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Primary Ewing sarcoma of renal origin with tumor thrombus into inferior vena cava: a case report

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Abstract

Background Renal-origin Ewing's sarcoma is an extremely rare malignancy often misdiagnosed owing to its nonspecific presentation and similarities to other renal tumors. Accurate diagnosis requires a combination of clinical evaluation and advanced diagnostic techniques. Limited case reports make understanding its clinical course and management challenging. This case report aims to raise awareness of renal-origin Ewing's sarcoma, highlight diagnostic challenges, and discuss effective multidisciplinary management strategies to improve patient outcomes.

Case presentation A 32-year-old Iranian female patient presented with a chief complaint of progressive dyspnea, anorexia, and night sweating in the last 2 weeks before her admission. Computed tomography scan showed a tumoral lesion in the left kidney with thrombosis extending into the left renal vein and inferior vena cava up to the right atrium. The patient underwent open cardiac surgery and a radical nephrectomy. During surgery, the mass protruded from the inferior vena cava into the right atrium; it was ultimately diagnosed as renal-origin Ewing's sarcoma, and EWSR1 rearrangement was confirmed on pathology.

Conclusion and key clinical message This case highlights the importance of a thorough diagnostic approach in patients presenting with a renal mass and the value of a multidisciplinary strategy, combining clinical presentation, imaging, histopathology, immunohistochemistry, and molecular studies to achieve an accurate diagnosis. It underscores the critical need for increased awareness and research into the rare entity of renal-origin Ewing's sarcoma, as clinical and pathological information on this condition is limited. Furthermore, this case emphasizes the necessity of timely diagnosis and tailored management to optimize treatment outcomes and improve survival rates in such rare and challenging presentations.

Clinical trial number: not applicable.

Keywords Ewing's sarcoma, Kidney tumor, Cancer, Neuroectodermal tumor, Oncology

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Introduction

Ewing's sarcoma is a highly aggressive malignancy that primarily affects the bones and soft tissues, commonly presenting in adolescents and young adults [1]. It is most frequently found in the long bones, pelvis, and chest wall. Approximately 6% of cases are extraosseous. The most common extraosseous sites include the trunk, extremities, head and neck, and retroperitoneum [2], but its occurrence in the kidneys is exceedingly rare [3]. Renal Ewing's sarcoma (RES) accounts for less than 1% of all reported cases of Ewing's sarcoma, making it a highly unusual manifestation [4].

Owing to its rarity, renal Ewing's sarcoma often presents diagnostic challenges, as its clinical and radiological features can mimic other more common renal malignancies such as renal cell carcinoma or Wilms' tumor. Proper diagnosis relies on a combination of imaging techniques, histopathology, and molecular confirmation through genetic markers, particularly the EWSR1 gene translocation [4].

This case report aims to highlight a rare presentation of primary Ewing's sarcoma originating in the kidney. We describe the patient's clinical course, radiological findings, pathological features, and treatment approach, emphasizing the importance of early diagnosis and multidisciplinary management in improving outcomes. Given the scarcity of RES cases, this report contributes valuable insight into the clinical spectrum of Ewing's sarcoma and underscores the need for heightened awareness of this rare entity among clinicians.

Case presentation

A 32-year-old Iranian female presented to Rajaei Hospital Cardiac Center in Tehran, Iran with a chief complaint of progressive shortness of breath (dyspnea), which persisted even at rest. The patient was referred for an outpatient hematology consultation to assess for inherited coagulopathies and to further evaluate the etiology of the thromboembolic events. Initial clinical and paraclinical evaluations, including echocardiography and computed tomography (CT) angiography, were performed owing to the high clinical suspicion of pulmonary embolism; the diagnosis of pulmonary thromboembolism (PTE) was confirmed. Anticoagulation therapy with heparin was promptly initiated, and the patient was transitioned to oral rivaroxaban after stabilization. She was discharged in stable condition, with close follow-up recommendations.

Subsequently, 2 weeks later, the patient returned with worsening dyspnea accompanied by systemic symptoms, including fever, chills, night sweats, and anorexia. Abdominal ultrasonography and contrast-enhanced abdominopelvic CT scan revealed a renal mass involving the inferior vena cava (IVC) with a tumor thrombus extending into the right atrium. Given these findings, the patient was referred to the emergency general surgery department at our referral hospital for further management and surgical evaluation.

The patient had no significant past medical or family history and denied smoking, alcohol use, or illicit drug use. On presentation, her vital signs included a body temperature of 37 °C, blood pressure of 100/60 mmHg, respiratory rate of 20 breaths per minute, and a pulse rate of 110 beats per minute. Physical examination revealed a painless, palpable abdominal mass located in the right flank region without tenderness, guarding, or percussion abnormalities. No signs of hepatosplenomegaly or lymphadenopathy were detected, and other systemic examinations were unremarkable.

Diagnostic assessment and therapeutic interventions

Laboratory assessments, including complete blood count (CBC), blood biochemistry, urinalysis (UA), and arterial blood gas (ABG) analysis, yielded normal results. A summary of these findings is provided in Table 1.

The initial spiral CT scan of the lungs, mediastinum, abdomen, and pelvis with and without contrast revealed an enlarged heterogeneously enhancing solid mass located at the mid to lower pole of the left kidney, measuring 70 mm ×75 mm×105 mm with tumor thrombosis extending into the left renal vein and IVC superiorly over a craniocaudal length of ~23 cm, terminating below the right atrium. In addition, mild hypodense fluid was noted in the pelvic cavity. Pulmonary findings revealed filling defects in the right main pulmonary artery and its segmental branches, consistent with pulmonary thromboembolism and a 7 mm ground-glass nodule detected in the left lower lobe (LLL) superior segment. No signs of appendicitis, cholecystitis, pancreatitis, diverticulitis, hydronephrosis, urinary stones, gastrointestinal obstruction, or free air were observed, and major vascular structures remained open without gross pathology in other abdominal or pelvic regions (Fig. 1).

Echocardiography showed normal systolic function with an ejection fraction (EF) of 55%. There was mild to moderate tricuspid regurgitation (TR), mitral regurgitation (MR), and pulmonary insufficiency (PI), with a mean pulmonary artery pressure (PAP) of 27 mmHg and a peak instantaneous pressure gradient (PIPG) of 17 mmHg. A large, rope-like, hyperechoic mass with tissue texture was identified in the inferior vena cava (IVC), measuring 14 cm × 2.7 cm. The mass protruded from the IVC into the right atrium, highly suggestive of massive vein thrombosis.

With a possible diagnosis of renal tumor with extensive tumor thrombus into the inferior vena cava and

Table 1 Laboratory tests of the patient

Test	*Unit*	*Normal range*	*Before treatment*	*After treatment*
Blood count				
RBC	10^{12}/L	4.3–5.6	3.94	4.52
Hct	%	41–50	35	40.1
Hemoglobulin	g/dL	14–18	10.3	12
MCV	F lit	80–96	88.8	88.7
MCH	pg	27–33	26.1	26.5
MCHC	g/dL	31–36	29.4	29.9
WBC	10^{9}/L	4.4–11.3	4.7	6.3
Platelets	10^{3}/µL	150–450	236	297
Biochemistry				
CRP	mg/L	< 10 mg/L	75	10
ESR	mm/hour	< 20 mm/hour	117	12
FBS	mg/dL	70–100	82	108
BUN	mg/dL	8–20	37	38
Cr	mg/dL	0.9–1.3	0.9	0.9
Na^{+}	mmol/L	135–145	141	144
PK^{+}	mmol/L	3.5–5.0	43	3.6
Ca^{2+}	mg/dL	8.5–10.5	8.9	–
PO4	mg/dL	2.5–4.5	3.5	–
Mg^{2+}	mg/dL	1.7–2.2	1.8	–
AST	U/L	< 38	–	40
ALT	U/L	< 41	–	149
ALP	U/L	100–460	–	382
Total bilirubin	mg/dL	0.1–1.2	–	0.6
Direct bilirubin	mg/dL	< 0.3	–	0.2
Urine and blood test				
Urine culture (UC)	Qualitative	Qualitative	Negative	–
Urine analysis (UA)	Qualitative	Qualitative	Protein 1^{+} Blood 2^{+} RBC 10–12	–
Blood culture (from central vein line)	Qualitative	Qualitative	–	*Klebsiella pneumoniae*
Arterial blood gas (ABG)				
PH	mmHg	7.35–7.45	7.41	7.46
PCO2	mmHg	35–48	29.7	36.1

RBC, red blood cells; WBC, white blood cells; Hct, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; BUN, blood urea nitrogen; Na^{+}, sodium; K^{+}, potassium; Ca^{2+}, calcium; PO4, phosphate; Mg^{2+}, magnesium; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase ;FBS, fasting blood sugar]

right atrium, an open, left radical nephrectomy was performed by the urologist team, and then the cardiac surgery team performed IVC thrombectomy. During surgery, there was a huge intracardiac tumor (tumoral and fibrous in gross vision in the right atrium) that was resected, and then the IVC was evacuated from the tumor (extracardiac tumor) with cardiopulmonary bypass and abdominal exploration. The left kidney specimen, following radical nephrectomy, was preserved in formalin and submitted for pathological examination.

Macroscopic examination of the left radical nephrectomy specimen revealed a 7 cm×6.5 cm×5 cm mass in the lower pole of the kidney with extension to the renal sinus. On microscopic examination, sheet-like diffuse infiltration of small and round neoplastic cells with monomorphic nuclei, fine speckled chromatin pattern, and inconspicuous nucleoli was seen. The arrangement of the tumor cells in occasional pseudorosette-like structures was also identified (Fig. 2).

Results of immunohistochemical staining (IHC) were as follows: positive staining for NKX2.2, CD99,

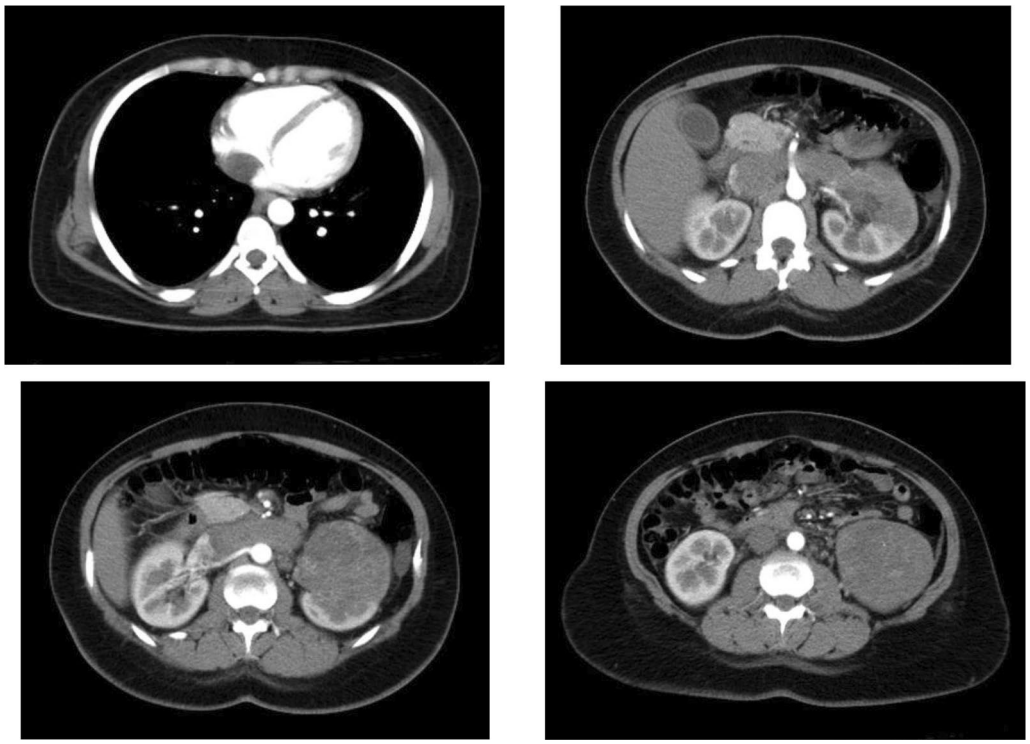

Fig. 1 Abdominal computed tomography scan

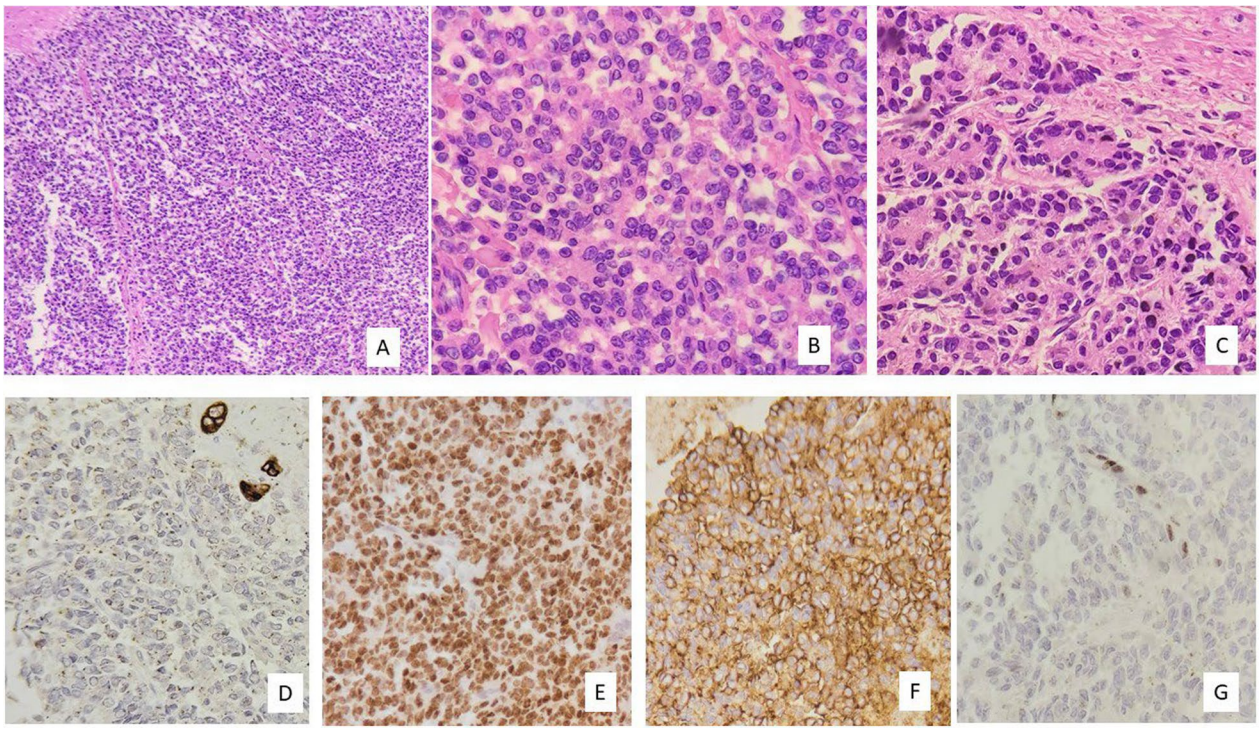

Fig. 2 Microscopic examination of hematoxilin and eosin sections shows: (**A**) sheet-like diffuse infiltration of neoplastic cells (40X); (**B**) the neoplastic cells are rather uniform with small round nuclei, inconspicuous nucleoli, scant cytoplasm, and occasional mitosis (400X); **C** scattered Homer Wright pseudorosettes are evident (400X). Immunohistochemistry study revealed (**D**) dot-like staining with CK AE1/AE3; (**E**) positive nuclear reaction with NKX2.2; (**F**) diffuse membranous staining with CD99; and (**G**) negative staining with TLE1

synaptophysin (Syn), and chromogranin; negative staining for CK7, CK20, CK, LCA, PAX8, AMACR, P63, CKA1/A3, and TLE 1; and non-diagnostic staining for Ki67. Finally, the peripheral primitive neuroectodermal tumor (PNET/Ewing sarcoma) was diagnosed with 20% tumor necrosis.

In the fluorescence in situ hybridization (FISH) study, translocation was identified at (11;22), indicating the presence of an EWSR1 gene rearrangement. This finding confirmed the final diagnosis of primitive neuroectodermal tumor (PNET) (Fig. 3).

Differential diagnosis

On the basis of the clinical and paraclinical findings, the physicians considered a differential diagnosis that included a kidney tumor with thromboembolism in the superior vena cava (SVC), extending into the right atrium.

Outcome and follow-up

The patient's postoperative course was largely uneventful, aside from some minor incisional pain, which was well managed with analgesics. She was discharged 1 week after the operation in stable condition with appropriate follow-up care. She initiated systemic chemotherapy as part of her comprehensive treatment plan 2 months postoperatively. Given the prothrombotic risk associated with both malignancy and chemotherapy, she has remained on anticoagulant therapy since her initial admission. This regimen was carefully maintained throughout her chemotherapy to minimize the risk of thrombotic complications, ensuring optimal management of her condition.

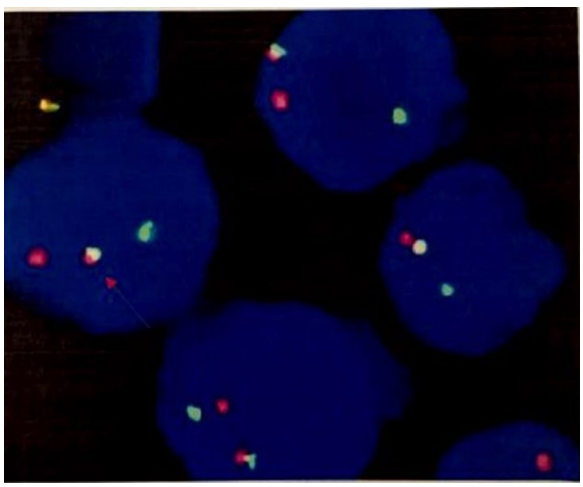

Fig. 3 EWSR1 gene translocation was detected by fluorescence in situ hybridization

Adjuvant therapy

Following surgery, the patient was initiated on interval-compressed therapy with alternating cycles of vincristine/doxorubicin/cyclophosphamide (VDC) and ifosfamide/etoposide (IE), which was administered every 14 days with hematopoietic growth factor support. Our radiation oncology team indicated that there was no need for radiotherapy. The treatment demonstrated a favorable response, and the final management plan included an autologous stem cell transplant to consolidate the response. However, after 12 weeks of therapy, some adjustments were necessary owing to significant toxicity and the onset of cytopenia. To mitigate these side effects, doxorubicin was replaced with dactinomycin, and the duration of each cycle was extended from 2 to 3 weeks to accommodate the patient's tolerance and recovery better.

Spiral CT scan

At the end of the eighth cycle of chemotherapy, 4 months later, we evaluated the patient using spiral CT. Multislice CT spiral imaging before and after oral and intravenous contrast revealed normal findings in the lungs, pleura, mediastinum, heart, chest wall, liver, pancreas, spleen, right kidney, adrenal glands, aorta, IVC, retroperitoneum, bowel loops, stomach, bladder, and pelvic organs. The left kidney was absent owing to prior nephrectomy, and no lymphadenopathy, ascites, or abnormalities in the bones were detected. A chemotherapy port was noted on the left upper chest wall. All findings were stable compared with the previous multislice CT spiral.

Discussion

The Ewing's sarcoma family of tumors is one of the most common osseous malignancies, especially in pediatrics [5]. Extraskeletal presentation, such as primary presentation in the kidney, is an exceedingly rare and aggressive tumor, which has been reported in case reports and has resulted in misdiagnosis or management delays [6]. RES mostly affects young people and has a high rate of recurrence and poor outcomes. It can be easily misdiagnosed for other renal neoplasms, such as Wilms' tumor, renal cell carcinoma, or lymphoma, owing to its nonspecific clinical and radiological features [6, 7].

The pathophysiological mechanisms behind cancer-associated thrombosis, particularly in the context of renal Ewing sarcoma, require further exploration to identify potential therapeutic targets and preventive strategies. Cancer promotes a prothrombotic state by driving mechanisms that enhance coagulation, which are compounded by common clinical risk factors such as hospitalization, surgery, catheter placement, and cancer treatments [8–10]. Cancer cells may release or express procoagulant

proteins, such as tissue factor, which initiates the coagulation cascade. The hypercoagulable state in patients with cancer can lead to conditions such as venous thromboembolism, arterial thromboembolism, microcirculatory thrombosis, or superficial thrombophlebitis [8–10]. Certain cancers, including pancreatic, gastric, brain, and ovarian cancers, have a particularly high incidence of thrombosis [11]. A recent study reported a 6.7% 5-year cumulative incidence of venous thromboembolism in patients with Ewing sarcoma, particularly in those aged 18 years and older, with catheter-related upper-extremity thrombosis being the most common manifestation [12].

Clinical signs and symptoms are usually nonspecific, such as abdominal or acute flank pain, hydronephrosis, hematuria, and palpable mass [13]. Diagnosing RES can be challenging, especially when presenting with atypical symptoms such as dyspnea and thromboembolic events, as observed in this case. Most of the diagnoses come from postoperative pathology results; they are based on a combination of histopathology, IHC, chromosomal analysis, and FISH [14, 15].

Histologically, RES consists of uniform small round cells that overlap with other diagnoses such as Wilms' tumor, malignant lymphoma, synovial sarcoma, among others, with various morphologies, for example, uniform cells with an even chromatin pattern and rosette formation [16–18]. In our case, there was a diffuse, sheet-like infiltration of small, round neoplastic cells characterized by uniform nuclei, a fine speckled chromatin pattern, and inconspicuous nucleoli. In addition, occasional pseudorosette-like arrangements of tumor cells were observed. IHC analysis in previous studies revealed the highly positive rate of CD99 and FLI-1 [18, 19]. IHC analysis in the present case was positive for NKX2.2, CD99, synaptophysin (Syn), and chromogranin. Over 85% of Ewing sarcoma can be present by a DNA translocation t(11;22)(q24;q12), and some patients are identified by t(21;22)(q22;q12) [20, 21]. In the present case, a t(11;22) translocation of an EWSR1 gene rearrangement was detected by FISH and can lead to various malignancies, often characterized by mesenchymal or neuroectodermal features. Histopathological and IHC examination played a critical role in confirming the diagnosis.

Nowadays, complete surgery—radical nephrectomy followed by chemotherapy—is necessary for the long-term survival of patients with RES, and studies appear to show that the most frequent chemotherapy regimens are VDC/IE [22]. In this case, the patient underwent radical nephrectomy followed by adjuvant chemotherapy with the VDC/IE regimen, which is the gold standard of Ewing's sarcoma management. However, the long-term management of IVC thrombosis in the context of malignancy requires a multidisciplinary approach.

Conclusion

This report emphasizes the importance of integrating clinical and paraclinical results for an appropriate diagnosis and management. To improve patient outcomes, early detection, including surgery and adjuvant chemotherapy, is essential. This case emphasizes the importance of unusual and aggressive tumors such as RES in the differential diagnosis of renal masses in young adults, which is crucial to ensure early intervention and timely management and consider rare presentations. Further investigations are needed to enhance our understanding of this rare renal tumor.

Abbreviations

RES	Renal-origin Ewing's sarcoma
IVC	Inferior vena cava
CT	Computed tomography
IHC	Immunohistochemical staining
FISH	Fluorescence in situ hybridization
VDC	Vincristine/doxorubicin/cyclophosphamide
IE	Ifosfamide/etoposide
PNET	Primitive neuroectodermal tumor

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Author contributions

Case presentation—Ahmad Khajeh-Mehrizi, Masoud Mortezazadeh, Hamidreza Zarei, and Fatemeh Nili. Writing—Mehdi Karimi and Hoda Haghshenas. Conceptualization—Mehdi Karimi, Hoda Haghshenas, Masoud Mortezazadeh, and Ahmad Khajeh-Mehrizi. Critical review and editing—Mehdi Karimi, Hoda Haghshenas, and Ahmad Khajeh-Mehrizi. Supervision—Ahmad Khajeh-Mehrizi, Mehdi Karimi, and Masoud Mortezazadeh.

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Data availability

All data related to the case are reported in the manuscript. Please contact the corresponding author if you require any further information.

Declarations

Ethics approval and consent to participate

This case report was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of Rajaei Hospital Cardiac Center, Tehran University of Medical Science (TUMS), Tehran, Iran.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

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