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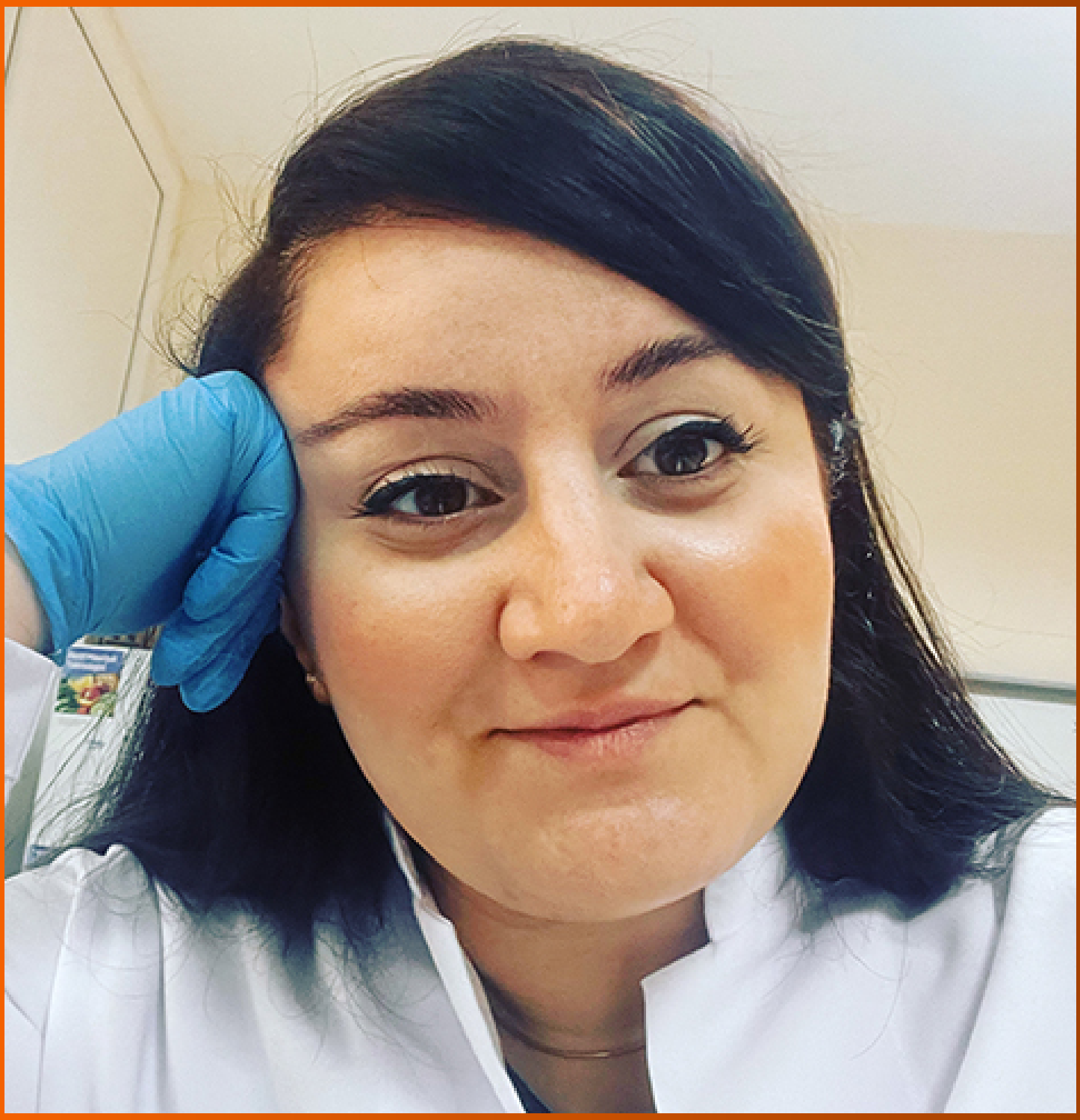

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Contents

Thrice Monthly Volume 12 Number 29 October 16, 2024

EDITORIAL

6250 Post competency training in standardized training of resident physicians and integrated postgraduates

Zeng Y, Yang J, Zhang JW

6255 Solid pancreatic masses: What's hidden beneath? Insights into rare pancreatic lesions

Balaban DV

6258 Medical imaging for the diagnosis, recurrence and metastasis evaluation of clear cell sarcoma

Wang WJ, Wang X, Hui DM, Feng JB, Li CM

6262 Metastatic clear cell sarcoma of the pancreas: An overview

Ait Addi R

6266 Advancing the predictive accuracy of PNTML in rectal prolapse: An ongoing quest

Meng J, Wang ZG, Zhang LM, Chen DY, Wang Y, Bai HX, Ji CC, Liu DL, Zhao XF, Liu Y, Li BY, Wang L, Wang TF, Yu WG, Yin ZT

6271 Challenges in integrating traditional Chinese medicine and gut microbiota research for insomnia treatment

Bilal M, Nashwan AJ

ORIGINAL ARTICLE

Observational Study

6275 Quran memorisation and heart rate variability: How do they correlate?

Ghazali AR, Abd Warif NM, A Yazit NA, Juliana N, Ishak I, Ibrahim FW, Mat Ludin AF, Harun D, Abd Rahman S, Che Wan Mohd Rozali WNA

SYSTEMATIC REVIEWS

6285 Spectrum of delayed post-hypoxic leukoencephalopathy syndrome: A systematic review

Srichawla BS, Garcia-Dominguez MA

CASE REPORT

6302 Recurrent acute pancreatitis as an initial presentation of primary hyperparathyroidism: A case report

Karim MM, Raza H, Parkash O

6307 Combination treatment with telitacicept, mycophenolate mofetil and glucocorticoids for immunoglobulin A nephropathy: A case report

Shen Y, Yuan J, Chen S, Zhang YF, Yin L, Hong Q, Zha Y

6314 Ruptured venous aneurysm associated with a dural arteriovenous fistula: Two case reports

Kim YS, Yoon W, Baek BH, Kim SK, Joo SP, Kim TS

6320 Novel procedure for hepatic venous outflow block after liver resection: A case report

Higashi H, Abe Y, Abe K, Nakano Y, Tanaka M, Hori S, Hasegawa Y, Yagi H, Kitago M, Kitagawa Y

6327 Comprehensive interventions for adult cyclic vomiting syndrome complicated by superior mesenteric artery syndrome: A case report

Liu B, Sun H, Liu Y, Yuan ML, Zhu HR, Zhang W

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Thrice Monthly Volume 12 Number 29 October 16, 2024

Contents

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EDITORIAL

Metastatic clear cell sarcoma of the pancreas: An overview

Rachid Ait Addi

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Abstract

Clear cell sarcoma (CCS) is a rare soft-tissue sarcoma that accounts for less than 1% of all cases and was originally reported in 1965. The incidence of CCS is estimated to be approximately 0.014/100000 depending on the surveillance, epidemiology and end results databases. CCS is a highly invasive type that mainly metastasizes to the lungs, followed by the bones and brain; however, pancreatic metastasis is relatively rare. It has a high probability of recurrence or metastasis and has a poor prognosis with a high mortality rate. Finally, even after recovery, it is fundamental to keep regular postoperative follow-up for CCS patients.

Key Words: Clear cell sarcoma; Pancreas; Metastasis; Follow-up; Case report

Core Tip: In this editorial, we comment on a case report by Liu *et al*. According to the authors of this article, the objective of presenting this case was to bring to attention of metastatic clear cell sarcoma (CCS) of the pancreas. CCS is an uncommon soft-tissue sarcoma, making up less than 1% of all cases, and was first documented in 1965. The estimated incidence of CCS is around 0.014 per 100000 individuals, varying based on data from surveillance, epidemiology, and end results databases.

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INTRODUCTION

In this editorial we comment on the article by Liu *et al*[1]. The authors of this article aimed to highlight metastatic clear cell sarcoma (CCS) of the pancreas by presenting this case[1]. CCS is an uncommon soft-tissue sarcoma, making up fewer than 1% of all cases, and was first documented in 1965[2,3]. The estimated incidence of CCS is around 0.014 *per* 100000 individuals, varying based on data from observation, disease monitoring, and outcome databases[4].

CLINICAL FEATURES OF METASTATIC CCS OF THE PANCREAS

CCS comes from the tendon and aponeurosis, displaying a distinctive feature of locally invasive growth into the tendon and surrounding soft tissues[5]. CCS is an extensively invasive type, with primary metastasis often occurring in the lungs, then the bones and brain; although, metastasis to the pancreas is comparatively uncommon[4-9]. In the Liu *et al*'s study, it is about a 47-year-old male was diagnosed with metastatic CCS of the pancreas and subsequently underwent surgery for pancreatic metastases[1]. The patient had a smooth recovery after surgery with no complications and remained free of discomfort until the last follow-up at 6 months post-operation, declining further therapy or examinations. The study of Huang *et al*[10] reported the first case of CCS in the pancreas of the literature. This case illustrates the pancreas as a possible location for primary CCS of soft tissues, highlighting the pivotal role of cytogenetics and/or molecular techniques in the diagnosis[11].

Additionally, the most frequent primary tumor to metastasize to the pancreas is renal cell carcinoma[12,13]. Colorectal cancer, melanoma, breast cancer, lung cancer, and sarcoma are among the other common tumors that can metastasize to the pancreas[12]. The presence of metastatic sarcoma in the pancreas can pose challenges in diagnosis and treatment, given its uncommon occurrence and the challenge of distinguishing between primary and metastatic tumors based on radiological features, particularly in cases of solitary masses[14,15]. Also, tumors found in the body or tail of the pancreas frequently do not cause any symptoms[15,16]. In the Liu *et al*'s study, no irregularities were detected during physical examination and the tumor was discovered through an abdominal computed tomography (CT) scan[1]. Likewise, the study of Sun *et al*[17] had found no abnormal findings on physical examination. However, Lee *et al*[18] found epigastric area tenderness on physical examination and Dhillon[19] found a mass on the left hand with tenderness, limited range of motion, and adenopathy in the left armpit.

DIAGNOSIS OF METASTATIC CCS OF THE PANCREAS BASED ON GENETIC ANALYSIS

Genetic analysis for detecting the Kirsten rat sarcoma viral oncogene (*KRAS*) mutations in the identification of metastatic CCS of the pancreas is very helpful. The *KRAS* gene encodes the *KRAS* protein, which is the most frequently altered protein in solid tumors, highlighting the importance of effective targeting.

Cancer-causing mutations in *KRAS* usually take place at specific hotspots, with 95% of mutations found in codons 12, 13, and 61[20]. In pancreatic cancer, the most frequent mutations happen at codon 12, where a single amino acid missense mutation results in glycine being replaced by aspartate (*G12D* approximately 40%), valine (*G12V* approximately 29%), arginine (*G12R* approximately 15%), or cysteine (*G12C* approximately 1%)[21].

Less frequent mutations include those at G13 and Q61. The *KRASQ61H* mutation may happen in 5% of cancer affecting the pancreas cases and is linked to reduced mortality. Nonetheless, the *KRASG12D* mutation is linked to poorer outcomes [22].

TREATMENT AND PROGNOSIS OF METASTATIC CCS OF THE PANCREAS

Therapeutic strategies can significantly differ between primary pancreatic cancer and metastatic sarcoma[15,23-26]. Extended survival following surgery for isolated or resectable pancreatic metastatic sarcoma has been documented[25, 26]. Pancreatic carcinoma carries a high mortality rate because it typically remains asymptomatic until reaching an advanced stage. Thus, precise diagnosis and early detection are crucial Kim *et al*[27] and Lüttges *et al*[28] classified clear cell carcinoma as tumors where the clear cells comprise more than 75%, 90%, and 95% of the tumor cells, respectively[29]. The diagnostic criteria for clear cell carcinoma of the pancreas, particularly regarding the proportion of clear tumor cell components, have varied among previous studies. Clear criteria for defining clear cell carcinoma of the pancreas have not been established yet[30]. In pancreatic ductal carcinoma, *MUC-1*, as well as cytokeratins 7, 8, 18, and 19, are overexpressed, showing predominantly membranous staining with a variable cytoplasmic pattern[31].

CCS carries a bleak prognosis, with conventional postoperative treatments such as chemotherapy and radiotherapy proving to be inadequate. While targeted therapy or immunotherapy shows promise in certain studies, there is a lack of definitive clinical trials to confirm their efficacy[30]. Even with optimal management of local disease, CCS has a high likelihood of recurrence or metastasis. By stages III and IV, the 5-year survival rate decreases significantly to 15%-35% [31]. Patients with CCS require long-term follow-up due to the potential emergence of new metastatic lesions over time. Effective postoperative management is crucial for detecting early metastases in CCS.

CONCLUSION

In summary, CCS is a rare type of soft tissue sarcoma, comprising fewer than 1% of all cases CCS. We may find no irregularities during physical examination and discover the tumor through abdominal CT. Genetic analysis for detecting *KRAS* mutations would help in the identification of CCS. Also, CCS has a high probability of recurrence or metastasis and has a poor prognosis with a high mortality rate. Finally, even after recovery, it is fundamental to keep regular postoperative follow-up for CCS patients.

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