

Superior Vena Cava Syndrome

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Superior vena cava syndrome (SVCS) was first described in 1757 in a patient with a syphilitic lesion of the aorta.¹ The causes of SVCS have changed since that time. In the 1950s, SVCS was primarily caused by aortic aneurysm and infections such as tuberculosis and fibrous mediastinitis. In the 1980s and 1990s, malignant disorders have become the dominant cause of SVCS. In most patients with SVCS, primary malignancies of the mediastinum are the causative factor. Benign disorders account for less than 10% of cases of SVCS. Modern antibiotic treatment of infectious disorders is postulated to be the cause of the changing etiologies of SVCS.²⁻¹¹ This article reviews the anatomy of the superior vena cava and the pathophysiology, malignant and benign causes, clinical presentation, and diagnosis of SVCS. Treatment and prognosis are also discussed.

ANATOMY OF THE SUPERIOR VENA CAVA

The superior vena cava is a thin-walled, readily compressible vessel that transmits blood to the heart at low pressure. The superior vena cava is located in the middle mediastinum and is encircled by rigid structures, including the trachea, right bronchus, aorta, thymus, and pulmonary artery. The superior vena cava extends approximately 8 cm from the innominate vein to the right atrium. The distal 2 cm of the superior vena cava are within the pericardial sac. The azygous vein enters the superior vena cava posteriorly and is a significant venous collateral channel. Encircling the superior vena cava are subcarinal, perihilar, and paratracheal lymph nodes. These nodes drain the right lung and the lower lobe of the left lung.²⁻⁴

PATHOPHYSIOLOGY

Any pathology of the previously noted structures produces external pressure on the superior vena cava or internally obstructs the vessel as a result of either thrombosis or direct invasion by the disease process. In addition, enlargement of the lymph nodes may also compress the superior vena cava. In most cases, extrinsic compression develops gradually and the symptoms are initially mild because collateral circulation has sufficiently developed. If the obstruction develops sudden-

ly, as in the case of a malignancy, the collateral circulation has not developed and the patient rapidly becomes symptomatic. Thrombosis of the superior vena cava may progress to involve all the major collateral vessels, and the resulting thrombosis eventually undergoes fibrosis that results in permanent occlusion of the superior vena cava. In this case, thrombolytic therapy is of little or no benefit unless the treatment is directed at the primary cause of SVCS.

MALIGNANT AND BENIGN CAUSES

Malignant Causes

The most common malignancy associated with SVCS is lung cancer, followed by lymphomas and metastatic tumors to the mediastinum (**Table 1**).

Lung tumors. Approximately 5% to 15% of patients with bronchogenic carcinoma develop SVCS. The syndrome is four times more likely to occur in patients with right-sided tumors of the thoracic cavity. These lesions often cause obstructive pneumonitis, which usually occurs with involvement of right hilar and mediastinal lymph nodes. Among the types of lung cancers, all histologic cell types are associated with SVCS.

Lymphomas and metastatic tumors. The second group of malignancies that commonly cause SVCS are lymphomas, especially non-Hodgkin's lymphoma. SVCS occurs in 3% to 8% of patients with lymphoma. The lymphoma usually originates in the anterior mediastinum and produces SVCS by external compression. Metastatic tumors, more commonly breast and testicular tumors, cause SVCS in approximately 5% to 20% of patients.²⁻⁹

Benign Causes

Many benign disorders can cause SVCS (**Table 2**). As noted previously, however, benign disorders account for less than 10% of cases of SVCS. Benign causes of SVCS include thymoma, cystic hygroma, benign cystic teratoma, substernal thyroid goiter, dermoid cyst, and postirradiation therapy. Infections notable for causing SVCS are tuberculosis, histoplasmosis, actinomycosis,

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Table 1. Malignant Causes of Superior Vena Cava Syndrome

Malignancy	Histologic Subtypes
Lung cancer	Small cell
	Large cell
	Adenocarcinoma
	Undifferentiated
Lymphoma	Lymphoblastic
	Lymphocytic
	Mixed
	Nodular
Metastatic tumor	Non-Hodgkin's
	Breast
Other malignancy	Testicular
	Kaposi's sarcoma

syphilis, and pyogenic infections. In addition, the increased current use of invasive monitoring devices, such as central lines, cardiac pacemakers, catheters for total parenteral nutrition, and Swan-Ganz monitoring devices, is associated with increasing reports of thrombosis of the superior vena cava. Finally, aneurysms of the aorta and aortic branches are occasionally responsible for causing SVCS.²⁻⁹

CLINICAL PRESENTATION

The typical symptoms of SVCS are most obvious when obstructive disease is almost complete. Patients with SVCS most often present with complaints of facial edema and erythema, swelling of the neck and/or arms, and visible dilatation of the veins in the upper extremity. Patients with SVCS may also complain of dyspnea, persistent cough, and orthopnea. As the disease progresses, the symptoms may include hoarseness, peri-orbital edema, dysphagia, headaches, dizziness, syncope, lethargy, and chest pain. Other findings may include confusion and laryngeal and/or glossal edema.

In some cases, the nerves that cross the superior mediastinum (ie, vagus and phrenic nerves) are affected by SVCS. This nerve involvement can lead to hoarseness and paralysis of the diaphragm. These symptoms may be worsened by positional changes such as bending forward, stooping, or lying down. Patients with SVCS and vagus or phrenic nerve involvement find significant symptom relief when they are in an upright position, and many of these patients sleep in a chair to avoid dyspnea.

Table 2. Benign Causes of Superior Vena Cava Syndrome

Infectious
Tuberculosis
Histoplasmosis
Actinomycosis
Syphilis
Pyogenic
Tumors
Cystic hygroma
Substernal goiter
Teratoma
Thymoma
Dermoid cyst
Cardiac
Atrial myxoma
Pericarditis
Intrapericardial band
Mitral stenosis
Complication of central catheter
Complication of congenital heart surgery
Complication of total parenteral nutrition line
Vascular
Aortic aneurysm
Arteriovenous fistula
Polycythemia
Idiopathic thrombosis
Other causes
Sarcoidosis
Postirradiation
Mediastinal hematoma
Pneumothorax
Behçet's disease

The venous hypertension associated with SVCS can sometimes produce cerebral vessel thrombosis and hemorrhage with dire results. Of all the symptoms of SVCS, the most life-threatening complications are cerebral or laryngeal edema.²⁻¹⁰

DIAGNOSIS

The diagnosis of SVCS can be made simply on physical examination. In cases in which the extent of disease

Table 3. Findings on Chest Radiography in Patients with Superior Vena Cava Syndrome

Mediastinal widening
Pleural effusion(s)
Right hilar mass
Bilateral lung infiltrates
Cardiomegaly
Calcified paratracheal lymph nodes
Anterior mediastinal mass

Adapted with permission from Parish JM, Marschke RF Jr, Dines DE, Lee RE: Etiologic considerations in superior vena cava syndrome. *Mayo Clin Proc* 1981;56:407-413.

is minimal, the physical findings may not be prominent and the diagnosis may be more difficult to establish. Today, establishing the underlying diagnosis and etiology of SVCS has become more important because certain disorders that cause SVCS may be more amenable to specific treatment regimens. For example, small cell lung carcinoma and lymphoma respond dramatically to chemotherapy/irradiation, whereas thrombosis from a central line catheter does not respond to this treatment.⁴⁻¹²

Laboratory Studies

Chest radiography. The initial diagnostic test for suspected SVCS is chest radiography. Although this test is not specific for SVCS, chest radiography may be helpful in identifying the cause of the disorder. Findings on chest radiography that may be helpful include widening of the superior mediastinum, pleural effusions, and a hilar or mediastinal mass, usually on the right side (Table 3). These radiologic findings usually suggest an underlying malignancy, whereas calcified lymph nodes may be more predictive of granulomatous disease. However, the results of chest radiography may appear normal despite an obstruction in the superior vena cava. In the absence of previous catheterization or surgery, a normal result on chest radiography in a patient with SVCS is almost pathognomonic of chronic fibrous mediastinitis.²⁻¹²

Contrast venography. The extent and site of obstruction as well as the nature of obstruction must be identified when SVCS is diagnosed. Identification of these features may be achieved by a number of radiologic imaging studies. Contrast venography can provide information regarding the patency of the superior vena cava, the degree of superior vena cava obstruction, and the differentiation between intrinsic and extrinsic causative factors responsible for the obstruction. Contrast

venography also provides assessment of collateral vessel formation, the degree of venous distension of the neck and arms, measurement of actual venous pressure, and the presence of the internal jugular vein reflux.

Contrast venography is essential prior to planning any surgical bypass operation. Surgical bypass operations are easier to accomplish when the brachiocephalic veins are not involved. However, if all the intrathoracic veins are obstructed, extrathoracic bypass operations can be undertaken, but the operation is more technically difficult and the results are less favorable.⁴

Contrast venography is also very helpful in documenting obstructions caused by thrombus formation. When thrombosis is present, treatment with fibrinolytic agents (eg, urokinase, streptokinase) is pursued and repeat venography can be used to evaluate treatment efficacy. In the rare cases in which fresh thrombosis is detected in the superior vena cava, thromboembolectomy may be an alternate method of treatment.

Radionuclide venography. Radionuclide venography can also be used to diagnose SVCS. This test is less invasive than contrast venography but is also less specific in defining patency and flow. Radionuclide venography may be of value in long-term follow-up studies.

Computed tomography scanning. Computed tomography (CT) scanning provides an effective, non-invasive evaluation of the superior vena cava and its collateral circulation. CT scanning provides anatomic details of the mediastinal and thoracic organs, allows identification of the cause and extent of the obstruction, documents collateral circulation, provides guidance for percutaneous biopsies, and guides the formulation for radiotherapy.²⁻⁶

Magnetic resonance imaging. Magnetic resonance imaging (MRI) is also used extensively in the diagnosis of SVCS, and this test is often very important in determining the cause of SVCS. Although the collateral circulation is easier to detect by CT scan, MRI, by virtue of its multidimensional capabilities, shows the relationships of vessels, lymph nodes, and other mediastinal structures better than the information provided by CT scanning.²⁻⁷

Diagnostic surgery. When all other diagnostic procedures fail to provide information about the cause of SVCS, surgery may be the last alternative. Exploratory thoracotomy is successful in obtaining diagnostic tissue in patients with SVCS in virtually every case. A surgical approach has several advantages—surgery allows direct visualization of the underlying disease process, assessment of the extent of disease involvement, and accessibility for tissue biopsy. However, compared to the previously described diagnostic methods, this procedure is the most invasive and is associated with increased risks.²⁻¹⁰

Other diagnostic techniques. Other diagnostic techniques used in the evaluation of SVCS include bronchoscopy, retinoscopy, cell cytology, and mediastinoscopy. In each case, the risks of intervention, such as bleeding and perforation of the collateral circulation, should be carefully weighed against the benefits for and safety of the patient. Today, SVCS is seldom a medical emergency and all efforts should be made to identify the etiology. Although the specific etiology of SVCS can be obtained by tissue diagnosis in a few cases, this procedure may be difficult and even hazardous to the patient.

TREATMENT

Depending on the underlying condition, multiple treatment options are available for superior vena cava obstruction.^{1, 9-19} The primary treatment options include radiation, chemotherapy, thrombolytic therapy, anticoagulation, stents and balloon angioplasty, and surgery.

Radiation

Indications. The majority of cases of SVCS are caused by malignancy; thus, most patients receive radiation treatment at some point in their illness. Emergency radiation treatment has been administered to some patients with life-threatening cerebral or laryngeal edema prior to a tissue diagnosis of malignancy. The relief of obstructive symptoms by radiation therapy may provide sufficient time to work up the cause of SVCS, thus allowing for more specific treatment. Radiotherapy for the treatment of a thoracic malignancy or lymphoma may be appropriate, whereas radiotherapy for the treatment of an underlying thrombosis or granulomatosis causing the obstruction would be inappropriate. Therefore, delaying treatment for 1 to 2 days if necessary to establish a firm tissue diagnosis is appropriate.

Dosage. Radiation treatment is initiated at high-dose fractions daily for the first few days. This treatment regimen is usually followed by conventional low daily doses. The total dose is dependent on the underlying tumor histology. Lymphomas are generally treated with 3000 to 4000 cGy, whereas carcinomas require 4000 to 5000 cGy or more to achieve control. Lower doses of radiation treatment may be considered in cases in which systemic disease is present and short-term palliation is the goal. Because of the limited tolerance of the heart and spinal cord to radiation, short duration, high-dose programs are used. Physicians must be aware of this dosage intensity in treating patients who are receiving chemotherapeutic agents such as doxorubicin, which can enhance radiation toxicity.⁹

Response to treatment. The response to radiation in most patients occurs within 3 to 4 days. Resolution of facial edema and venous distension of the upper extremities in addition to radiographic improvement occur within 1 to 3 weeks. Radiation therapy is usually not effective when thrombosis is causing the occlusion, which emphasizes the importance of a complete and thorough evaluation of the venous system in the diagnostic workup of SVCS. When radiation therapy is successful, prolonged survival has been reported, especially in cases in which full courses of treatment are completed. Of all patients with SVCS with malignancies, 10% to 20% survive more than 2 years.

Side effects. Radiation therapy is associated with a number of complications that include persistent fever, bleeding or superior vena cava perforation at the site of tumor invasion, nausea, vomiting, anorexia, leukopenia, hemoptysis, skin irritation, and esophagitis. Pulmonary or mediastinal fibrosis may also occur as a late complication.^{5,8,9}

Chemotherapy

Chemotherapy may be used as a primary therapy or as an adjunct to radiotherapy for the treatment of SVCS, depending on the underlying etiology of the obstruction. The treatment of choice for SVCS caused by mediastinal lymphoma is a combination of chemotherapy and radiotherapy.

Thrombolytic Therapy

The role of thrombolytic therapy and subsequent anticoagulation for SVCS has become increasingly important within the past decade. Pericatheter thrombosis has been demonstrated by venography in approximately 50% of non-anticoagulated patients with long-term central venous catheters. Depending on the acuteness or chronicity of the thrombosis, thrombolytic therapy can be used. In patients with an acute occurrence, thrombolytic therapy can achieve excellent results.¹

Anticoagulation

Patients with SVCS are at increased risk for deep vein thrombosis and pulmonary embolism. In patients for whom thrombosis is the cause of SVCS, anticoagulation therapy should be administered after successful thrombolytic treatment. Once the symptoms subside after thrombolytic therapy, anticoagulation should be maintained as long as the central venous catheter is present. Recently, low dose warfarin has been noted to significantly decrease thrombosis in patients with central venous catheters.⁸

Stents and Balloon Angioplasty

Recent advances in interventional radiology have contributed expandable wire stents and balloon angioplasty. These stents can be placed across the stenotic portion of the vena cava. The stents have little thrombogenic potential and usually remain widely patent without narrowing for months. Today, placement and use of stents is limited when intraluminal thrombosis is present. However, after thrombolytic therapy, stent placement has been noted to be a more successful approach. After stent placement, patients experience instantaneous relief of symptoms. The placement of stents is performed under local anesthesia by radiologists. The placement of a stent appears to be suitable therapy for the palliation of the symptoms of SVCS in cases for which other therapeutic modalities cannot be used or are ineffective.¹¹ For localized lesions, balloon angioplasty with or without stenting has also been shown to significantly reduce the symptoms of SVCS.

Surgical Treatment

Surgical bypass is an additional alternative to relieve SVCS. The surgical option is usually recommended to patients with benign disease and to only a few patients with malignancy. Patients selected for surgery should have the venographic sign of total superior vena cava obstruction associated with thrombosis of caval branches and distension of the veins of the upper extremity. Surgery in cases of fibrosing mediastinitis can be extremely complicated. Because of the gradual onset of this disorder, the collateral circulation is extensive and serious bleeding can occur if any of these vessels is transected. In addition, because of the associated venous hypertension, all the collateral circulation is under high pressure.

The advantages of surgery are the expeditious and definitive removal of the obstruction and the convenience of direct tissue diagnosis. Venous thrombectomy may be indicated in select patients with catheter-induced thrombosis of the superior vena cava when the foreign material can be removed in addition to the obstructing catheter. However, most data after surgical bypass are obtained from patients soon after surgery. Long-term results after surgical bypass are lacking, chiefly because most of these patients have a malignancy and their life expectancy is short.^{1, 11-17}

Other Treatment Options

Additional measures used to treat SVCS include the administration of steroids or diuretic agents and salt restriction. Diuretic agents may provide symptomatic

relief of edema; this relief is often immediate but not long term. Steroids are useful in the presence of respiratory compromise but the long-term use of steroids may be considered harmful because of significant side effects.

PROGNOSIS

The prognosis of SVCS depends on the underlying obstruction. Malignancies of the mediastinum are the most common cause of SVCS today, and the overall prognosis for these patients is poor. In past studies, the average survival time for patients with SVCS caused by malignancies of the mediastinum has been approximately 6 to 9 months. Most patients with SVCS can be successfully managed with medical or radiation therapy. For patients with severe unremitting symptoms caused by malignant disease, thrombolysis, balloon angioplasty, and stenting appear to be clinically acceptable forms of therapy. Surgical bypass is primarily reserved for the few patients with persistent symptoms of SVCS secondary to a benign pathology. **HP**

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