JACC: CARDIOONCOLOGY VOL. 2, NO. 5, 2020

CLINICAL CASE CHALLENGES

Early T Cell Precursor Leukemia Presenting With Superior Vena Cava Syndrome and Cardiac Tamponade

Krishna Santosh Vemuri, MD,[a] Pruthvi C. Revaiah, MD,[a] Dinakar Bootla, MD,[a] Rajeev Chauhan, MD,[a] Krishna Prasad Nevali, MD,[a] Aditya Jandial, MD,[b] Man Updesh Singh Sachdeva, MD,[c] Dushyant Singh, MBBS,[b] Manoj Kumar Rohit, MD[a]

Superior vena cava (SVC) syndrome is a constellation of symptoms and signs resulting from obstruction of the SVC (1). It results in increased venous pressure in the upper body causing edema of the head, neck, and upper limbs, along with facial plethora and engorged skin and subcutaneous vessels. This obstruction can be extrinsic or intraluminal (1). Extrinsic compression of the SVC results from anterior or middle mediastinal masses secondary to metastases, enlarged lymph nodes, lymphomas, thymomas, inflammatory processes, or aortic aneurysms (1), with the most common malignant causes being lung cancer (non-small cell [24%] and small cell [22%]) and lymphoma in 8% (2). Intraluminal obstruction occurs secondary to the use of intravascular devices or malignancy-associated thrombosis (2). The severity of symptoms depends on the rapidity of onset and degree of narrowing of the SVC. We herein present a unique case of early T cell precursor leukemia presenting as SVC syndrome and cardiac tamponade.

A 22-year-old woman was referred to our center reporting progressive breathlessness for 2 months. At presentation, she noted orthopnea, as well as generalized weakness, body aches, facial puffiness for 1 month, and dysphagia for 20 days. There was also a history of a 4-kg weight loss over the prior 2 months. She had no history of comorbid medical illness, prolonged fever, or indwelling catheters.

On admission, the patient was tachycardic (pulse 102 beats/min) and tachypneic (respiratory rate 28 breaths/min), with a supine blood pressure of 100/60 mm Hg with pulsus paradoxus and 15 mm Hg inspiratory fall, and room air saturation of 95%. Her jugular venous pressure was elevated, with prominent x descent and absent y descent. On auscultation, her heart sounds were muffled, and breath sounds were reduced in the mid and basal left lung fields. Abdominal examination revealed an enlarged liver (4 cm below the right costal margin) and spleen (3 cm below the left costal margin). Small subcentimeter lymph nodes were noted in deep cervical, posterior cervical, and submandibular regions.

Chest radiography showed cardiomegaly with a left-sided pleural effusion. Electrocardiography showed sinus tachycardia. Two-dimensional echocardiography revealed a medium-sized pericardial effusion and features of cardiac tamponade with complete right ventricular diastolic collapse. A right atrial mass was also noted. Echocardiography-guided pericardiocentesis was performed, and 1.5 l of serosanguineous fluid was removed. The brain type natriuretic peptide level was 415 pg/ml (normal range <100 pg/ml). Other cardiac biomarkers were within normal limits. The complete blood count revealed a hemoglobin level of 10.6 g/dl,

From the [a]Department of Cardiology, Post Graduate Institute of Medical Education & Research, Chandigarh, India; [b]Department of Internal Medicine, Post Graduate Institute of Medical Education & Research, Chandigarh, India; and the [c]Department of Hematology, Post Graduate Institute of Medical Education & Research, Chandigarh, India.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received August 30, 2020; revised manuscript received October 23, 2020, accepted October 25, 2020.

ISSN 2666-0873 https://doi.org/10.1016/j.jaccao.2020.10.009

ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

CT = computed tomographic

DOAC = direct oral anticoagulant agent

FDG = fluorodeoxyglucose

LMWH = low-molecular weight heparin

PET = positron emission tomographic

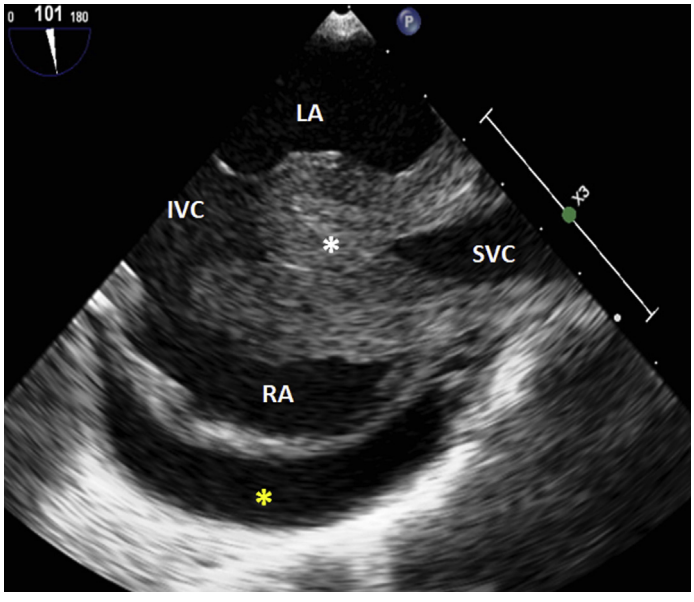
SVC = superior vena cava

white blood cell count of 4.2 × 10^9/l, and platelet count of 284 × 10^9/l. Renal, liver, thyroid, and coagulation function test results were normal. Results of laboratory screening for connective tissue disorders (antinuclear antibody and anti-double-stranded deoxyribonucleic acid) and for thrombophilia (factor V Leiden and G20210A mutation of thrombin, proteins C, S, and antithrombin III) were all negative. Pericardial fluid analyses showed a total leukocyte count of 1,700 cells/μl, with blasts and mature lymphoid cells. The blasts were 1.5 to 3 times the size of mature lymphocytes with irregular nuclear contour, opened up chromatin, and pale granular cytoplasm with nuclear cupping.

Repeat 2-dimensional transthoracic and transesophageal echocardiography revealed a large right atrial mass that involved the right atrium in its entirety, with elongated flagellated masses extending from the SVC into the right atrium obstructing drainage of the SVC (Figure 1). The differential diagnosis included thrombus, tumor, and tumor thrombus. Venous Doppler ultrasound did not reveal deep venous thrombosis in the bilateral lower and upper limbs. Contrast-enhanced computed tomographic imaging of the chest revealed a large 37 × 28 × 26 mm soft tissue mass in the right atrium causing luminal narrowing of the SVC and extending to the inferior vena cava, with attenuation of 74 HU. Positron emission tomographic (PET) scanning showed an ^{18}F-fluorodeoxyglucose (FDG)-avid right atrial mass with a standardized uptake value of 7.2 extending into the SVC and inferior vena cava and subcentimeter cervical and mediastinal lymph nodes (Figure 2). There was no evidence of any mediastinal mass or lymph nodes causing extrinsic (extraluminal) compression of the right atrium or SVC.

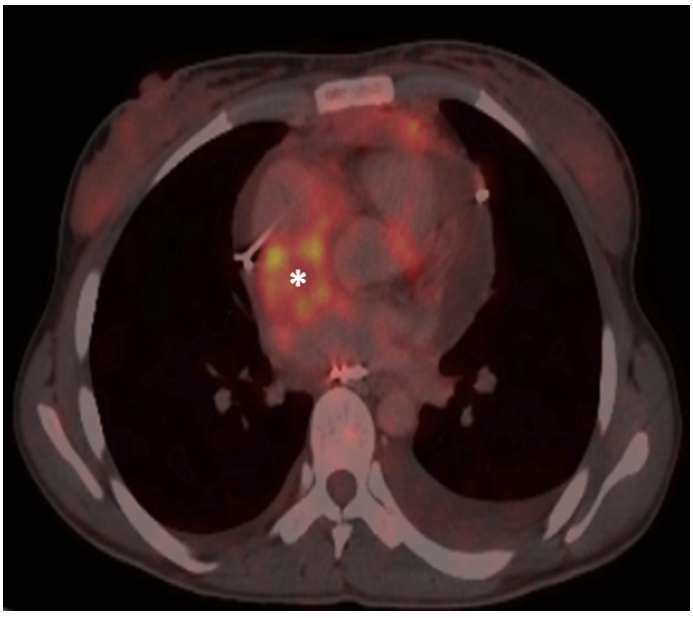
In view of the possibility of malignancy, peripheral blood analysis was performed. This revealed 63% circulating blasts. Subsequently, bone marrow aspirate was performed, which showed 70% blasts with a reduction in myeloid and erythroid series of cells that were negative for myeloperoxidase. Bone marrow trephine biopsy showed the presence of blasts replacing normal hematopoietic elements. Immunophenotyping by flow cytometry showed a blast population expressing bright CD7, cytoplasmic CD3, CD56, and dim expression of CD5. These were negative for other myeloid lineage and B cell markers. Blasts expressed immaturity markers CD34 and TdT but lacked HLA-DR. Overall, the features were consistent with the diagnosis of early T cell precursor leukemia.

FIGURE 1 Transesophageal Echocardiography: Bicaval View



Demonstrating right atrial mass **(white asterisk)** extending from superior vena cava (SVC) to right atrium (RA) obstructing the RA, as well as the pericardial effusion **(yellow asterisk)**. IVC = inferior vena cava; LA = left atrium.

FIGURE 2 FDG Positron Emission Tomography/Computed Tomography



Showing fluorodeoxyglucose (FDG)–avid soft tissue lesion in the right atrium (maximum standardized uptake value 7.2) **(white asterisk)** with intraluminal polypoidal soft tissue component extending into superior and inferior venae cava.

Given the concern for tumor thrombus, the patient was started on anticoagulation with low-molecular weight heparin (LMWH) at a dose of 1 mg/kg twice daily along with head-end elevation, diuretic agents, and dexamethasone. After the results of flow cytometry confirmed a diagnosis of early T cell precursor leukemia, she was treated with a modified BFM-90 (Berlin-Frankfurt-Münster) protocol consisting of cyclophosphamide, vincristine, daunorubicin, L-asparaginase, and corticosteroids. Within 1 week of chemotherapy, her pericardial effusion decreased, and the pigtail catheter was removed. Repeat bone marrow examination after 1 month of chemotherapy showed a reduction of blast cells to 3%. Her facial puffiness, engorged veins, and dyspnea on exertion improved significantly. Repeat transthoracic and transesophageal echocardiography showed a dramatic reduction in the size of masses in the right atrium and SVC. The patient is continuing anticoagulation with LMWH for 3 months. There are no clear guidelines regarding the anticoagulation regimen in patients with SVC obstruction and right atrial masses, particularly in the setting of hematologic malignancies. She has been under regular follow-up for the past 2 months and is doing well.

This case demonstrates the following: 1) early T cell precursor leukemia can present as SVC syndrome due to tumor in the right atrium and SVC and cardiac tamponade; 2) multiple imaging modalities were integral to the diagnosis and management; and 3) chemotherapy with BFM-90 protocol and anticoagulation with LMWH was effective in controlling the early T cell leukemia with the resolution of right atrial and SVC mass and pericardial effusion on follow-up.

We present the case of a patient with T cell precursor leukemia with SVC syndrome and cardiac tamponade. SVC syndrome, in this case, was due to the leukemic tumoral mass invading the right atrium and SVC. Multiple imaging modalities were used to guide the diagnostic process. The initial echocardiographic findings were grossly abnormal, with an apparent mass infiltrating the right atrium and SVC. The additional imaging modalities, including contrast-enhanced CT imaging and PET/CT imaging, further characterized the tissue and supported the suspicion of malignant infiltration. Although the nonenhancing nature suggested a thrombotic component, an attenuation of 74 HU on chest CT imaging could not completely differentiate between thrombus and tumor thrombus. Hence ^{18}F-FDG PET imaging was done, which showed an FDG-avid mass in the right atrium and SVC, providing additional evidence for the malignant nature of this tumor. The diagnosis was further established by bone marrow biopsy and flow cytometry.

Tumor thrombosis involving the SVC is usually the result of direct invasion of an adjacent malignancy from the lungs, mediastinum (lymphoma/metastases), pleura, or trachea and rarely by hematogenous spread (3). The most common presentation of metastatic cardiac involvement is in the form of pericardial effusion, followed by intracardiac masses. Cardiac involvement in the form of a right atrial mass has been reported with malignancies of the lung, breast, and kidney (4). Echocardiography is the initial investigation of choice for detection of cardiac masses and effusions. CT, cardiac magnetic resonance (CMR), and PET imaging modalities are also used to assess tissue characteristics that favor specific pathologies. Advanced imaging can guide surgical candidacy and planning as well as assess response to therapy (5). FDG uptake on PET/CT imaging has been used more frequently in recent years to help differentiate benign and malignant tumors. Malignant tumors generally have high FDG uptake in the 8.0 to 10.8 range, whereas benign tumors have mild FDG uptake (the mean standardized uptake value for benign tumors is 2.8 $\pm$ 0.6) (6). CMR with T1- and T2-weighted imaging, resting first-pass perfusion, and early and late gadolinium enhancement also provides complete and multiplanar noninvasive evaluation of cardiac masses (7). The CMR signal characteristics also correlate well with histopathology.

Management of SVC syndrome involves treating the underlying malignancy and relief of obstruction. Radiotherapy provides rapid response in cases of malignant SVC obstruction secondary to lymphomas, small-cell and non-small cell lung cancers. Systemic chemotherapy is useful in patients with chemosensitive tumors such as non-Hodgkin lymphoma, small-cell lung cancer, and germ cell tumors, providing complete relief. Interventional procedures such as stent placement and surgery are often necessary in patients with severe refractory respiratory symptoms and resistance to chemotherapy or radiotherapy (1).

The presentation of early T cell precursor leukemia as SVC syndrome and a right atrial mass with pericardial tamponade is not common. The intraluminal obstruction seen in malignancies could be due to the tumor mass itself or thrombosis or both. Of all hematologic malignancies, acute myeloid leukemia is associated with the highest thrombosis risk (25%) (4). Large-bore intravascular catheters for chemotherapy also increase thrombosis risk. In this case, there were large masses extending into the right atrium and another large mass in the right atrium involving the posterolateral wall and interatrial septum and extending up to the inferior vena cava, which could potentially embolize and cause acute pulmonary thromboembolism. The options for management of thrombosis include direct oral anticoagulant agents (DOACs), LMWH, and vitamin K antagonists, preferably DOACs or LMWH (8). In a recent meta-analysis comparing LMWH with DOAC, there was a lower risk for recurrent venous thromboembolism but a higher risk for clinically relevant nonmajor bleeding with DOACs compared with LMWH, observed mostly in those with gastrointestinal malignancies (9). In our patient, LMWH was used rather than DOACs for accessibility reasons and availability of antidote.

The case reported here was a rare presentation of early T cell precursor leukemia as cardiac tamponade and SVC syndrome. Multimodality imaging and a multidisciplinary approach can aid in the prompt diagnosis and management of such rare presentations.

AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Prof. Manoj Kumar Rohit, Department of Cardiology, Advanced Cardiac Center, Postgraduate Institute of Medical Education and Research, Chandigarh, Sector-12 160012, India. E-mail: cardiopgimerchd@gmail.com. Twitter: @PruthviCR1, @dinakartweet, @krishnanevali, @rajeevafmc, @rohitmanoj6.

REFERENCES

1. Wilson LD, Detterbeck FC, Yahalom J. Superior vena cava syndrome with malignant causes. N Engl J Med 2007;356:1862–9.

2. Rice TW, Rodriguez RM, Light RW. The superior vena cava syndrome: clinical characteristics and evolving etiology. Medicine (Baltimore) 2006;85:37–42.

3. Sonavane SK, Milner DM, Singh SP, Abdel Aal AK, Shahir KS, Chaturvedi A. Comprehensive imaging review of the superior vena cava. Radiographics 2015;35:1873–92.

4. Houssou B, Orou-Guiwa GG, Habbal R, Qachouh M, Quessar A. Massive thrombosis of the right atrium extended to the superior vena cava at the diagnosis of acute myeloid leukemia. Case Rep Cardiol 2016;2016:6802429.

5. Motwani M, Kidambi A, Herzog BA, Uddin A, Greenwood JP, Plein S. MR imaging of cardiac tumors and masses: a review of methods and clinical applications. Radiology 2013;268:26–43.

6. Rahbar K, Seifarth H, Schafers M, et al. Differentiation of malignant and benign cardiac tumors using ^{18}F-FDG PET/CT. J Nucl Med 2012;53:856–63.

7. Parwani P, Co M, Ramesh T, et al. Differentiation of cardiac masses by cardiac magnetic resonance imaging. Curr Cardiovasc Imaging Rep 2020;13.

8. Key NS, Khorana AA, Kuderer NM, Bohlke K, Lee AYY, Arcelus JI, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: ASCO clinical practice guideline update. J Clin Oncol 2020;38:496–520.

9. Sabatino J, De Rosa S, Polimeni A, Sorrentino S, Indolfi C. Direct oral anticoagulants in patients with active cancer. J Am Coll Cardiol CardioOnc 2020;2:428–40.

KEY WORDS **cardiac tamponade, precursor T cell lymphoma, superior vena cava syndrome, tumor thrombosis**