CCS can invade and manifest in atypical locations such as the pancreas, posing diagnostic and treatment challenges. The importance of continuous information gathering in the case of uncommon diseases is emphasized.

FOOTNOTES

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