DIAGNOSTIC AND THERAPEUTIC CHALLENGES IN A CRITICALLY ILL PATIENT IN ICU WITH SUPERIOR VENA CAVA SYNDROME

- Case Report -

Pragny Adipta Mishra*, Rajini Kausalya*
and Rajiv Jain**

Abstract

Purpose

To highlight the diagnostic and therapeutic challenges associated with the treatment of a patient with superior vena cava syndrome and a coexisting coagulopathy.

Clinical features

This case report describes a bone marrow transplant patient with graft versus host diseases (GVHD) who was admitted to our intensive care unit with bronchiectasis complicated with nosocomial pneumonia. When he was recovering from pneumonia after prolonged ventilatory support, he developed superior vena cava (SVC) syndrome due to mediastinal lymphadenopathy. The diagnosis was delayed due to associated confounding clinical factors. Because of the rapid deterioration in patient's condition, immediate tissue diagnosis of mediastinal lymph nodes and re-canalization of vena cava by stenting were our priority. He had many other medical problems such as thrombocytopenia, deranged coagulation profile, old cerebral infarction with hemiplegia, seizure disorder and cardiac arrhythmias which complicated the treatment plan. USG guided biopsy followed by stenting of the SVC was done after discussing the risks and benefits with patient's relatives. But, he had bleeding from biopsy site due to deranged coagulation profile. Again for the same reason, he was not given any anticoagulants. Within 24 hours the stent was blocked by clot which was diagnosed by the deteriorating clinical features and repeat CT scan. Then he was given enoxaparin in therapeutic dose and the clot cleared within a day possibly partly due to enoxaparin and partly coagulopathy.

* Department of Anesthesia and Intensive Care Unit.
** Department of Radiodiagnosis.
Sultan Qaboos University Hospital, Muscat, Oman.
Corresponding author: Dr. Pragny Adipta Mishra, Department of Aneshtesia and Intensive Care Unit. Tel: +968-92488259, E-mail: pragyandeep@gmail.com

Conclusion

In a bone marrow transplant patient with GVHD, the associated complications can confound the diagnosis of SVC syndrome. Physician has to show high degree of suspicion as it may develop even if patient has coagulopathy due to other factors such mediastinal lymphadenopathy. SVC stent may clot even if the patient has coagulopathy. So, it is advisable to defer the invasive diagnostic procedures such as mediastinal lymph node biopsy till the patient is well stabilized after the stent placement in SVC as it will prevent further use of anticoagulants. Enoxaparin may be helpful in the treatment of stent thrombosis in such patients with multiple complications.

Introduction

Superior vena cava (SVC) syndrome is an uncommon complication of many disease conditions, which include malignancies, hematological disorders and patients with transvenous pacemakers and central venous catheters[1-3]. Most cases are caused by malignancies and SVC obstruction due to malignancy usually progresses rapidly leading to complete obstruction which can cause a patient's condition to deteriorate rapidly[4]. Benign cases are increasing in large part due to iatrogenic injuries from central venous catheters (CVC) and transvenous pacemakers. Obstruction due to benign disease may be indolent. SVC obstruction usually presents with swelling of face and upper extremities, conjuctival suffusion, periorbital swelling, proptosis, dyspnea, respiratory distress and pleural effusion and rarely life-threatening complications such as pulmonary embolism (PE) and intracranial hypertension[1,5,6]. Because some of the complications such as respiratory distress, systemic hypotension, and intracranial hypertension are life threatening, this condition has to be treated on an emergency basis with definitive strategies, which vary from anticoagulation and medical management to radiological stenting, chemotherapy, radiotherapy or surgical bypass[7-14]. We present an interesting case of SVC syndrome in a patient admitted to our intensive care unit.

Case Report

A twenty year old patient who had undergone allogenic bone marrow transplantation for acute myeloid leukemia two years earlier presented to our emergency department with breathing difficulty. He also had bronchiectasis with history of multiple admissions to our emergency department and medical ward for exacerbation. His immunoglobulin A level was found to be low and he had grown extended spectrum beta lactamase resistant organism (Klebsiella) in sputum, sensitive only to meropenem in the previous admissions 2 months earlier. He had multiple other complications arising from bone marrow transplant such as liver graft versus host disease (GVHD), transfusional iron overload and has been on monthly venesection and desoferol, 6 month old watershed cerebral infarct involving right middle cerebral artery & anterior cerebral artery with hemiparesis, 4 month old chronic subdural hematoma with regular neurosurgical follow ups and past history of seizures on valproic acid.

Patient's vital parameters on admission were as follows, respiratory rate 40/min, pulse rate 128/min, blood pressure 126/60 mmHg left arm partially propped up position. Chest was full of rhonchi and crepitations with saturation on pulse oxymeter of around 75% on 10 L/min O_2 flow by facemask with reservoir bag. Arterial blood gas showed respiratory acidosis due to CO_2 retention (pCO_2 = 16 kPa). He was admitted to the intensive care unit (ICU) and given noninvasive ventilation (NIV) without any improvement. His trachea was intubated and started on pressure controlled mechanical ventilation. Patient had a turbulent course in ICU. He developed multiple complications such as nosocomial infection with septic shock, right-sided heart failure, uncontrolled seizures and arrhythmias such as intermittent paroxysmal supraventricular tachycardia (PSVT). A CVC was inserted in his right internal jugular vein to monitor central venous pressure and for giving various intra venous medications. A CT scan of chest done during ICU stay showed significant bronchiectactic changes with bilateral upper lobe fibrosis and his arterial CO_2 was always between 10 to 12 kPa due these lung changes. Patient was tracheostomised in the ICU in anticipation of prolonged ventilatory support due to his

primary lung pathology and associated complications. Once his respiratory and hemodynamic parameters stabilized, we gradually tried to wean him off the ventilatory support. His ventilatory requirements came down from a pressure controlled mode to a pressure support mode (PSV). He could not be weaned further. The possibility of home ventilation was discussed with the family members, which was not accepted. He intermittently complained of headache and pain in the upper chest, which we attributed to hypercarbia and tracheostomy wound. The tracheostomy tube tie was loosened and some analgesics were prescribed.

On day 26 of ICU stay, patient developed significant puffiness of the face, neck and both upper extremities (Fig. 1). Along with that, patient became tachypneic, irritable and drowsy. His mode of ventilation had to be changed back to control mode. He showed a decrease in his urine output and increase in frequency of PSVT with intermittent atrial fibrillation (AF). It was initially thought that he was developing some renal impairment, possibly due to recurrent sepsis and nephrotoxic drugs such as amikacin, amphotericin B and cyclosporine which patient was taking at that time. But, over a period of two days the swelling became worse in the same region without involving the lower extremities. From

Fig. 1
Patient showing significant swelling of face, chest and upper extremity

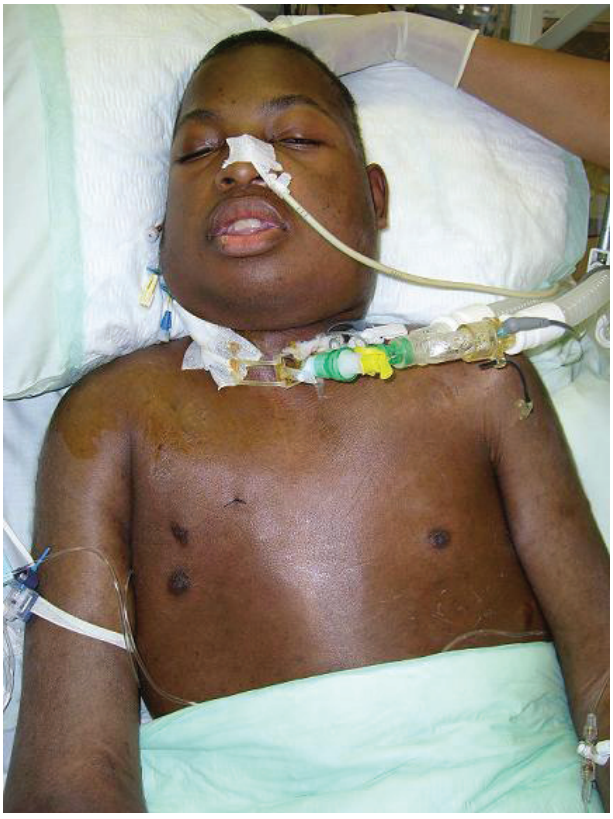


Table 1
Coagulation parameters and platelet count of the patient during the ICU stay

DAY IN ICU	PT(Sec)	APTT(Sec)	INR	PC($\times 10^9$/L)
1	21.3	1.67	47	67
4	22	1.67	46	79
8	22	1.67	44	96
16	22.4	1.70	48	75
24	22.7	1.70	73	86
26(05.10 hours)	24	1.83	66	92
26(19.00 hours)	30	2.33	61	98
27(05.45 hours)	28	1.83	53	64
27(17.00 hours)	28.5	1.83	57	75
30	22.4	1.70	49	72

It shows significantly derangement from first day of ICU due to GVHD involving liver. Around day 26 of ICU stay, it deteriorated further may be because of worsening of clinical condition of the patient. (PT- Prothrombin time, APTT- Activated partial thromboplastin time, INR- International normalized ratio, PC- Platelet Count).

the day of admission his coagulation profile was deranged due to GVHD (Table 1). He received many units of fresh frozen plasma and platelet concentrates before invasive procedures during the ICU stay such as CVC cannulation, tracheostomy, rectal biopsy etc. Although patient had coagulopathy, SVC syndrome was suspected due to external compression of superior vena cava by mediastinal lymphadenopathy from post transplant lymphoproliferative disorder or a relapse of the primary malignancy (AML). After an inconclusive bedside doppler ultrasonography (USG), it was decided to proceed with a CT scan to determine the cause. The CT scan confirmed the diagnosis of a superior venacaval obstruction by enlarged mediastinal lymph nodes. A femoral venous catheter was immediately inserted for administration of intravenous medication, but the CVC in the right internal jugular vein (IJV) was retained as advised by the radiologist for potential future radiological interventions.

Normal range: PT (10.8-15.3 Seconds), INR (0.83-1.16), APTT (24-38 Seconds), PC (150 to 450×10^9/L).

A decision was made to perform an USG guided mediastinal lymph node biopsy for tissue diagnosis and SVC stenting in the same sitting. The radiologist, under general anesthesia, performed the mediastinal biopsy followed by stenting of SVC (Fig. 2 and 3). But, biopsy site started to bleed. Patient remained hemodynamically stable. Local pressure was applied to stop the bleeding and wound was sutured. It was decided not to transfuse any blood products for the above bleeding episode due to fear of thrombosis of the stent. CVC in IJV was withdrawn and fixed just above the stent by the radiologist for possible future use. He was not given any post-stenting anticoagulant due to the deranged coagulogram and possibility of bleeding from biopsy site.

But on the next day (day 27 of ICU stay), there was a significant increase in facial and upper limb swelling. Along with that he had diminished air entry at lung bases on both sides. In fact, there was no decrease in CVP (20 mmHg) after the stenting as measured through the CVC in right IJV. He was now complaining of more chest pain. There was sudden decrease in urine output and increase in blood urea and creatinine possibly due to contrast induced nephropathy. His lung compliance was deteriorating steadily with a parallel increase in pCO_2 in spite of full ventilatory support.

Fig. 2
Superior venacavogram
AP projection of study performed through the right internal jugular venous access showing the narrowed segment of the SVC (between arrows) and multiple collateral channels in the neck including reversal of flow in the left brachiocephalic vein.

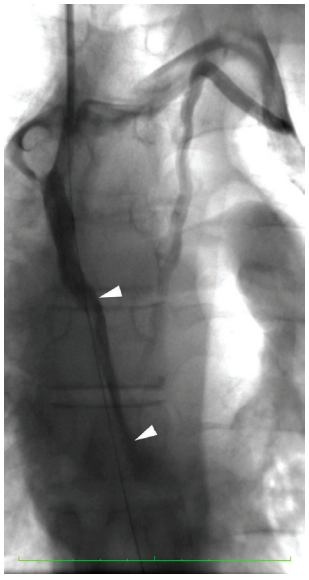
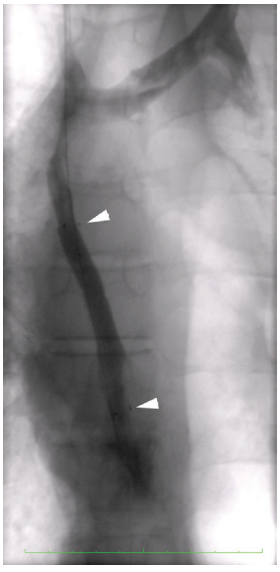


Fig. 3
Superior venacavogram
AP projection of study performed through the right internal jugular venous access following insertion of self-expanding metallic stent of 8mm diameter. The image shows improved diameter and flow through the SVC and reduction of flow through the multiple collateral channels in the neck and the left brachiocephalic vein.



Cardiac arrhythmias (PSVT and AF) worsened and amiodarone was started in spite of fibrotic lungs as he showed no response to sotalol which he was already on for PSVT. Urgent CT scan showed thrombosis of stent in SVC with extension to right subclavian vein along with bilateral pleural effusion. He was started on enoxaparin in therapeutic dose (60 mg twice daily). Thrombolytic therapy or intravenous heparin was withheld for fear of possible rebleed from mediastinal biopsy site and also from chronic subdural hematoma and old cerebral infarct site. Vascular surgeon ruled out the possibility of surgical intervention due to poor general condition of the patient. The biopsy of the mediastinal lymph node was reported as crushed tissue. Hence no definitive treatment for the enlarged nodes was possible. Instead it was decided to repeat the CT scan and give local thrombolytic therapy (with Alteplase) through the CVC in the right IJV if found to have persistent thrombosis. A repeat mediastinal lymph node biopsy was deferred due to the possibility of rebleed. Fortunately, the radiologist found the SVC to be patent. So he was continued on enoxaparin without any further intervention.

Discussion

Superior vena cava syndrome generally occurs due to impairment of normal venous return through superior vena cava by either compression by adjacent tumor mass or lymph nodes or thrombosis of SVC due to long term indwelling extraneous devices and hyper-coagulable states[1-5]. Even though the diagnosis depends on a high degree of alertness on the part of the treating physician, it can be quite challenging to diagnose SVC syndrome in a critically ill patient like ours.

Our patient had undergone allogenic bone marrow transplant two years earlier for acute myeloid leukemia (AML). There were neither any history nor any sign, symptom or laboratory reports, which would suggest post transplant lymphoproliferative disorder or relapse of AML during the current episode of acute illness. The main problem which led to ICU admission and respiratory failure was acute exacerbation of bronchiectasis which was later complicated by severe ventilator associated pneumonia (VAPS) and ARDS. He successfully recovered from all these problems.

On retrospective analysis, this patient showed many symptoms of SVC compression before the full blown syndrome was evident. He had respiratory distress in the form of inability to wean from ventilatory support. He never tolerated T-piece trial for more than minutes which was previously contributed to his main lung pathology, bronchiectasis and many other pathological conditions such as lung fibrosis, low muscle bulk and power. His chest pain was attributed to tracheostomy wound and the initial low-grade facial swelling to progressing renal failure from nephrotoxic drugs. The magnitude of deranged coagulation profile was against SVC syndrome due to CVC, although it cannot rule it out absolutely. As the swelling progressed on face and upper limbs without involving lower limbs, patient was investigated in the line of SVC syndrome.

The treatment option for SVC syndrome depends on the primary pathology and progress of the disease. Any malignant condition such as bronchogenic carcinoma or lymphoma etc. has to be managed by treatment of primary disease by radiotherapy or chemotherapy after confirming the tissue diagnosis[9,12,13]. But if the symptoms progress rapidly leading to respiratory distress, neurological deterioration or hemodynamic instability, immediate intervention may be required in the form of balloon angioplasty, stenting or surgical intervention[10,11,14]. Benign condition leading to SVC syndrome usually responds to medical treatment in the form of head elevation, anticoagulants, thrombolysis, diuretics and steroids[1,7,8]. But, nowadays it is increasingly being treated by angioplasty, local thrombolysis and stenting[15,16].

USG or CT guided biopsy are time tested methods of tissue diagnosis of mediastinal mass with few contraindications. The absolute contraindications include uncontrollable cough and suspicion of hydatid cyst, whereas relative contraindications include bleeding diathesis, vascular lesions, pulmonary hypertension, uncooperative patient, and advanced emphysema[17]. In this patient, CT scan revealed mediastinal lymph nodes compressing the SVC. Irritation of SVC by compressing lymph node could have been a focus of the atrial arrhythmias[18]. Mediastinal biopsy was planned to find out tissue diagnosis for possible chemotherapy to treat the AML relapse or any secondary malignancy. Retrospectively

thinking, the decision to do USG guided biopsy along with angioplasty and stenting of SVC was a therapeutic misadventure on our part. It prevented us from giving anticoagulation for maintaining the patency of the stent. Allowing the patient to stabilize after stenting would have decreased the collateral vessels in mediastinum to create a better condition for biopsy.

The condition of patient was deteriorating rapidly and the coagulation profile was quite deranged on that day. It was expected that the stent would not clot with this type of deranged coagulation profile. But, the next day when the symptoms increased, repeat CT scan showed thrombosed stent. Because this patient had a six month old cerebral infarction and chronic subdural hematoma, he was at high risk for intracranial bleed from thrombolysis and intravenous heparin therapy. So, enoxaparin was started in therapeutic doses in spite of his deranged coagulogram and all risk factors. Fortunately, the stent became patent radiologically with in 24 hours.

So, we conclude that associated complications can confound the diagnosis of SVC syndrome in a very sick bone marrow transplant patient with GVHD. Physician has to show high degree of suspicion as it may develop even if patient has coagulopathy due to other factors such mediastinal lymphadenopathy. SVC stent may clot even if patient has coagulopathy. So, it is advisable to defer the invasive diagnostic procedures such as mediastinal lymph node biopsy till the patient is well stabilized after the stent placement in SVC as it will prevent further use of anticoagulants. Enoxaparin may be helpful in the treatment of stent thrombosis in such patients with multiple complications.

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