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Case Report

Abdominal distention, immunopositivity, and aggressive nature: A rare Ewing's sarcoma of the adrenal gland ☆,☆☆

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ABSTRACT

This case report describes a 32-year-old Pakistani male patient with an Ewing sarcoma (ES) of the adrenal gland. Presenting complaints were abdominal distention, pain, low-grade fever, and weight loss. Initial studies, including imaging and tumor markers, ruled out any other possible origins of the mass. A percutaneous biopsy verified the tumor's neuroendocrine origin. Extensive involvement of nearby anatomical structures was discovered through exploratory laparotomy, rendering total resection difficult. Based on the presence of malignant, round, blue cells that were positive for specific immunostaining markers, the histopathology report supported the diagnosis of an ES with a staging of T3N0M0. Chemotherapy, in accordance with the VAC-IE protocol, was administered after debulking surgery. Subsequent imaging and close monitoring revealed no metastatic or residual tumors. Adrenal ES is an uncommon, aggressive tumor that mandates prompt diagnosis and management. This case report highlights the value of early detection and multimodal therapy in enhancing patient outcomes for this rare malignancy.

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Introduction

Ewing's sarcomas (ES) are a family of rare malignant tumors composed of small, round, basophilic cells. They typically grow in the bones or soft tissues surrounding the bones but can also occur in other locations, including the thorax, abdomen, and limbs. The incidence of extraosseous ES is 0.4 per million [1]. Primary ES of the adrenal gland is a sporadic, aggressive tumor; to our knowledge, less than 40 cases have been described in the existing scientific literature [2]. Our case report is singular in describing the presentation and management of a primary adrenal ES that has extensively spread to adjacent tissues, including the inferior vena cava, lesser sac, lesser curvature of the stomach, liver, porta hepatis, and body of pancreas.

Case report

A 32-year-old Pakistani male brought to our outpatient department presented with abdominal distention associated with pain. For the past 2 months, he had experienced intermittent low-grade fever and a weight loss of 6 kilograms. The patient had no known comorbidities and insignificant past medical and surgical histories. He did not endorse any history of smoking, alcohol use, or recreational drug abuse. On physical examination, pallor was observed, and the patient seemed to be in mild discomfort. His abdomen was distended, and there was mild tenderness in the right quadrant. An abdominal examination of the patient revealed a palpable mass in the right upper quadrant measuring 20 × 15 cm. There was no palpable lymphadenopathy. The patient was advised to undergo comprehensive imaging and laboratory testing to establish a working diagnosis. Laboratory tests revealed normal levels of urine metanephrine (160 mcg/24 hours; N: 140-785 mcg/24 hours), urine dopamine (128 mcg/24 hours; N: 65-400 mcg/24 hours), blood free metanephrine (73 pg/mL; N: 0-90 pg/mL), blood free normetanephrine (118 pg/mL; N: 0-190 pg/mL), and an elevated level of urine normetanephrine (600 mcg/24 hours; N: 75-375 mcg/24 hours). Tumor markers were normal, including serum alpha-fetoprotein (3.0 ng/mL; N: 0-8 ng/mL), CA 19-9 (<2.06 U/mL; N: 0-37 U/mL), and carcinoembryonic antigen (1.97 ng/mL; N: 0-2.5 ng/mL).

A CT scan of the abdomen and pelvis revealed a large, lobulated mass measuring 24 × 16 × 23.8 cm in the epigastric region with both cystic and solid components (Figs. 1a and b). The mass was displacing the inferior vena cava and gallbladder to the right, the duodenum and pancreas posteriorly, and lifting the hepatic hilum. The right adrenal gland was not visualized separately; however, the mass was distinguishable and separate from the right kidney. After careful consideration of the imaging findings, the mass appeared to be of adrenal origin. A percutaneous biopsy was performed to identify the origin of the tumor. The biopsy report revealed that the mass was positive for synaptophysin, cytokeratin, and S-100, demonstrating the tumor's neuroendocrine origin.

Given the adrenal location of the mass, differentials were formulated considering this specific anatomical context.

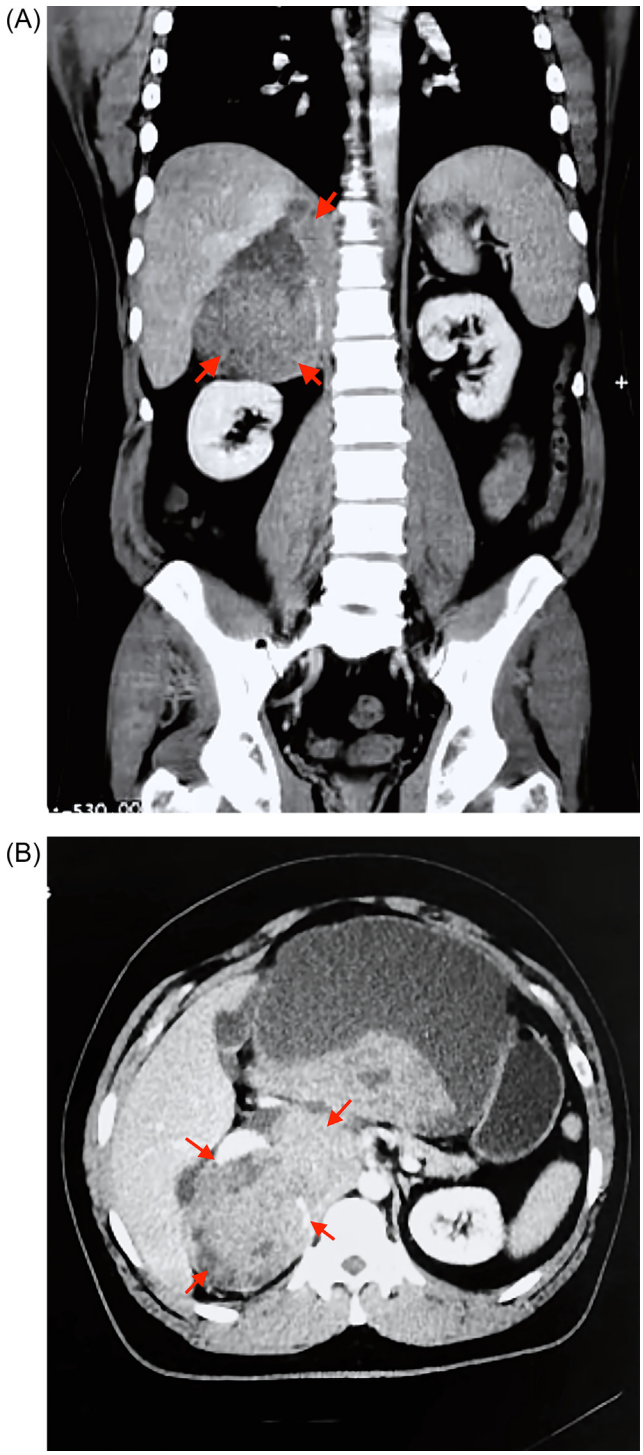

Fig. 1 – (A and B): Coronal (frontal) and axial (transverse) views of the CT scan of the patient's abdomen and pelvis disclosed a discernible left adrenal gland, while the right adrenal gland remained obscured by the mass (red arrows).

These included adrenocortical carcinoma, a tumor originating from the adrenal cortex, pheochromocytoma, a neuroendocrine tumor arising from the adrenal medulla, and Ewing sarcoma/primitive neuroectodermal tumor (PNET), which can arise from soft tissues and bones, including rare cases in the

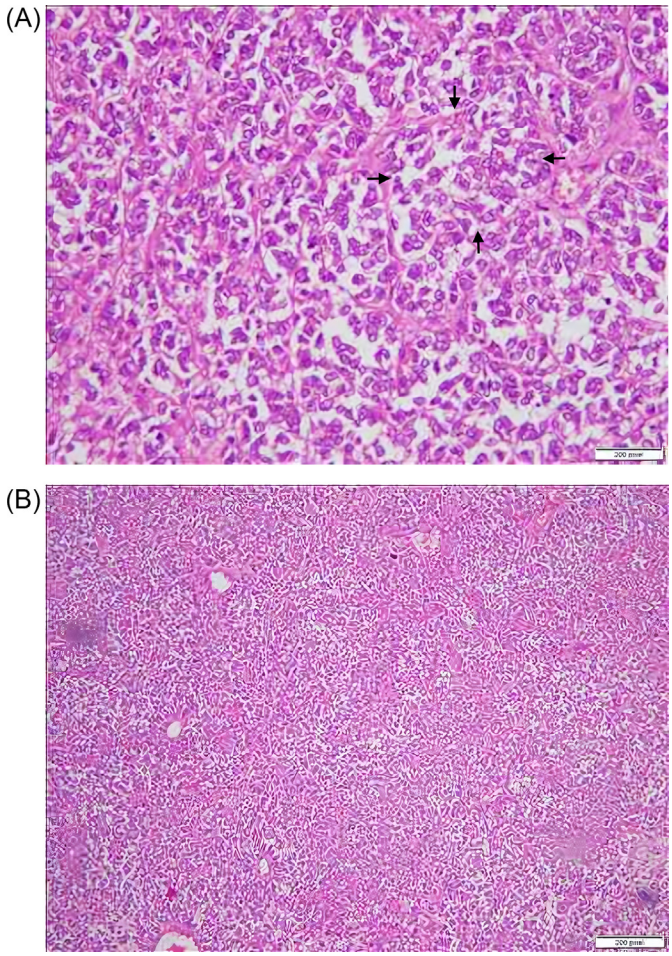

Fig. 2 – (A and B): Histopathological examination of the mass unveiled a tumor exhibiting a distinctive nesting pattern, with tumor nests (arrows) comprised of round cells characterized by prominent hyperchromatic nuclei, clear cytoplasm, and a heightened nucleus-to-cytoplasmic (N:C) ratio.

adrenal gland. Additionally, considering the neuroendocrine nature of the tumor, pancreatic neuroendocrine tumor (PanNET) was also considered. Other differentials were considered irrespective of the adrenal location, including gastrointestinal stromal tumor (GIST) and metastatic malignancy, considering the extensive involvement of adjacent structures observed on imaging.

To definitively diagnose and manage the patient, an exploratory laparotomy and resection of the tumor were scheduled. In preparation for surgery, the patient was kept nil per os (NPO) for 12 hours, and the bowel was prepared via enema. The surgery was performed under general anesthesia. On exploration, the tumor was found to be originating from the adrenal gland, and it extensively involved the stomach, liver, porta hepatis, and body of the pancreas. The tumor encased the portal vein and directly extended into the inferior vena cava. Due to the tumor's involvement of major blood vessels, it could not be resected; however, tumor debulking was performed. An excisional biopsy of the mass was performed for a detailed histopathological analysis.

The histopathology report stated the consistency of the mass as malignant, round, blue cells arranged in nests with marked hyperchromatic nuclei, clear cytoplasm, and a high nucleus-to-cytoplasmic (N:C) ratio (Figs. 2a and b). On immunostaining, the mass was positive for CD-99, FLN-1, and NKX2-2. Based on the findings, percutaneous biopsy, and histopathological analysis, a diagnosis of Ewing's sarcoma (ES) of the adrenal gland was suspected. TNM staging of the tumor was described as T3N0M0.

Upon follow-up 1 week after the surgery, a whole-body CT scan was performed to check for residual tumor mass and possible metastasis, both of which were negative. The patient was transferred to the oncology department for chemotherapy. The patient was administered chemotherapy based on the VAC-IE protocol with an initial cycle of vincristine, doxorubicin, and cyclophosphamide, followed by nine cycles of etoposide, ifosfamide, and mesna. The patient is currently undergoing the fourth cycle of chemotherapy and is being considered for radiotherapy.

Discussion

Ewing sarcoma (ES) is a rare and highly aggressive primitive neuroectodermal tumor (PNET) characterized by CD99, FLI-1,

and NKX2.2 immunopositivity as well as the t(11;22)(q24;q12) [3] translocation. While ES commonly presents in bones, primary adrenal ES is an uncommon manifestation. Only a few cases have been reported in scientific literature describing such a widespread tumor managed with adjuvant chemotherapy after debulking surgery. ES typically affects young adults with a median age of 23.4 years at presentation [4]. A few reported patients were over 50 years old at diagnosis, with the oldest reported age of 74 [5]. A retrospective analysis of 18 cases of intra-abdominal and retroperitoneal neuroectodermal tumors reported a mean tumor diameter of 7.2 cm in contrast with our case, which measures twice as big, with a maximum diameter of 24 cm [6].

The most common presentation of primary adrenal ES includes abdominal pain and swelling [4], distinguishing it from the skeletal counterparts. The aggressive nature of adrenal ES is underscored by its rapid spread and the need for immediate intervention.

The diagnosis of primary adrenal ES often begins with imaging studies, with CT scans being the modality of choice which was used in our case for initial detection, extent determination, and surgical planning. The imaging characteristics typically include a substantial necrotic heterogeneous density with both cystic and solid components. A 2017 retrospective study reporting radiological findings of 7 adrenal PNET cases reported that all cases had heterogeneous enhancement on contrast [7]. Another case series reported that contrast-enhanced CT scans demonstrated mild rim enhancement (due to cystic features) and several feeding arteries within the masses. They speculated that these imaging characteristics may indicate retroperitoneal and intra-abdominal neuroectodermal tumors [6]. Based on a literature review, only 4 other cases have demonstrated the involvement of the inferior vena cava either by direct extension or via thrombus formation [2]. In our case, the tumor's large size resulted in encasement of the portal vein, a unique feature not previously reported.

Differential considerations for adrenal masses include other neuroectodermal tumors, and imaging alone may not provide a definitive preoperative diagnosis. While calcification is uncommon, the presence of massive masses with cystic degeneration and necrosis complicates differentiation from other adrenal tumors. Immunohistochemistry, histopathology, and cytogenetic analysis are essential for an accurate diagnosis [2,8].

Histopathologically, primary adrenal ES is identified by small, round blue cells with specific nuclear features, including round to oval nuclei, coarsely stippled chromatin, indistinct nucleoli, and scant cytoplasm [8]. Our case exhibited similar histology, suggesting a neuroendocrine neoplasm. Immunohistochemistry plays a crucial role in confirming the diagnosis, with CD99, FLI-1, and NKX2.2 showing high specificity for ES. Ewing sarcoma family of tumors (ESFT) are typically diagnosed using CD99 and FLI-1; an immunohistochemical panel with at least these two markers is advised [9]. Positive results for these markers were evident on immunostaining in our case. The t(11;22)(q24;q12) translocation, which results in the fusion gene EWS-FLI1, is the most prevalent type found in 85% of ES cases. The t(21;22)(q22;q12) translocation is the second most frequent type, resulting in the production of the EWS-ERG fusion gene, and has been detected in approximately 5%-10% of cases [10]. Our patient did not undergo translocation studies due to financial limitations and a heavily resource-limited setting.

The National Comprehensive Cancer Network (NCCN) recommends local treatment (surgery and/or radiation) along with chemotherapy for ES [1]. Surgical approaches, including laparoscopic techniques, have been successful in some cases, but the extent of local spread may necessitate debulking surgery, as seen in our case [2].

The prognosis of adrenal Ewing sarcoma has been explored in a comprehensive literature review conducted by Eddaoualline et al. [4], revealing valuable insights into the clinical course of this rare malignancy. The follow-up duration for affected individuals ranged from 6 months to 5 years, with local recurrence occurring in 4 patients and metastatic recurrence in 5 patients. The median progression-free survival (PFS) periods for local and metastatic recurrences were 16 months and 7 months, respectively. Notably, metastatic recurrence predominantly involved the lungs, liver, and brain. Patients with totally resected tumors for localized ESFT had a good prognosis, even in cases of rapid local spread. Those with incomplete resection can have a poor prognosis, and such cases must be treated with radiotherapy [11]. Chemotherapy for adrenal ES mirrors the regimen used for skeletal ES involving Vincristine, Doxorubicin, and Cyclophosphamide (VAC) alternated with Ifosfamide and Etoposide (IE). Locoregional recurrence of malignancy has been previously observed in cases of ES of the adrenal gland that lacked adjuvant or neoadjuvant chemotherapy [2].

Conclusion

In conclusion, we described a rare instance of an aggressive Ewing sarcoma (ES) that originated in the adrenal gland. The tumor displayed an extensive local distribution and encased several major blood vessels. Immunostaining was positive for specific markers, which was used to confirm the working diagnosis. Debulking surgery followed by adjuvant chemotherapy was employed to treat the malignancy. This case report emphasizes the value of prompt detection, early identification, appropriate management, and a multimodal strategy for ES. To achieve better prognoses and for further research, physicians need to be aware of this aggressive malignancy and the best approach for its management.

Patient consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article (case report).

Data availability statement

Not applicable.

Authorship

all authors had access to the data and a role in writing this manuscript.

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