

Thrombogenic superior vena cava syndrome from long-standing central venous access in a 5-year-old patient treated with balloon-expandable stents

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ABSTRACT

Thrombogenic superior vena cava syndrome is an uncommon, dangerous complication of long-standing central venous catheter use. The increased use of central venous catheters has resulted in more non-malignant cases of superior vena cava syndrome across all age groups. We present a 5-year-old male with superior vena cava syndrome associated with acute onset of severe upper extremity and facial swelling, dyspnea, and a right subclavian central venous catheter malfunction. The patient was ultimately treated with percutaneous stenting of the superior vena cava with balloon-expandable Palmaz stents following unsuccessful angioplasty, catheter-directed thrombolysis, and percutaneous thrombectomy. This case highlights a relatively uncommon complication in children from long-term central venous catheter access and describes an emerging, minimally-invasive therapeutic alternative that allows for preservation of age-appropriate superior vena cava luminal diameter as patients grow.

CASE REPORT

CASE REPORT

A 5-year-old male presented in April 2015 with acute onset of severe upper extremity and facial swelling, shortness of breath, and a right subclavian central venous catheter (CVC) malfunction. The indwelling subclavian CVC was surgically placed during infancy for total parenteral nutrition dependency associated with short gut syndrome due to history of necrotizing enterocolitis. His past medical history included CVC-associated thrombosis related to venous stenosis from a previous long-standing CVC in the superior vena cava (SVC) and brachiocephalic vein one month prior in March 2014 which was treated with therapeutic anticoagulation. He was placed on prophylactic anticoagulation in September 2014

after completing a course of uncomplicated therapeutic anticoagulation with a negative thrombophilia workup by the hematology service.

Expansive acute thrombosis of the right internal jugular, subclavian, and brachiocephalic veins as well as the superior aspect of the SVC (Figures 1a-1c) was identified sonographically in the setting of known chronic occlusion of the left innominate vein. Venography revealed poorly developed collateral flow from the right arm through mediastinal collaterals (Figure 2a) that eventually drained into the azygos system. The subclavian catheter tip was in the SVC and was removed. Angioplasty was performed through new right internal jugular vein access. Through and through access

via the right femoral vein was also obtained in case there was a need to stent the SVC during the initial procedure. However, there was improved flow through the SVC following angioplasty (Figure 2b), so a new right internal jugular tunneled CVC was placed. The patient rapidly improved clinically before suffering acute SVC thrombosis and abrupt return of symptoms 4 days later. Pharmacologic catheter-directed thrombolysis was then performed via two separate infusion catheters placed across the SVC/internal jugular veins (from a femoral access site) and across right the subclavian/brachiocephalic veins (from a right brachial vein access site). Two infusion catheters were used in an attempt to improve inflow through the SVC. Tissue plasminogen activator (tPA) was divided equally and administered through both infusion catheters at a total rate of 0.03 mg/kg/hr.

Despite overnight pharmacologic TPA thrombolysis, there was no appreciable recanalization of the occluded veins on venography the following day. Thus, the decision was made to perform percutaneous mechanical thrombectomy with the Indigo Mechanical Thrombectomy System (Penumbra, Alameda, CA) of the occluded segments and perform an additional 24 hours of catheter-directed pharmacologic thrombolysis at the same tPA infusion rate divided equally between two infusion catheters. Following a second night of catheter-directed thrombolysis, SVC occlusion persisted and the patient was clinically unchanged. A venogram from the right brachial vein access demonstrated persistent SVC occlusion (Figure 3), leading to the decision to place a stent in the occluded portion of the SVC. The occluded segments were stented using three balloon-expandable Palmaz XL (Cordis, Milpitas, CA) unmounted stents with dilatation of the cranial-most aspects of the stents to 8 mm and the most caudal aspects of the stents to 12 mm. The stents extended from the caudal right internal jugular vein across the confluence with the subclavian vein into the SVC. Of note, crossing the subclavian vein with stents in the setting of SVC syndrome has been shown to have no significant differences in clinical efficacy [1]. Post-stent venogram from the right internal jugular vein (Figure 4) demonstrated brisk flow from the internal jugular vein into the right atrium. A new right common femoral tunneled CVC was placed. The patient's symptoms resolved in the first 24-48 hours after stent placement. The patient was discharged and underwent an uneventful course of 6 months of therapeutic enoxaparin anticoagulation and remains on prophylactic anticoagulation.

A scheduled follow-up venogram was performed 30 months after initial stent placement showing growth of the internal jugular vein related to the stent (Figure 5a). The superior portion of the stent was then dilated to 10 mm (Figure 5b) allowing for age-appropriate luminal diameter of the brachiocephalic vein and internal jugular vein, while the inferior/central diameter of the stent was maintained at 12 mm. The patient remains clinically asymptomatic 32 months after the procedure and will continue to be scheduled for serial dilations of the stent until adult-sized luminal diameters of the stented vessels are achieved.

DISCUSSION

Etiology & Demographics:

SVC syndrome is caused by obstruction or compression of venous return from the upper extremities, head, and neck. The increased use of indwelling CVCs in clinical practice has yielded an increasing number of non-malignant cases of SVC syndrome, which has historically been associated with malignancy, in patients of all ages [2]. Although the precise prevalence of SVC syndrome in pediatric patients is unknown [3], it is known that malignancy accounts for 60-80% of cases, with the remainder due to benign causes [4]. Although relatively rare, one of the most dangerous complications with the use of CVCs is central venous stenosis and/or occlusion associated with long-term central venous access, resulting in SVC syndrome due to impaired venous drainage [4,5]. Infection and thrombosis are the most common complications of long-standing CVCs. Pediatric variants of SVC can be incidental, associated with cardiac anomalies, and may first be identified at imaging performed for venous access [6]. Risk factors for SVC syndrome in children include intrathoracic malignancies (non-Hodgkin lymphoma), thrombosis, infection (syphilis and tuberculosis), post-radiation fibrosis, and mediastinitis. All causes of thrombosis must be considered, including genetic thrombophilias, tumor, and vascular stenosis. Additionally, SVC syndrome in children is not gender specific and does not have a particular age predilection.

Clinical & Imaging Findings:

The SVC is formed by the confluence of the right and left brachiocephalic veins. Venous blood return from the upper extremities, head, and neck primarily occurs through the SVC. When the SVC becomes obstructed, collateral venous return to the heart most commonly develops via the azygos/hemiazygos system. The brachiocephalic veins, their tributaries, and the mediastinal venous plexus serve as collateral venous pathways and become identifiable at imaging in cases of SVC obstruction. Gradual development of adequate collateral venous return will minimize the progression of SVC syndrome. However, acute obstruction, as seen with thrombosis, can cause life threatening SVC syndrome and present with clinical findings of facial and neck swelling, facial flushing, bilateral upper extremity swelling, neurological signs, dyspnea, headache and cough [4,5]. Children with long-standing CVCs may be at an increased risk of central venous stenosis leading to thrombogenic SVC syndrome, although this has not been definitively studied. As children grow (with unchanged length of existing CVCs), the distal tip is typically retracted from the cavoatrial junction into the SVC and brachiocephalic veins. Placement within these vessels, and the subsequent turbulent flow, may lead to this increased risk. Additionally in children, if external compression of the SVC is the primary etiology of SVC syndrome, the compression of the superior vena cava may be associated with compression of the trachea as well. The trachea in children is relatively narrow, flexible, and soft as compared with an adult. Airway obstruction may occur and manifest as difficulty breathing, stridor, and wheezing.

Imaging plays a vital role in diagnosis and management of various conditions that affect the SVC. Indirect signs on chest radiography, such as superior mediastinal widening or presence of a mediastinal mass, may indicate the presence of malignancy arising from the lung, pleura, or trachea [6]. These radiographs may also be used to evaluate the positioning of CVCs in certain benign cases. Computed tomography and magnetic resonance imaging can also be used to demonstrate the level and extent of venous blockage, identify and map collateral pathways of venous drainage, and often identify the underlying cause of venous obstruction if the etiology is unknown [6]. In the setting of acute, thrombogenic SVC syndrome, venography is often required as part of an intervention to evaluate the location and extent of occlusion of the superior vena cava and the collateral drainage [6]. Acute, expansile thrombosis in the internal jugular, subclavian, and brachiocephalic veins is common on Doppler ultrasound in the setting of SVC syndrome.

Treatment & Prognosis:

The goal of treatment is to relieve the SVC stenosis or obstruction and to alleviate the inciting cause. The prognosis and mortality are determined by the underlying cause. Without treatment, SVC syndrome is associated with a 10-20% mortality within 6 months. For malignant cases of SVC syndrome, the traditional treatment therapy is radiation therapy, chemotherapy, or a combination of both. With the increased number of benign cases of SVC syndrome and the expanding acceptance of percutaneous and minimally invasive treatment options, the treatment of SVC syndrome with angioplasty and stenting has become more common in adults [7,8]. While venous angioplasty and intravascular stents have been used to reestablish patency in patients with benign SVC stenosis or occlusion, balloon angioplasty is the mainstay of treatment [6].

SVC syndrome is not typically seen in childhood, and treatment can be quite difficult, particularly in small children, due to the small size of the occluded vessels. The placement of an endovascular stent restores venous return and provides rapid and sustained symptom palliation in patients with SVC syndrome [1]. However, evaluation of this therapeutic alternative in children has not been critically analyzed, particularly in patients who may have a normal life-expectancy at the time of diagnosis and smaller vessels. Two primary types of stents have been used to treat SVC syndrome in adults: 1) Self-expanding stents, and 2) Balloon-expandable stents. Palmaz, unmounted, balloon-expandable stents (Cordis, Milpitas, CA) allow for gradual balloon dilation as the patient ages [9]. Overtime, the stents can be dilated until an "adult-sized" SVC (12 -16 mm) is achieved. This same gradual dilation is not possible with self-expanding stent technology. Other advantages of balloon-expandable stents are the accurate positioning with which they can be placed and the ability to increase the diameter as needed during initial deployment [10,11]. Balloon-expandable stents represent a therapeutic alternative to treat SVC syndrome, even in very small children, when other less-permanent endovascular interventions are unsuccessful.

Differential diagnoses:

Acute Thrombogenic SVC Syndrome

Acute thrombosis is the most common cause of SVC syndrome in children. This is primarily due to the increased use of long-standing central venous access in children. The risk may be exacerbated by either a pre-existing thrombophilia or central venous stenosis. If stenosis is present, percutaneous stent placement may be required for adequate therapy, in addition to anti-coagulation and thrombolysis, such as was required in this case.

External Compression of the SVC

If the mediastinum is shown to be widened on chest X-ray, the differential includes an external compression of the SVC. Although less common in children, SVC compression is seen on CT/MRI in the setting of various mediastinal masses (such as lymphoma, germ cells tumors, and thymic masses), primary lung tumors (such as pleuropulmonary blastoma and carcinoid tumor), and fibrosing mediastinitis. Ultrasound will most likely not provide any additional findings other than venous thrombosis.

Conclusion:

Until now, percutaneous treatment of SVC abnormalities in children has been primarily performed by interventional cardiologists as SVC abnormalities are most commonly encountered in children with congenital heart disease [12]. With the increase of thrombotic causes of SVC syndrome in children due to the rise in the use of CVCs, this case serves to educate pediatric interventional radiologists on the increased incidence of SVC syndrome in children without congenital heart disease and that treatment with balloon-expandable stents is a clinically viable alternative that can be employed after other conventional therapies have failed while allowing for long-term preservation of an age-appropriate luminal diameter of the SVC.

TEACHING POINT

Balloon-expandable, percutaneous SVC stent placement is a minimally-invasive therapeutic alternative that allows for preservation of long-term, age-appropriate SVC luminal diameter in children with catheter-associated, thrombogenic SVC syndrome.

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FIGURES

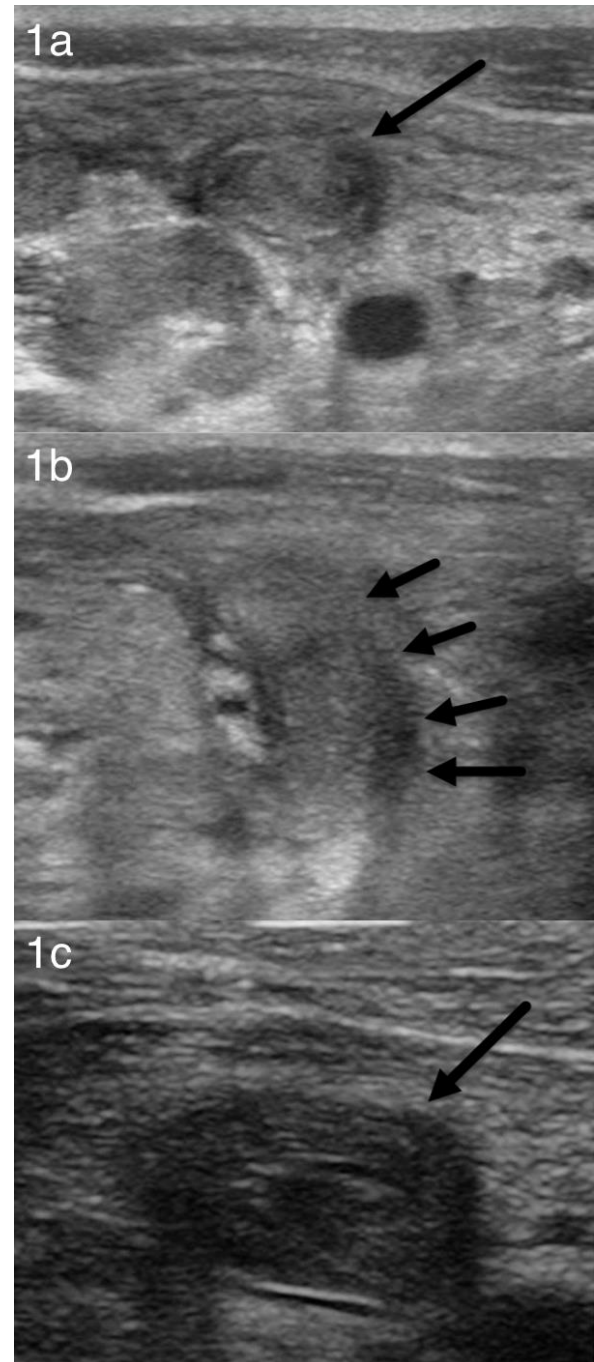


Figure 1: A 5-year-old male with acute, thrombogenic SVC syndrome.

a) Grayscale ultrasound demonstrates expansile, acute thrombosis in the right internal jugular vein (arrow). This region was non-compressible. Image was obtained with a 12 MHz linear transducer.

b) Grayscale ultrasound demonstrates expansile, acute thrombosis in the right brachiocephalic vein extending into the superior/cranial portion of the SVC (arrows). Image was obtained with a 12 MHz linear transducer.

c) Grayscale ultrasound demonstrates expansile, acute thrombosis in the right subclavian vein (arrow) obtained with the ultrasound probe in a supraclavicular position. This region was non-compressible. Image was obtained with a 12 MHz linear transducer.

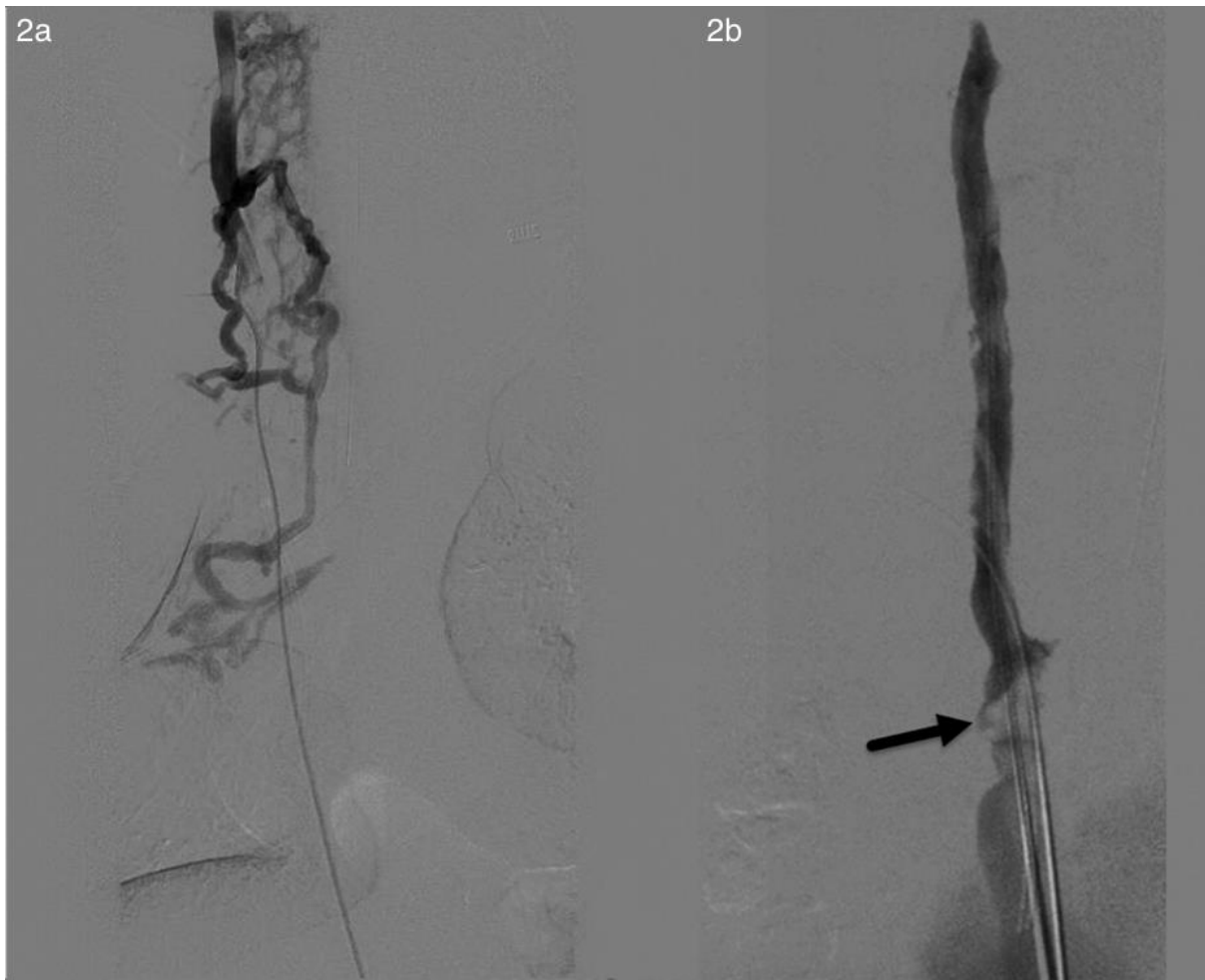


Figure 2: A 5-year-old male with acute, thrombogenic SVC syndrome.

a) Digital-subtraction venography with a 4F diagnostic angled catheter placed in the right brachiocephalic vein via an inferior right femoral vein access site demonstrates opacification of multiple mediastinal collateral vessels and occlusion of the SVC.

b) Following angioplasty of the occluded internal jugular vein, brachiocephalic vein, and SVC, inline flow of contrast is restored from the internal jugular vein through the SVC. Note the persistent luminal irregularity/stenosis (black arrow) in the SVC, likely from long-term central venous access.



Figure 3 (left): A 5-year-old male with acute, thrombogenic SVC syndrome. Digital-subtraction venography from a right brachial vein access site following 48 hours of pharmacologic thrombolysis and percutaneous mechanical thrombectomy demonstrates persistent occlusion of the SVC with opacification of mediastinal collateral vessels filling the azygos vein (arrow).

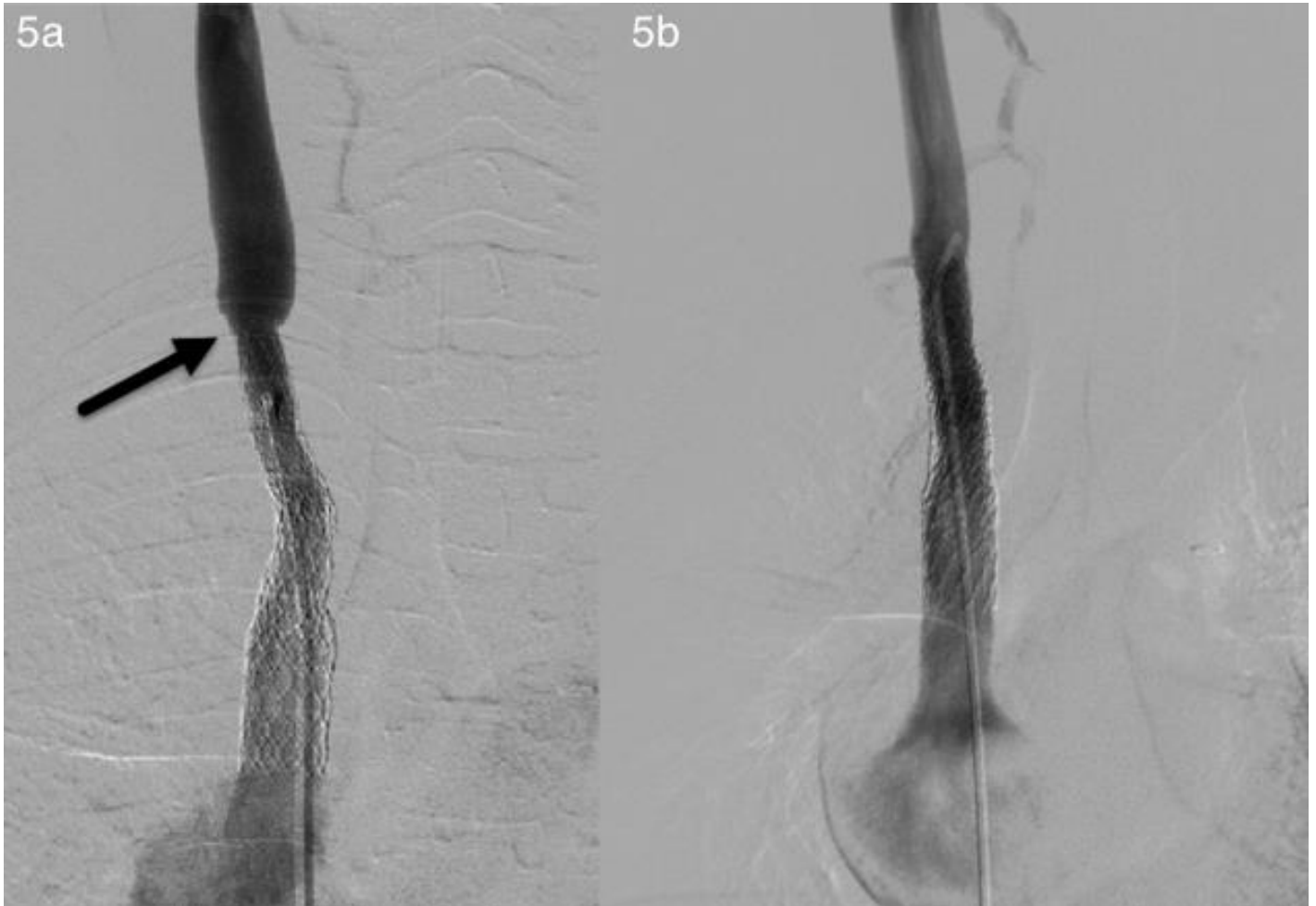


Figure 4 (left): A 5-year-old male with acute, thrombogenic SVC syndrome. Following deployment of 3 balloon-expandable, unmounted stents, in-line flow is restored from the internal jugular vein into the right atrium with resolution of SVC stenosis seen in Figure 1b. The superior/cranial diameter of the stents was dilated to 8mm. The central/caudal portion of the stents was dilated to 12mm.

Figure 5 (bottom): A 7-year-old male with acute, thrombogenic SVC syndrome.

a) 30-month follow-up venography via a 4F angled catheter from right common femoral venous access demonstrates growth of the patient's internal jugular vein related to the stent (arrow) with persistent stent patency.

b) Following dilation of the cranial aspect of the stent to 10mm, the patient's internal jugular vein is now similar in size to the stent allowing for preservation of an age-appropriate luminal diameter of the stented vessels.



Etiology	<ul style="list-style-type: none"> • Obstruction of blood flow through the SVC can be caused by invasion or external compression by adjacent pathologic processes involving the right lung, lymph nodes, or other mediastinal structures, or by thrombosis within the SVC.
Incidence	<ul style="list-style-type: none"> • Malignancy accounts for 60 to 80% of cases, with the remainder due to benign causes. Most common cause is non-Hodgkin lymphoma. • Benign causes now account for 20 to 40% of cases of SVC syndrome. Thrombosis has become a more common nonmalignant cause due to the increased use of intravascular devices that lead to turbulent flow, endothelial injury, and vascular stenosis.
Gender Ratio	<ul style="list-style-type: none"> • Not gender specific
Age Predilection	<ul style="list-style-type: none"> • Not related to age
Risk Factors	<ul style="list-style-type: none"> • Intrathoracic malignancies (non-Hodgkin lymphoma) • Thrombosis (due to intravascular devices) • Infection (syphilis and tuberculosis) • Post-radiation fibrosis • Mediastinitis
Treatment	<ul style="list-style-type: none"> • Treatment is relieving the SVC stenosis or obstruction and to treat the underlying disorder • Removal of intravascular device • Radiation with or without chemotherapy • Regional thrombolytic therapy and/or anticoagulation • Endovascular therapy including balloon angioplasty and/or stenting
Prognosis	<ul style="list-style-type: none"> • Prognosis is determined by the underlying cause of SVC syndrome. • Mortality is most affected by the underlying cause of SVC syndrome and not the syndrome itself • Without treatment, superior vena cava syndrome is associated with a 10-20% mortality within 6 months
Imaging Findings	<ul style="list-style-type: none"> • Chest X-ray: may be normal or reveal superior mediastinal widening or a tumor in the lung. An enlarged mediastinal shadow is not uncommon. Pleural effusions may be present. • Doppler US: Acute, expansile thrombosis in the internal jugular, subclavian, and brachiocephalic veins is common. The SVC is often not visible with US. • CT: superimposed thrombosis, a mediastinal mass or lymphadenopathy, collateral vessels and associated lung masses • MRI: same as CT • Venography: Occlusion of the SVC often with mediastinal and paraspinal collaterals connecting to the azygos and hemiazygos veins.

Table 1: Summary table for superior vena cava syndrome in children.

Differential Diagnosis	X-ray	US	CT/MRI	Angiography
Acute thrombogenic superior vena cava syndrome	Non-specific, but the study may be normal with no differential	All causes for thrombosis must be considered, including genetic thrombophilias, tumor, and vascular stenosis	Anatomic variant (left SVC), acute on chronic thrombosis, intra-cardiac tumor	Same as CT/MRI
External compression of the superior vena cava	If mediastinum is widened, then the differential includes mediastinal mass, primary lung tumor, or fibrosing mediastinitis causing external compression of SVC	Likely will have no additional findings other than venous thrombosis	Mediastinal mass, primary lung tumor, fibrosing mediastinitis	Same as CT/MRI

Table 2: Differential Diagnosis table for superior vena cava syndrome.

ABBREVIATIONS

CVC: central venous catheter
 SVC: superior vena cava
 tPA: tissue plasminogen activator

KEYWORDS

superior vena cava syndrome; pediatric interventional radiology; balloon-expandable stents; percutaneous venous stenting; long-standing central venous access

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