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Case Report

Histiocytic sarcoma involving multiple abdominal sites: A rare case with KRAS mutation and response to ICE chemotherapy ☆

Shahad Khalid Hussein Hussein, MD, Olga Tcacenco, MD*

Department of Radiology, Aalborg University Hospital, Aalborg, North Jutland, Denmark

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ABSTRACT

Histiocytic sarcoma (HS) is a rare and aggressive malignant neoplasm from histiocytic cells. This case report describes a 52-year-old male with HS involving multiple abdominal sites, diagnosed through imaging, histopathology, and immunohistochemical analysis, which identified a KRAS mutation. The patient underwent surgical resection followed by 6 cycles of ICE chemotherapy, resulting in significant clinical improvement and reduction of tumor burden. This case highlights the clinical presentation, diagnostic challenges, and potential treatment approach for this rare malignancy.

Introduction

Histiocytic sarcoma (HS) is a rare neoplasm originating from hematopoietic cells, characterized by the morphologic and immunophenotypic features of mature histiocytes [1–6]. The definition of "histiocytic sarcoma'' was first introduced by Mathe et al. in 1970, marking the early understanding of this rare malignancy [7,8]. HS commonly occurs in extranodal sites, including the skin, soft tissue, respiratory system, gastrointestinal tract, bone marrow, spleen, and central nervous system, rather than the lymph nodes [9–13].

HS affects a wide age range, with a slight male predominance [4,14–15]. Although primarily diagnosed in adults, cases in pediatric patients have been reported [4,16]. Diagnosis is confirmed through histologic and immunophenotypic examination, revealing noncohesive neoplastic cells that are typically large and abundant of eosinophilic cytoplasm, that are surrounded by reactive inflammatory cells. These cells are immunoreactive for markers such as CD4, CD45, CD68, CD163,

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* Corresponding author.
E-mail address: Shahadalmadhaty@gmail.com (S.K.H. Hussein).

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and lysozyme, but negative for markers like CD1a, CD3, CD20, CD21, and CD30 [9,11–13,17].

Despite its rarity, an increasing number of HS cases are being recognized, even though the diagnostic criteria have become more strict to aid in better diagnosis [7–18]. HS is often highly aggressive, and there is no established standard treatment approach [1,2,4]. A recent population-based study revealed a median survival of only 6 months, with a 5-year disease-specific survival rate of 42.3% for males and 33.6% for females. Most patients present with disseminated disease, and treatment options often involve surgery, chemotherapy, or radiotherapy depending on the extent of the disease [1,2].

Here, we present a case of HS involving multiple abdominal sites, focusing on the diagnostic and therapeutic approach.

Case

A 52-year-old man, previously only diagnosed with a history of reflux, osteoarthritis of the right shoulder, chronic back pain, and Asperger's syndrome, presented with abdominal pain in the lower abdomen radiation to the pelvis, along with severe constipation. His family history included a father who passed away from lung cancer and a sister who had surgery for a gastrointestinal stromal tumor. Between January and February 2024, as symptoms worsened and reflux developed, he was referred to the gastroenterology department. Treatment with proton pump inhibitors was ineffective. Both gastroscopy and colonoscopy, but not ileocolonoscopy, were performed, and no noteworthy findings were identified.

By March 2024, the patient's abdominal pain and constipation persisted, prompting a referral for a CT scan of the thorax, abdomen, and pelvis (CT-TAP), which raised suspicion of peritoneal carcinomatosis because of extensive changes in the peritoneal fat tissue, extending into the pelvis (Fig. 1). A subsequent positron emission tomography-computed tomography (PET-CT) scan showed signs of metastasis, including FDG-avid foci in the ileum and moderate FDG uptake in the posterior pelvis (Fig. 2)

In April 2024, The patient underwent an exploratory laparoscopy, and biopsies were obtained from the peritoneum, mesentery, and pelvic wall. Changes in the tissue around the appendix were also observed, and an appendectomy was performed. Histopathological analysis revealed pleomorphic tumor cells with a mixed infiltrate of xanthomatous and histiocytic cells, along with small mature lymphocytes. Immunohistochemical studies showed tumor cells positive for CD68, CD163, and CD4, while negative for S-100 and calretinin, consistent with a diagnosis of HS. A KRAS mutation was also identified.

A follow-up PET/CT scan in late April revealed strong FDG uptake in the left tonsil and in known abdominal lesions with continued blurring in the peritoneal fat tissue. Further imaging, including cardiac MRI and brain MRI, has ruled out Erdheim-Chester disease and other abnormalities. These conditions were initially considered as differential diagnoses, but the absence of typical radiological features and the immunohistochemical profile confirmed their exclusion.

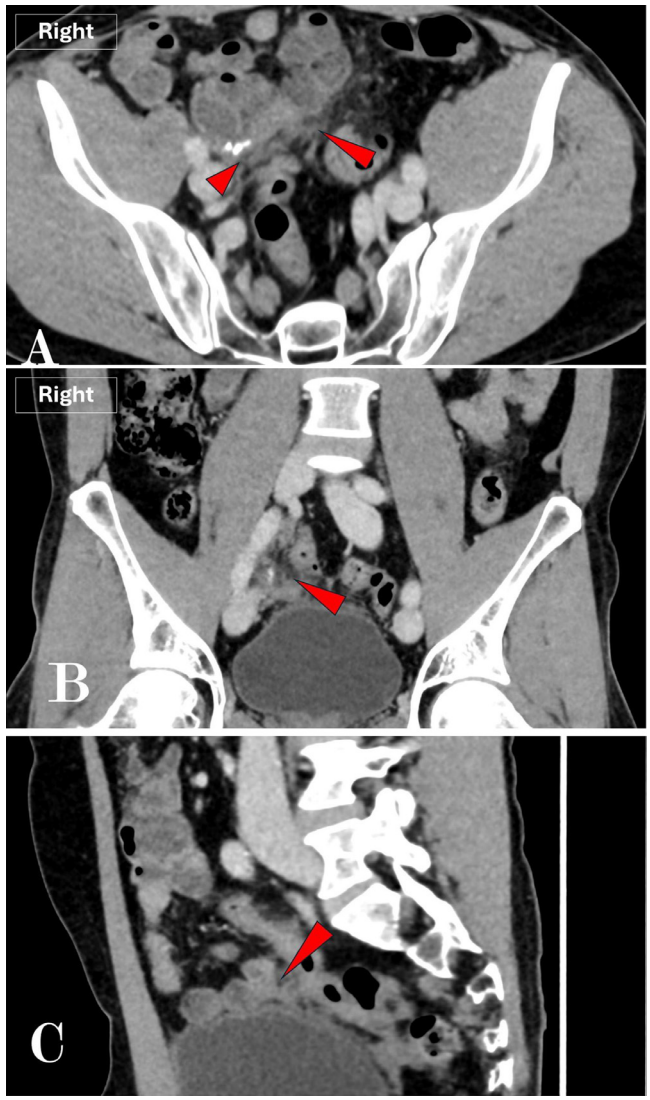

Fig. 1 – CT-TAB. (A) axial, (B and C) coronal view revealed blurring in the peritoneal fat tissue, extending into the pelvis, with a small amount of free fluid in the pelvic region, raising suspicion for peritoneal carcinomatosis (red arrowheads).

The patient commenced a treatment regimen of 6 cycles of ICE chemotherapy (ifosfamide, carboplastin and etoposide), followed by an allogeneic stem cell transplant, when a suitable donor is found. After 2 cycles, a PET-CT scan showed partial resolution of the blurring in the peritoneal fat tissue (Fig. 3). Following 6 cycles, the patient exhibited a significant improvement in both clinical condition and PET-CT findings (Fig. 4).

Discussion

Histiocytic sarcoma (HS), as classified by the World Health Organization (WHO), is a malignant neoplasm characterized by the abnormal proliferation of cells resembling mature histiocytes [1,2,5,6]. Derived from the monocytic-macrophage sys-

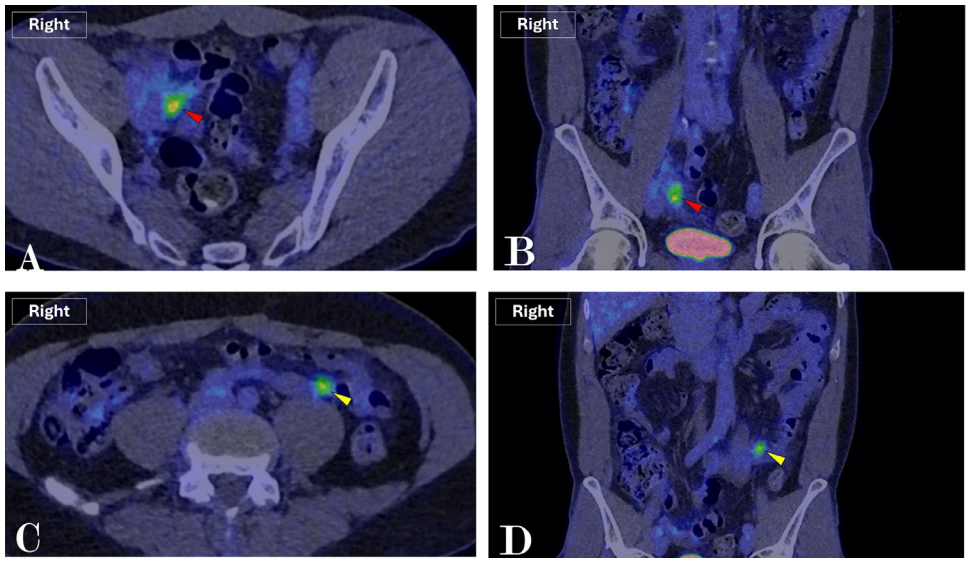

Fig. 2 – PET-CT. (A and B), showed strongly FDG-avid foci in the ileum, one with possible wall thickening (red arrowheads). Additionally, (C and D) showed free fluid with moderate FDG uptake was observed in the posterior small pelvis, along with peritoneal stranding/irregular changes without pathological FDG uptake (yellow arrowheads).

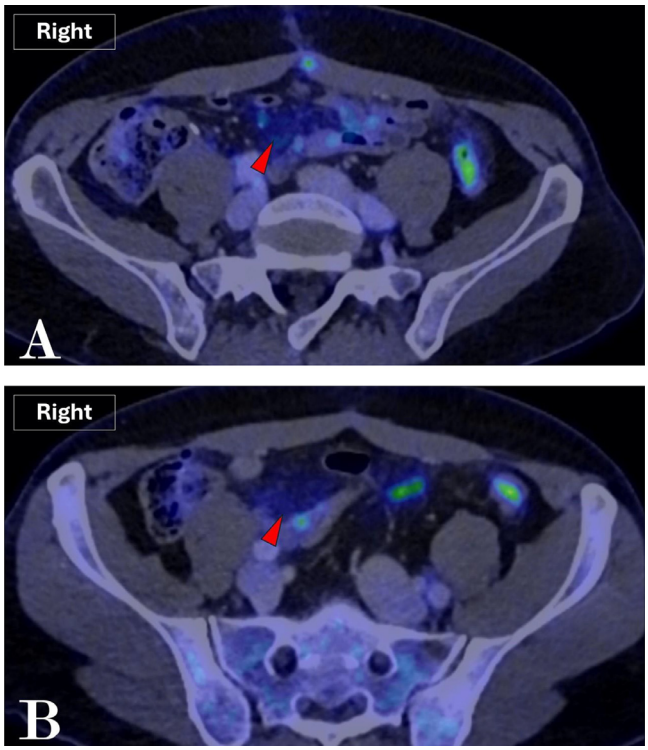

Fig. 3 – PET-CT. (A and B) after the second cycle of ICE, showing partial reduction of blurring in the peritoneal fat tissue (red arrowheads), especially on the left side of the abdomen, without pathological FDG uptake.

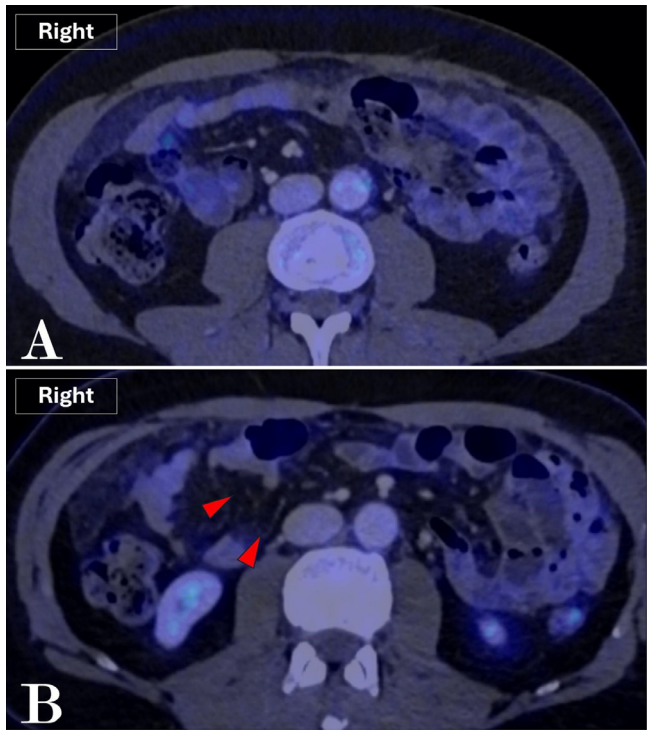

Fig. 4 – PET-CT (A and B) after 6 cycles of ICE showed persistent, slight blurring in the peritoneal fat tissue, especially on the right abdominal flank, with mild diffuse FDG uptake, (red arrowheads). No newly developed malignant lesions were identified.

tem [1,4], HS is extremely rare, with only a few hundred cases documented in medical literature [1] and accounts for less than 1% of lymph nodes or soft tissue tumors [1]. The pathogenesis remains poorly understood, but genomic studies have identified possible mutations in the RAS-MAPK and PI3K signaling pathway, including KRAS mutations, in a significant portion of cases [1].

Clinically, HS often presents as an asymptomatic mass, or with symptoms arising from compressions of nearby structures [1,5]. Systemic symptoms such as fever, night sweats, fatigue, and general weakness are also not uncommon [1,5]. Due to the rarity and nonspecific clinical presentation, HS is often misdiagnosed. Histological examination, immunohistochemistry, and radiological characteristics of HS typically involve exhibiting high metabolic activity on PET scans are crucial for accurate diagnosis, particularly in distinguishing HS from other histiocytic and nonhistiocytic neoplasms. In our case, the presence of high metabolic activity on PET scans, along with immunohistochemical staining revealing positivity for CD68, CD163, and CD4, is consistent with HS. Negative staining for markers such as CD1a and S-100 ruled out other diagnoses, including dendritic cell sarcomas and Erdheim-Chester disease.

The involvement of multiple extranodal sites, including the peritoneum and pelvic wall, mirrors previous reports of HS frequently affecting organs outside the lymphatic system, including the skin, central nervous system and gastrointestinal tract [9–13]. The gastrointestinal tract sites affected include the stomach, ileum, colon, rectum, and anus [22]. Histiocytic sarcoma in the small bowel typically appears as polypoid tumors, leading to intestinal obstruction [22]. Patients with histiocytic sarcoma have also been found to have multiple ulcerations, some of which result in fatal perforations, in the esophagus and duodenum [22]. Imaging studies, particularly PET-CT scans, played a critical role in assessing tumor spread and response to therapy. The strong FDG uptake in the ileum and left tonsil indicated aggressive metabolic activity, further supporting the diagnosis of HS.

One of the primary challenges in diagnosing HS is distinguishing it from other histiocytic or sarcoma-like conditions, particularly Erdheim-Chester disease. However, the absence of typical radiological features and immunohistochemical profile helped exclude this possibility. The presence of a KRAS mutation adds an additional layer of complexity layer, as this mutation is often implicated in other malignancies, including Erdheim-Chester disease, although its role in HS is not fully understood.

This patient responded well to ICE chemotherapy, with notable improvements in PET/CT findings after 6 cycles. Although HS has no established treatment protocol, chemotherapy regimens typically used for high-grade lymphomas or sarcomas, have shown efficacy in some cases (21). The inclusion of stem cell transplantation in the treatment plan highlights its potential role in managing this rare and aggressive malignancy, particularly in cases of younger patients or those who respond favorably to chemotherapy [19–21]. This patient's positive response to chemotherapy, with a reduction in tumor burden and improvement in clinical condition, is promising. However, long-term outcomes remain uncertain, and careful follow-up will be essential.

Conclusion

This case of HS involving multiple abdominal sites highlights the diagnostic complexity and aggressive nature of the disease. Histopathological examination, immunohistochemical profiling, and advanced imaging techniques together played a crucial role in making the diagnosis While the patient showed a good response to chemotherapy, the prognosis for HS remains poor. Further research into targeted therapies and the potential role of stem cell transplantation is essential for improving outcomes in patients with this rare malignancy.

Patient consent

Written informed consent was obtained from the patient regarding the publication of this case report, including all accompanying images.

REFERENCES

[1] Iyizoba-Ebozue Z, Burton C, Prestwich RJD. Histiocytic sarcoma of the base of tongue treated with radical radiotherapy: a case report and review of the literature. Clin Translation Radiat Oncol 2020;21(March):66–8. doi:10.1016/J.CTRO.2020.01.002.

[2] Gounder M, Desai V, Kuk D, Agaram N, Arcila M, Durham B, et al. Impact of surgery, radiation and systemic therapy on the outcomes of patients with dendritic cell and histiocytic sarcomas. Eur J Cancer 2015;51(16):2413–22. doi:10.1016/J.EJCA.2015.06.109.

[3] Cao M, Eshoa C, Schultz C, Black J, Zu Y, Chang CC. Primary Central nervous system histiocytic sarcoma with relapse to mediastinum: a case report and review of the literature. Arch Pathol Lab Med 2007;131(2):301–5. doi:10.5858/2007-131-301-PCNSHS.

[4] Hung YP, Qian X. Histiocytic sarcoma. Arch Pathol Lab Med 2020;144(5):650–4. doi:10.5858/ARPA.2018-0349-RS.

[5] Takahashi E, Nakamura S. Histiocytic sarcoma: an updated literature review based on the 2008 WHO classification. J Clin Experiment Hematopathol 2013;53(1):1–8. doi:10.3960/JSLRT.53.1.

[6] Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, et al. The 2016 revision of the World Health Organization Classification of Lymphoid Neoplasms. Blood 2016;127(20):2375–90. doi:10.1182/BLOOD-2016-01-643569.

[7] Vos JA, Susan L, Abbondanzo CL, Barekman J, Andriko AW, Miettinen M, et al. Histiocytic sarcoma: a study of five cases including the histiocyte marker CD163. Modern Pathol 2005;18(5):693–704. doi:10.1038/MODPATHOL.3800346.

[8] Mathé G, Gerard-Marchant R, Texier JL, Schlumberger JR, Berumen L, Paintrand M. The two varieties of lymphoid tissue 'reticulosarcomas' Histiocytic and histioblastic types. British J Cancer 1970;24(4):687. doi:10.1038/BJC.1970.82.

[9] Bang S, Kim Y, Chung MS, Park JS, Choi YY, Shin SJ. Primary histiocytic sarcoma presenting as a breast mass: a case report. J Breast Cancer 2019;22(3):491–6. doi:10.4048/JBC.2019.22.E32.

[10] Kommalapati A, Harsha Tella S, Durkin M, Go RS, Goyal G. Histiocytic sarcoma: a population-based analysis of incidence, demographic disparities, and long-term outcomes. Blood 2018;131(2):265–8. doi:10.1182/BLOOD-2017-10-812495.

[11] Trevisan F, Xavier CA, Pinto CAL, Cattete FG, Stock FS, Martins ML. Case report of cutaneous histiocytic sarcoma: diagnostic and therapeutic dilemmas. Anais Brasileiros de

Dermatologia 2013;88(5):807–10. doi:10.1590/ABD1806-4841.20132070.
[12] Petkova NY, Hristoskova RG, Guenova ML, Raynov JI. A rare case of primary histiocytic sarcoma of the stomach. Folia Medica 2018;60(2):318–22. doi:10.1515/FOLMED-2017-0075.
[13] May JM, Waddle MR, Miller DH, Stross WC, Kaleem TA, May BC, et al. Primary histiocytic sarcoma of the Central Nervous System: a case report with platelet derived growth factor receptor mutation and PD-L1/PD-L2 expression and literature review. Radiat Oncol 2018;13(1). doi:10.1186/S13014-018-1115-X.
[14] Hornick JL, Jaffe ES, Fletcher CDM. Extranodal histiocytic sarcoma: clinicopathologic analysis of 14 cases of a rare epithelioid malignancy. Am J Surg Pathol 2004;28(9):1133–44. doi:10.1097/01.PAS.0000131541.95394.23.
[15] Shimono J, Miyoshi H, Arakawa F, Sato K, Furuta T, Muto R, et al. Prognostic factors for histiocytic and dendritic cell neoplasms. Oncotarget 2017;8(58):98723. doi:10.18632/ONCOTARGET.21920.
[16] Venkataraman G, McClain KL, Pittaluga S, Koneti Rao V, Jaffe ES. Development of disseminated histiocytic sarcoma in a patient with autoimmune lymphoproliferative syndrome and associated Rosai-Dorfman disease. Am J Surg Pathol 2010;34(4):589–94. doi:10.1097/PAS.0B013E3181D5DDF8.
[17] Yoshida C, Takeuchi M. Histiocytic sarcoma: identification of its Histiocytic origin using immunohistochemistry. Intern Med 2008;47(3):165–9. doi:10.2169/INTERNALMEDICINE.47.0386.
[18] Arai, Eiichi WP, Daniel S, Patrick CR, Chin-Yang -Y L. Cutaneous histiocytic malignancy. Immunohistochemical re-examination of cases previously diagnosed as Cutaneous 'histiocytic lymphoma' and 'malignant histiocytosis. J Cutaneous Pathol 1993;20(2):115–20. doi:10.1111/J.1600-0560.1993.TB00226.X.
[19] Iwabuchi H, Kawashima H, Umezu H, Takachi T, Imamura M, Saitoh A, et al. Successful treatment of histiocytic sarcoma with cladribine and high-dose cytosine arabinoside in a child. Int J Hematol 2017;106(2):299–303. doi:10.1007/S12185-017-2202-8.
[20] Tomlin J, Orosco RK, Boles S, Tipps A, Wang H-Y, Husseman J, et al. Successful treatment of multifocal histiocytic sarcoma occurring after renal transplantation with cladribine, high-dose Cytarabine, G-CSF, and mitoxantrone (CLAG-M) followed by allogeneic hematopoietic stem cell transplantation. Case Rep Hematol 2015;2015:1–6. doi:10.1155/2015/728260.
[21] Tsujimura H, Miyaki T, Yamada S, Sugawara T, Ise M, Iwata S, et al. Successful treatment of histiocytic sarcoma with induction chemotherapy consisting of dose-escalated CHOP plus etoposide and upfront consolidation auto-transplantation. Int J Hematol 2014;100(5):507–10. doi:10.1007/S12185-014-1630-Y.
[22] Khan AA, Agarwal A, Chaddha SK, Gagliardi JA. Histiocytic sarcoma of the terminal ileum presenting as a large ulcerating lesion: CT diagnosis. Radiol Case Rep 2009;4(2):262. doi:10.2484/rcr.v4i2.262.