Oncological emergencies: Superior vena cava syndrome

Superior vena cava obstruction leads to the venous hypertension of the head, neck, upper extremities and upper part of the truncus. Its clinical manifestation, known as the superior vena cava syndrome, is a complication of malignancy, mainly of lung cancer and lymphoma. As it usually affects patients with advanced disease, the prognosis is poor. This article stresses the importance of early detection and adequate management of this oncological emergency. The diagnostic tools as well as treatment possibilities are discussed.

What is the Superior Vena Cava Syndrome?

The term superior vena cava syndrome (SVCS), introduced in 1865 by Trousseau, encompasses a range of signs and symptoms arising from obstruction or direct invasion of the superior vena cava (SVC) [1,2]. The SVC carries blood from the head, arms and upper torso to the heart. The blocked venous drainage leads to pleural effusions and edema of the face, neck, trachea and arms. Severe obstruction may cause cerebral edema with focal neurologic signs and unconsciousness as well as impaired cardiac filling [3].

Etiology

Over 90% of SVCS cases are caused by malignancies and are therefore cancer-related. Other causes include mediastinal fibrosis, vascular diseases (for example aortic aneurysm), infections (such as histoplasmosis, tuberculosis, syphilis, and actinomycosis) and benign mediastinal tumors. Among these the most frequent are: teratoma, cystic hygroma, thymoma, and dermoid cyst. SVC may also be a result of thrombosis from central venous catheters or cardiac pacemakers [4]. Over the last two decades, the benign causes have been reported to stand for more cases of SVCS than previously when the intravascular devices were uncommon [5].

Among the patients with malignancies, SVCS most often affects males aged 50-70 with primary or metastatic tumors of the mediastinum [6]. Advanced small-cell lung carcinoma and – less frequently – advanced non-small-cell lung carcinoma stand for 75% of all cases of SVCS. Next most common cause of the SVCs lymphoma (usually non-Hodgkin) with perihilar lymphadenopathy, that accounts for around 12% cases.


Among other malignancies causing the SVC obstruction metastases from different locations, germ cell cancers, thymoma and mesothelioma should be mentioned. Due to their anatomic proximity to the SVC, right-sided lesions are related to a higher risk than left-sided tumors [6].

Patophysiology

The SVC is located inside the rigid walls of the thoracic cavity, surrounded by inflexible structures such as the sternum, ribs, vertebral bodies, and aorta with its high intravascular pressure. Figure 1. shows the anatomic drainage of the SVC. The SVC is usually situated close to the right main bronchus. As a thin-walled structure with low intravascular pressure in a tight, non-expanding compartment, SVC can get easily compressed by extraluminal tumor or enlarged lymph nodes. SVCS may also be a result of intraluminal obstruction by thrombosis or tumor. The symptoms can occur rapidly or gradually and there can be a complete or partial obstruction. In some cases, the collateral venous drainage may develop. The blockage develops gradually and a minimal blood flow remains in most SVCS cases [1].

The development of SVCS depends on several factors, such as the hypercoagulable state in patients with cancer, the growth rate, extent and localization of the tumor, flow in the azygos vein and the ability to form collateral circulation [1]. Blood from the upper thoracic venous system may be redirected to the azygos vein, internal mammary veins, thoracic venous system, and vertebral veins [6]. The subcutaneous veins may also play a role in the formation of collateral circulation [7]. The extent of SVCS depends on the level of obstruction – if the drainage is impaired above the azygos vein, the pressure in the
SVC is lower and the symptoms are less significantly demonstrated.

**Symptoms**

The severity of symptoms of SVCS depend on the speed of the SVC obstruction development. With a gradual progression the clinical manifestation is mild [8]. Patients complain of swelling of the face, neck and arms, especially in the morning after sleeping in the supine position or upon position changes such as bending forward [1]. Distended neck and chest veins and facial plethora are often striking, but generally of little consequence. Figure 2 shows the dilatation of the vessels of the upper chest due to the development of the collateral drainage. If the development of the disease is acute, patients suffer from neurological and respiratory distress. Dyspnea and cough are the most frequently reported symptoms among patients with SVCS. They also complain of hoarseness and stridor. Severe edema of the larynx may be life-threatening as it makes intubation impossible. Neurologic symptoms include headache, syncope, dizziness and confusion. Cerebral edema may also be observed and lead to cerebral ischemia, herniation or even death. Typical symptoms of SVCS are listed in Table I [9,7].

**Diagnosis**

Patient evaluation should begin with a history and a thorough physical examination, which play a fundamental role in establishing a tentative diagnosis of SVCS. In most cases, symptoms of the SVCS progress over several weeks and get better over time. Further investigation allow the identification of SVCS causes. Chest computed tomography scans (CT) with contrast enhancement and chest magnetic resonance imaging (MRI) are the preferred radiological tools used to confirm SVC obstruction [9,11]. Chest X-rays may sometimes also be useful showing a lung or mediastinal mass and superior mediastinal widening [10].

The histological diagnosis is crucial. Invasive procedures are performed to collect tumor samples. These procedures are usually connected with a high risk of bleeding because of increased venous pressure in the head and neck [12]. The procedure should be adjusted to the type of tumor (e.g., mediastinoscopy is well established in the diagnosis of lung cancer) [13]. Bronchoscopy with brushings and biopsy of lymph nodes is also valuable [1]. In the case of pleural effusion, thoracentesis should be considered [12]. If the underlying malignancy tends to involve bone marrow, like in Hodgkin’s lymphoma or non-small-cell lung carcinoma, bone marrow biopsy may prove useful [7].

**Management**

The way of treatment depends on the reason for SVC obstruction. In the case of a malignancy-related syndrome, management includes treatment of the neoplasm itself and relief of the symptoms of SVCS. It should also be adjusted to the patient’s performance status, the severity of symptoms, the presence of thrombosis and comorbidities. Radiotherapy, chemotherapy and surgery are the main therapeutic options [6]. Radical treatment may be attempted especially in such cases as the small-cell lung carcinoma, Hodgkin’s lymphoma and germ cell tumors [1].

In life threatening cases emergency treatment should be started as soon as possible [3].

Radiotherapy is the most common treatment modality for the patients suffering from lung cancer [14]. The irradiated field should include the tumor mass with adequate margins and the mediastinal and hilar lymph nodes [15]. Daily radiation dose is 400 cGy administered for 5 consecutive days [16]. Radiotherapy is associated with significant clinical improvement, noticeable much sooner than the objective signs in radiological examinations [3]. Symptoms could be reduced after only several days [6]. The side effects depend on the irradiated field, the total dose of the radiation therapy and the patient’s general condition [17]. Fatigue, dyspnoea, cough, pneumonitis, pharyngitis, esophagitis, skin changes are the most common side effects [18].

The histological diagnosis of malignancy

**Table I**

Typical symptoms of the SVCS.

<table>
<thead>
<tr>
<th>Symptoms of SVCS</th>
<th>Cardiologic</th>
<th>Neurologic</th>
<th>Pulmonologic</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain</td>
<td>Seizures</td>
<td>Dyspnoea</td>
<td>Edema of the face, neck, upper thorax, breasts, arms and fingers</td>
<td></td>
</tr>
<tr>
<td>Tachycardia</td>
<td>Stupor, coma</td>
<td>Orthopnoea</td>
<td>Dilatation of the vessels of the upper chest</td>
<td></td>
</tr>
<tr>
<td>Jugular vein distention</td>
<td>Headache</td>
<td>Tachypnoea</td>
<td>Dysphagia and hoarseness</td>
<td></td>
</tr>
<tr>
<td>Cyanosis of the upper part of the body</td>
<td>Visual disturbances</td>
<td>Pleural effusion</td>
<td>Periorbital edema and engorged conjunctivae</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
<td>Nonproductive cough</td>
<td>Facial plethora</td>
<td></td>
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<tr>
<td></td>
<td>Syncope</td>
<td>Psychiatric changes</td>
<td></td>
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Figure 1

Venous drainage of the SVC.

Drenaż żył SVC.

SVC – superior vena cava
RBC – right brachiocephalic vein
LBC – left brachiocephalic vein
AV – azygos vein
HAV – hemiazygos vein
AHAV – accessory hemiazygos vein
Yellow – normal variants of venous connections

Figure 2

Dilatation of the vessels of the upper chest (collateral drainage).

Poszerzenie żył widoczne w górnej części klatki piersiowej (krążenie oboczne).
is required to initiate chemotherapy which is used to treat chemosensitive tumors, such as small-cell lung carcinoma or lymphoma. Systemic treatment of small-cell lung carcinoma is based on cisplatin with etoposide. Taxanes, anthracyclics, alkylating agents and nucleoside analogs may also be used [19]. In the case of non-Hodgkin’s lymphoma, the schedule of chemotherapy depends on the immunohistological diagnosis. In some cases, monotherapy with an alkylating agent or nucleoside analog may prove sufficient. In other cases, polychemotherapy with alkylating agents, anthracyclics, vinca alkaloids and immunomodulators is administered [20]. Symptoms relief is usually reported in 1–2 weeks after the first cycle of chemotherapy [7]. Combined chemoradiotherapy may also be considered provided that the tumor is radiosensitive [21].

Chemotherapy is also applied to patients with non-small cell lung carcinoma who have already received the maximum dose of radiotherapy to the mediastinum [22].

Surgery can be either minimally invasive like coronary intravascular stent placement, or an open-chest operation. Intravascular stenting is safe and provides the most immediate relief. It can be accomplished even if there is complete SVC obstruction or thrombosis. That is why percutaneous placement of the intravascular stent is the preferred first-line intervention. Anticoagulation is usually recommended after intravascular stent placement [23]. Angioplasty is typically performed in preparation for stenting as itself it does not prevent recurrences [24]. Complications of stenting such as occlusion, infection, pulmonary embolus, stent migration, haematomas at the insertion site, bleeding and perforation have been reported in 3–7% cases. Surgical bypass is rarely performed due to the success of endovascular devices, but when it is the treatment of choice, it is associated with few complications and good effectiveness. Sometimes, SVC gets locally resected and a reconstruction with a venous patch or graft replacement is carried out. Grafts are made of Dacron and polytetrafluoroethylene or they are autologous from saphenous vein. Surgical thrombectomy, stent angioplasty, angioplasty and thoracotomy with or without extensive resection and reconstruction of the SVC are also performed. The operative mortality of 5% and the patency of 80–90% are reported [25].

Pharmacotherapy is helpful in relieving symptoms. Corticosteroids should be administered in order to reduce edema and inflammation around the tumor. However, their effectiveness is controversial [26]. Diuretics may also prove useful, but they need to be administered very carefully for the risk of decreased vascular volume and hypovolemic shock [27]. Medical management of SVCS includes also the thrombolytic therapy used to treat intraluminal thrombosis. Tissue plasminogen activators can effectively lyse clots. In the case of catheter-induced thrombosis, the intravascular devices should be immediately removed [28]. Anticoagulants should also be prescribed to the patients with cancer-related SVCS as the presence of malignancy is a potential risk factor for thrombosis [29]. Attention must be paid to the risk of hemorrhage.

Authors want to stress the importance of early detection of the first signs of SVCS. It allows time for the final histological diagnosis which determines adequate treatment modality. In fact, the entire medical staff should assume a proactive role and ask patients at risk about the typical symptoms of SVCS. Diagnosing this syndrome is a challenge not only for general practitioners, medical oncologists, palliative care specialists and radiologists but also the remaining personnel.

Summary

SVCS is an emergency in oncology, resulting from compromised blood flow through the SVC. The treatment modality depends on the histological diagnosis. Radiation therapy, chemotherapy and surgery are the treatment options. Unfortunately, there are no evidence-based guidelines on how to manage SVCS. Most data come from case series. The prognosis is poor and the average life expectancy is 6 months [30]. To sum up, it is important to prevent SVCS development by early diagnosis and efficient treatment of cancer. Nevertheless, if it does arise, it should be promptly diagnosed and treated. That is why all the physicians have to take it into account while making the differential diagnosis, especially among the patients with cancer.

Acknowledgements

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References