REVIEW ARTICLE

Superior Vena Cava Syndrome – Possibilities of Intervention Therapy

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SUMMARY

Superior vena cava syndrome is a relatively frequent complication in patients with lung or mediastinal malignant disease. Standard treatment is usually based on radiotherapy or chemotherapy. During the last 20 years endovascular methods such as stent implantation and local thrombolysis have been increasingly employed, being more effective in the treatment of superior vena cava obstruction or stenosis.
Key words: superior vena cava syndrome, stent, thrombolysis. *Be*

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Superior vena cava syndrome is a complex of symptoms caused by deterioration of blood flow through the superior vena cava (SVC) to the right heart atrium, resulting in congestion of blood in the upper part of the body. The syndrome was first described by William Hunter in a patient with an aortic aneurysm in 1757 (1).

ANATOMY OF THE SUPERIOR VENA CAVA

SVC is a thin – walled vessel about 6-8 cm long, situated in the upper mediastinum. It is formed by the joining of two brachiocephalic veins and flows to the right atrium. It is in close contact with the trachea, right bronchus, aorta, pulmonary artery and thymus. It is also surrounded by lymph nodes. Dorsally, the azygous vein flows into the SVC and may represent an important collateral circulation if the SVC is obstructed (2, 3).

ETIOLOGY

The causes of superior vena cava obstruction have changed during the years. While until the first half of the last century the syndrome was mainly caused by the pressure of tuberculous or syphilitic aortic aneurysms (4), nowadays more than 80 % of SVC syndromes are triggered by an advanced malignant disease, most frequently by bronchogenic carcinoma and particularly its small–cell type, by non-Hodgkin lymphoma (NHL) and by metastatic mediastinal tumours (5, 6). Thyroid carcinomas and thymomes are more rare causes. SVC syndrome may be caused either by an external SVC compression, or possibly by a stenosis-related thrombosis or a direct infiltration of a tumour into the vessel. Approximately 5-15 % of patients with bronchogenic carcinoma and 3-8 % of patients with NHL develop SVC syndrome (7). Benign etiology is a more rare cause of SVC syndrome, occurring in approximately 15-20 % of all cases (6, 7), but considering the increasing frequency of central venous catheters and stimulating electrodes implementing, SVC thrombosis related to venous catheters and cardiostimulating electrodes is not infrequent. On the other hand, mediastinal fibrosis is a less common cause, resulting most often from previous lung and mediastinal radiotherapy (8).

CLINICAL PICTURE

SVC syndrome symptoms follow from the venous congestion in the drained areas. The seriousness of the syndrome depends on its onset rapidity and on the duration of the SVC obstruction, as well as on the related possibility of the dilatation of collateral circulation. Moreover, it depends on the location of obstruction. If there is a stenosis or obstruction above the azygous vein ostium, the collateral flow is ensured via this vein contrary to the obstruction below the azygous vein ostium (9).

Venous hypertension can produce headaches, a feeling of pressure in the neck and head, dizziness, syncopes and coughing. There may be other apparent symptoms of SVC syndrome, such as oedemas of the face, neck and arms, a noticeable dilatation of neck and arms veins, lips and face cyanosis or even a coma in the final stage (10, 11).

DIAGNOSIS

If the syndrome is fully expressed, the diagnosis is already evident from the medical history and physical examination. The diagnosis can, however, be specified by a quantity of non-invasive and invasive examination methods.

An X-ray of the heart and lungs may reveal a widened mediastinum, pleural exudate and mediastinal or hilar tumour, particularly on the right side (6). Sometimes dilatation of the azygous vein can be apparent (12).

A Duplex ultrasonic examination is a non-invasive method that cannot picture the superior vena cava directly, but it well represents the subclavial and possibly brachiocephalic veins. On the basis of indirect signs, such as breathing variability of blood flow or dilata-

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tion during the Valsalva manoeuvre, a duplex ultrasonic examination can reveal suspicion of central obstruction.

Computer tomography (CT) is a non-invasive examination making it possible to display in detail anatomical structures, the cause and extent of obstruction and of the collateral circulation.

Nuclear magnetic resonance (NMR) provides a higher-quality image of anatomical structures than CT; however, in our context NMR availability is still limited, and it is contraindicated in patients with an implanted pacemaker.

Contrast phlebography remains the gold standard in diagnostics. It makes it possible to display the level and extent of the obstruction and of the collateral circulation, as well as potential presence of thrombi. In specialised departments an endovascular intervention can be carried out simultaneously. The phlebographic findings are the cornerstone of the Standford-Doty classification of the obstruction types: I. type: < 90 % SVC stenosis and a patent azygous vein, II. type: 90-100 % stenosis of SVC and a patent azygous vein, III. type: 90-100 % stenosis of SVC with a reverse circulation in a patent azygous vein and IV. type: occlusion of SVC and its supplying veins (3). The main disadvantage of a phlebographic examination is its invasive character and the necessity use of a contrast agent.

There are other alternatives of examination of the primary disease aetiology, such as bronchoscopy, pleural exudate puncture and mediastinoscopy.

TREATMENT

Treatment of the superior vena cava syndrome depends on the cause of obstruction, gravity of symptoms, the patient's prognosis and wishes.

Pharmacotherapy

In addition to the elevation of the upper part of the body, we use diuretics and corticosteroids to induce regression of the swelling and anticoagulant therapy to prevent thrombosis progression. This treatment, however, has very limited clinical effect (10, 13).

Radiotherapy, chemotherapy

If the aetiogogy of the SVC syndrome is a malignancy, radiotherapy, chemotherapy or a combination of the two - depending on the histological type of the tumour - form the basis of treatment. Most studies are aimed at bronchogenic carcinoma, which is the main cause of SVC stenosis or occlusion. Radiotherapy in radiosensitive and chemotherapy in chemosensitive tumours represents a standard treatment and brings symptomatic relief due to the reduction in tumour tissue volume. The effect of radiotherapy ranges from 46 to 90 % within 2 weeks (14-16) while the effect of chemotherapy oscillates between 62 to 80 % in the treatment of small-cell bronchogenic carcinoma (17, 18). Furthermore, a combination of both treatment methods can be used (17). Analysis from the Cochrane Clinical Trials Register including 2 randomised and 44 non-randomised studies of the treatment of SVC obstruction in bronchogenic lung carcinoma (and more particularly in its small-cell type) notes the effect of chemotherapy and/or radiotherapy on the regression of difficulties caused by the SVC syndrome in 77 % with recurrence in 17 %. In non-small-cell varieties of bronchogenic carcinoma chemotherapy and/or radiotherapy led to the regression of symptoms only in 60 %, with recurrence in 19 %. These traditional methods lead to a clinical effect with a delay of 2-4 weeks (17, 19, 20).

Surgical treatment

Until recently a bypass operation was the only alternative treatment in the event of failure of conservative therapy with a very good and long patency, and it still remains an alternative if there is failure of endovascular treatment or if a radical resection of a tumour can be effected. Owing to a very good and long patency – 88 % of patient bypasses with an average observation period of almost 11 years (20) – some authors prefer this method for cases of benign causes of the SVC syndrome (21-24). In patients suffering from a malignant disease that are in a general bad state, the necessity of sternotomy is the main inconvenience.

Stent implantation, local thrombolysis

The history of metal stents use in the superior vena cava started in 1986, when Charnsangajev carried out successful angioplasty of SVC for the first time, with a stent implantation in 7 dogs with the mediastinal fibrosis (25). Since then the method has become an appropriate alternative to a standard conservative treatment. Its technical success with a subsequent rapid clinical effect has ranged from 90 to 100 % in most of the published studies. In the above-mentioned meta-analysis from the Cochrane Clinical Trials Register, stent implantation led to a regression of symptoms in 95 %, with a recurrence of SVC syndrome in 11 %, but another recanalization was possible in most cases; therefore the long-term patency was 92 % (17). In the event of an extensive SVC thrombosis stent implantation is accompanied by local thrombolysis. In his study, Kee effected local thrombolysis in 27 patients with an acute SVC thrombosis of malignant etiology that in itself led to recanalization in 4 patients (15 %), while the remained patients underwent a stent implantation. During the local thrombolysis one patient with a small-cell carcinoma of lung died of pulmonary embolism of thrombotic and tuberculous masses (26). Other papers show a similar or better technical and clinical effect (27-31). The rapidity of endovascular therapy is also advantageous – the clinical effect comes in a short interval of 2-4 days (26-31). Local thrombolysis effected before proper stent implantation decreases the volume of thrombotic material that could embolise during the procedure. The dissolution of the thrombotic mass also reveals the cause of SVC obstruction, thus reducing the number and length of stents necessary for the recanalization of the obstruction - which, incidentally, brings a considerable economic benefit (26). The evident disadvantage of this therapy is an increased risk of bleeding complications in patients with an increased risk of potentially fatal bleeding due to their principal tumour disease. According to the published studies, fatal bleeding complications during the local thrombolysis occur in 0-5 %; only one small study with 10 patients noted a complication rate of 10 % (1 patient died) (26-31).

OWN EXPERIENCES

During the period of October 2002 to December 2004 three patients with acute superior vena cava syndrome of malignant etiology were admitted to the ward of angiologic intensive care of the 2nd internal clinic of cardiology and angiology, 1st Medical Faculty of Charles University in Prague. Two patients had already undergone unsuccessful treatment in another hospital – 1x systemic thrombolysis and 1x percutaneuous aspiration thrombectomy were performed without any considerable effect. The aetiology was as follows: a relapse of malignant thymoma, Ewing's sarcoma and stomach adenocarcinoma. SVC thrombosis in the patient with Ewing's sarcoma was associated with the central venous catheter.

Intervention performance

After sonographic or CT verification of the SVC obstruction, we bilaterally spiked the brachialis vein and inserted the 6F case by Seldinger method, in local anaesthesia under sonographic or X-ray control. Via the cases we performed a phlebography to reveal the character and the extent of the disease. The thrombosis and the com-

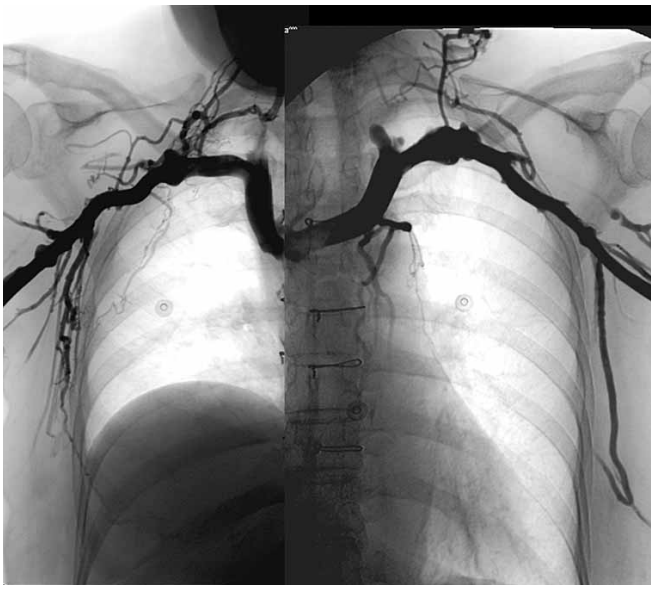

Figure 1. The first patient: phlebography from both brachial veins, a complete occlusion of SVC, there is a thrombus in a junction of brachiocephalic veins

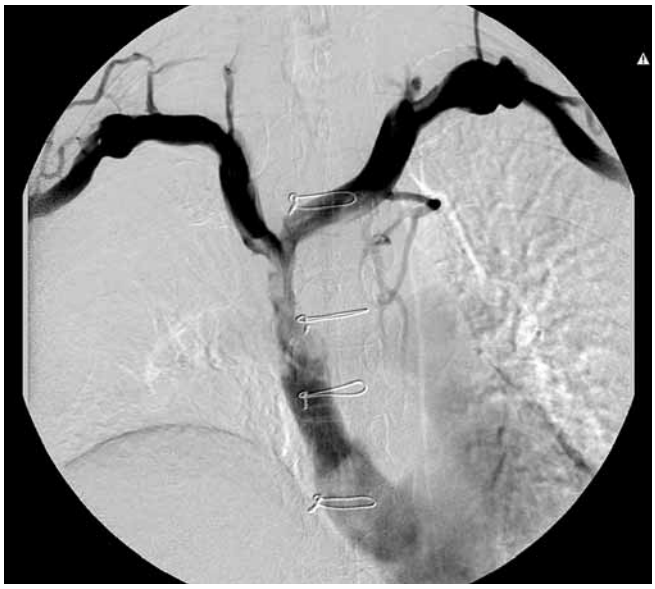

Figure 2. The first patient after 22 hours of thrombolysis (partial SVC recanalization with residual thrombi)

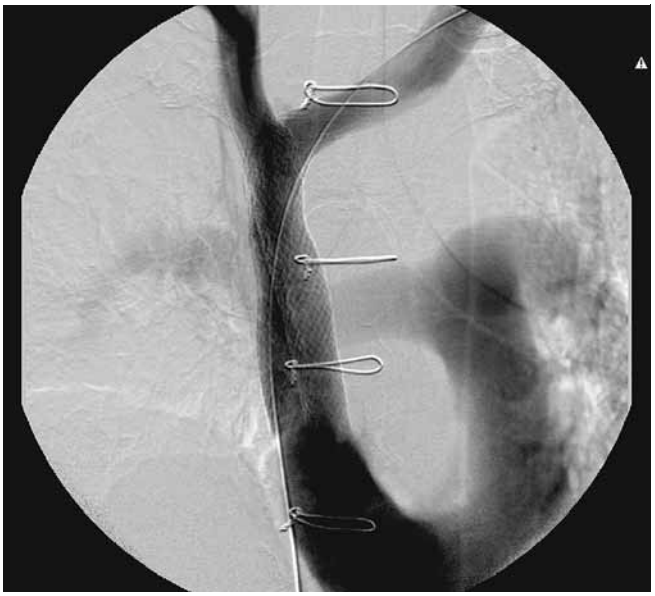

Figure 3. The first patient after 44 hours of local thrombolysis and implantation of 2 self-expanding stents

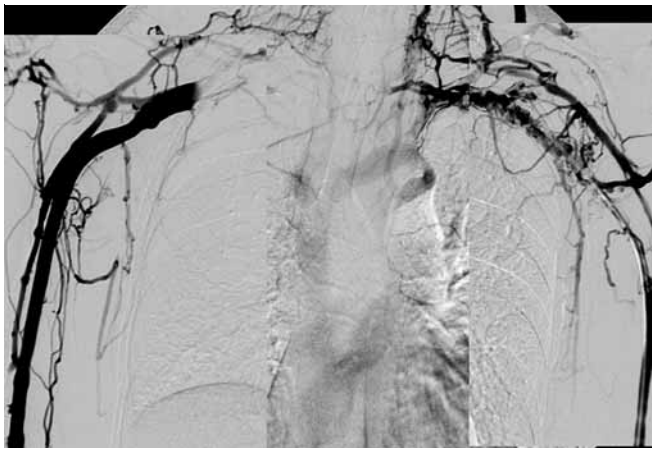

Figure 4. The second patient: phlebography from both brachial veins, thrombosis of axillar vein on the left, both subclavial veins and both brachiocephalic veins are occluded, the superior vein cava fills poorly

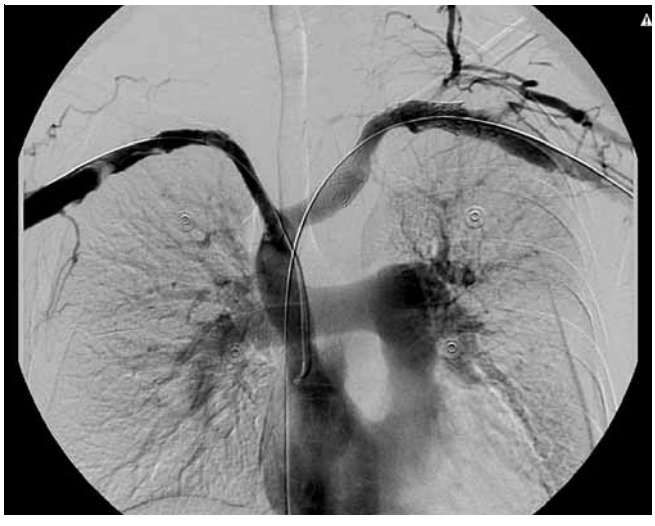

Figure 5. The second patient after 60 hours of local thrombolysis and bilateral implantation of 2 self-expanding stents on boundary of subclavial and brachiocephalic veins (residual thrombosis in the subclavial vein on the right, contrast agent however flows away very well from the periphery)

plete SVC obstruction were present in all three cases. The first patient had patent brachiocephalic veins (Fig. 1, 2, 3). The second patient had a thrombosis of both SVC and left brachiocephalic vein (Fig. 4, 5) and the third patient had a thrombosis of SVC, both brachiocephalic and subclavia veins and a unilateral thrombosis of the left axillaris vein. We administered Heparin 5000 U IV and via the cases, by means of soft hydrophilic conductors, we inserted local thrombolysis catheters with lateral orifices into the coagulum. We commonly use the recombinant tissue-plasminogen activator (rt-PA, Actilyse®, alteplasum) in the total dose of 1 mg/h into the catheters, and we applied heparin in an initial dose of 1250 U/h into the inserted case, with the dose adjustment according to APTT. The target value should be between 2-3 multiples of normal values. We performed a control phlebographic examination at intervals of 12 to 24 hours to consider the treatment effect and reposition of inserted catheters. The total time of local thrombolysis was on average 57.6 hours (38-60 hours); in one case the local thrombolysis alone led to

a complete opening of the venous vascular system, while in the two remaining cases an intervention performance followed – the implantation of stents into the SVC or into the brachiocephalic trunks and the subclavian vein. A quick regression of the swelling of the upper part of body and the regression of subjective symptoms came in all cases. In all patients we continued anticoagulant treatment by low-molecular heparin and a subsequent warfarinization after the performance. No complications appeared in our patients during the local thrombolysis and during their stay in our ward (on average 6.6 days). Subsequently 2 patients died during the following observation – one died of intracranial bleeding caused by brain metastases (using the therapy of low-molecular heparin) 2 weeks after the operation. The second patient died of the progression of his malignant disease after 3 months. The third patient has been without clinical signs of relapse of SVC syndrome, and the intervented veins have still been patent according to the executed examination as well.

CONCLUSION

Superior vena cava syndrome is a relatively frequent complication in patients with lung or mediastinal malignancy. The standard treatment on the basis of radiotherapy or chemotherapy is successful in a wide range of 45-80 %; however the clinical effect comes with a delay of 2-4 weeks. Endovascular treatment – stent implantation – is a highly effective method in short lesions, with a technical and clinical successfulness of 90-100 % and a quick effect. Local thrombolysis followed by angioplasty and possibly stent implantation is an appropriate method in an extensive thrombosis of SVC and other veins draining the upper part of body. The risk of fatal bleeding in local thrombolysis is 4-10 % according to the published papers. In contrast to radiotherapy, endovascular treatment allows reintervention in cases of relapse of SVC syndrome. The high cost of the intervention performance is a disadvantage, but it is still a fraction of sum expended for the total treatment cost of patients with the malignant disease.

The surgical treatment is an alternative for the cases of failure of conservative and intervention therapy or for patients with benign causes of the superior vena cava obstruction.

Abbreviations

aPTT – Activated Partial Tromboplastin Time
CT – computer tomography
SVC – superior vena cava
NHL – non-Hodgkin lymphoma
rt-PA – recombinant tissue-type plasminogen activator

LITERATURE

1. **Hunter, W.:** The history of an aneurysm of the aorta with some remarks on aneurysms in general. Med. Obs. Inq (Lond), 1757, 1, pp. 323-357.
2. **Skinner, D. B., Alzman, E. W., Scannell, J. G.:** The challenge of superior vena caval obstruction. J. Thorac. Cardiovasc. Surg., 1965, 49, pp. 8244-8253.
3. **Standford, W., Doty, D. B.:** The role of venography and surgery in the managment of patients with superior vena cava obstruction. Ann. Thorac. Surg., 1986, 41, pp. 158-163.
4. **Mcintire, F., Sykes, E. M. Jr.:** Obstruction of the superior vena cava: A review of the literature and report of two personal cases. Ann. Intern. Med., 1949, 30, pp. 925-960.
5. **D' Louge, G., Rigsby, L.:** Evaluating the superior vena cava syndrome. J. Am. Med. Assoc., 1981, 245, pp. 951-953.
6. **Parish, J. M., Marschke, R. F. Jr., Dines, D. E. et al.:** Etiologic consideration in superior vena cava syndrome. Mayo Clin. Proc., 1981, 56, pp. 407-413.
7. **Nieto, A. F., Doty, D. B.:** Superior vena cava obstruction: Clinical syndrome, etiology, and treatment. Curr. Probl. Cancer, 1986, 10, pp. 441-484.
8. **Gray, B. H., Olin, J. W., Graor, R. A. et al.:** Safety and efficacy of thrombolytic therapy for superior vena cava syndrome. Chest, 1991, 99, pp. 54-59.
9. **Bhimji, S.:** Superior vena cava syndrome. Hospitál Physician, 1999, 1, pp. 42-63.
10. **Baker, G., Barnes, H.:** Superior vena cava syndrome: etiology, diagnosis and treatment. Am. J. Crit. Care, 1992, 1, pp. 54-61.
11. **Kalra, M., Gloviczki, P., Andrews, J. C. et al.:** Open surgical and endovascular treatment of superior vena cava syndrome caused by non-malignant disease. J. Vasc. Surg., 2003, 38, pp. 215-223.
12. **LagunaDel Estal, P., Gazapo Navarro, T., Murillas Angoitti, J. et al.:** Superior vena cava syndrome: A study based on 81 cases. Ann. Med. Interna, 1998, 15, pp. 470-475.
13. **Escalance, C. P.:** Causes and managment of superior vena cava syndrome. Oncology, 1993, 7, pp. 61-68.
14. **Armstrong, B. A., Perez, C. A., Simpson, J. R. et al.:** Role of irradiation in the managment of superior vena cava syndrome. Int. J. Radiat. Oncol. Biol. Phys., 1987, 13, pp. 531-539.
15. **Davenport, D., Ferree, C., Blake, D. et al.:** Response of superior vena cava syndrome to radiation therapy. Cancer, 1976, 38, pp.1577-1580.
16. **Ghosh, B. C., Cliffton, E. E.:** Malignant tumors with superior vena cava obstruction. NY State J. Med., 1973, pp. 283-289.
17. **Urban, T., Lebedu, B., Chastang, C. et al.:** Superior vena cava syndrome in small-cell lung karcer. Arch. Intern. Med., 1993, 153, pp. 384-387.
18. **Wurschmidt, F., Bunemann, H., Heilmann, H. P.:** Small cell lung cancor with and withaut superior vena cava syndrome: a multi-variate analys of prognostic factor in 408 cencases. Int. J. Radiat. Oncol. Biol. Phys., 1995, 33, pp. 77-82.
19. **Rowll, N. P., Gleeson, F. V.:** Steroids, radiotherapy, chemotherapy and stents for superior vena caval obstruction in carcinoma of the bronchus: a systematic review. Clin. Oncol., 2002, 14, pp. 338-351.
20. **Nicholson, A. A., Ettles, D. F., Arnold, A. et al.:** Treatment of malignant vena cava obstructio: metal stents or radiation therapy. J. Vasc. Interv. Radiol., 1997, 8, pp. 781-788.
21. **Doty, J. R., Flores, J. H., Doty, D. B.:** Superior vena cava obstruction: bypass using spiral vein graft. Ann. Thorac. Surg., 1999, 67, pp. 1111-1116.
22. **Doty, D. B., Doty, J. R., Jones, K. W.:** Bypass of superior vena cava. Fifteen years' experience with spiral vein graft for obstruction of superior vena cava caused by benign disease. J. Thorac. Cardiovasc. Surg., 1990, 99, pp. 889-895.
23. **Doty, D. B.:** Bypass of superior vena cava: Six years' experience with spiral vein graft for obstruction of superior vena cava due to benign and malignant disease. J. Thorac. Cardiovasc. Surg., 1983, 1, pp. 326-338.
24. **Yellin, A., Rosen, A., Reichert, N., Lieberman, Y.:** Superior vena cava syndrome: The myth-the facts. Am. Rev. Respir. Dis., 1990, 141, pp. 1114-1118.
25. **Charnsangajev, C., Carrasco, C., Wallace, S. et al.:** Stenosis of the vena cava: preliminary assessment of treatment with expande metalic stents. Radiology, 1986, 161, pp. 295-298.
26. **Kee, S. T., Kinoshita, L., Razavi, M. K. et al.:** Superior vena cava syndrome: treatment with catheter-directed thrombolysis and endovascular stent placement. Radiology, 1998, 206, pp. 187-193.
27. **Dyet, J. F., Nicholson, A. A., Cook, A. M.:** The use of the Wallstent endovascular prosthesis in the treatment of malignant obstruction of the superior vena cava. Clin. Radiol., 1993, 48, pp. 381-385.
28. **Thony, F., Moro, D., Witmeyer, P. et al.:** Endovasular treatment of superior vena cava obstruction in patients with malignancies. Eur. Radiol., 1999, 9, pp. 965-971.
29. **Wilson, E., Lyn, E., Lynn, A. et al.:** Radiological stenting provides effective palliation in malignant central venous obstruction. Clin. Oncol., 2002, 14, pp. 228-232.
30. **Zhang, F., Wu, P., Huang, J.:** Treatment of superior vena cava syndrome in cancer patients with intravascular stent and local thrombolysis. Zhonghua Zhong Liu Za Zhi, 2000, 22, pp. 507-509.
31. **GMathias, K., Jager, H., Willaschek, J. et al.:** Interventional radiology in central venous obstructions. Dilatation, stent implantation, thrombolysis. Radiologie, 1998, 38, pp. 606-613.

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