

Case reports

Superior vena cava obstruction caused by radiation induced venous fibrosis

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Abstract

Superior vena cava syndrome is most often caused by lung carcinoma. Two cases are described in whom venous obstruction in the superior mediastinum was caused by local vascular fibrosis due to radiotherapy five and seven years earlier. The development of radiation injury to greater vessels is discussed, together with the possibilities for treatment of superior vena cava syndrome.

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Compression of the superior vena cava (SVC) can lead to oedema of the face and upper extremities, plethora, dizziness, headache, and syncope. Following compression of the SVC, five major venous collateral pathways via the paravertebral, azygos-hemiazygos, internal mammary, lateral thoracic and anterior jugular veins can develop. Each system is elaborately interconnected, providing many possibilities for variations in flow and, as a result, in the severity and presentation of superior vena cava syndrome (SVCS). Prior to the mid 20th century a large percentage of cases of SVCS were caused by non-malignant diseases such as luetic aortic aneurysms, fibrotic mediastinitis, and tuberculosis. Nowadays SVCS is caused by malignancy in about 90% of cases, predominantly lung cancer. We present two cases, one with SVCS and the other with obstruction of the left brachiocephalic vein, both caused by local vascular fibrosis due to radiotherapy.

Case 1

The first patient, aged 47 years, had a central squamous cell carcinoma in the right upper lobe, staged pT2N0M0, which required a pneumonectomy. Two years later he developed general malaise and mediastinal metastases were found in the paratracheal lymph nodes adjacent to the SVC. The tumour and mediastinum were irradiated with a total dose of 60 Gy in 30 fractions, 40 Gy to the tumour and mediastinum followed by a boost dose of 20 Gy to the tumour alone. A three field technique was used with 6 MV photon beams. For several years he remained well and no signs of metastases were found. Five years later he developed dyspnoea and dizziness when leaning forward and swelling

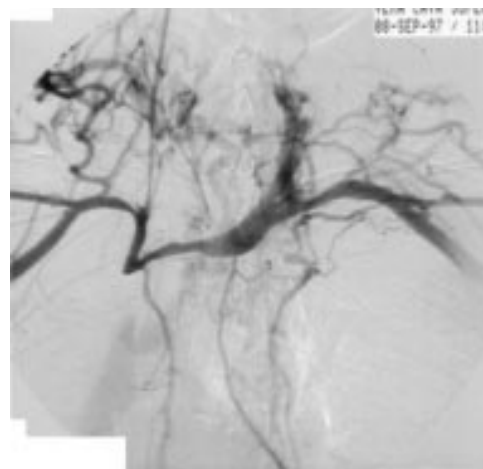


Figure 1 Venography showing obstruction of the superior vena cava in patient 1.

of his lower eye lids and neck. Distended veins were found on his lower rib cage. A contrast enhanced computed tomographic (CT) scan showed no mediastinal mass, the azygos vein was filled through the SVC, and directly above the right heart chamber an SVC obstruction of about 4 cm was observed. Venography showed extensive collaterals and, in the same tract of the SVC, a local stenosis was observed without evidence of thrombosis (fig 1). No distant metastases were found. Whole body PET scanning of the thorax showed no activity suspicious for malignancy. A wall stent was placed in the SVC and oral anticoagulation was started with acenocoumarol. Nine months later he remains free from symptoms.

Case 2

The second patient, aged 36, had radical resection of the right orbita and ethmoid sinus followed by local postoperative radiotherapy because of a carcinoma of the right maxillary sinus. Two years later he developed a cervical lymph node metastasis on the right side. The cervical and supraclavicular regions were irradiated on both sides with 50 Gy in daily fractions of 2 Gy using photons, followed by a boost dose to the right cervical lymph node of 20 Gy in 10 fractions using electron beams. A three field technique was used. Seven years later the patient developed swelling of his left arm. A chest radiograph showed widening of the upper left side of the mediastinum and a contrast

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enhanced CT scan of the chest showed thickening of the wall from the left brachiocephalic vein. Venography following injection of contrast material in the left and right cubital vein showed no flow of contrast through the left brachiocephalic vein, but an extensive network of collateral circulation without signs of thrombosis. Flow of contrast through the right subclavian vein to the SVC was normal. A mediastinoscopy was performed, followed later by a sternotomy, because of suspected lymph node metastases. On both occasions only fibrous tissue was found and there was no sign of malignancy on pathological examination of multiple biopsy specimens from this area. Distant metastases were not found. Whole body PET scanning of the thorax showed no activity suspicious for malignancy. Anticoagulation with acenocoumarol was started although there were no signs of thrombosis. The symptoms gradually resolved and 12 months later no signs of metastasis have been observed.

Discussion

Radiotherapy of any neoplasm is limited by the tolerance of the surrounding normal tissue. Dose fractionation and dose reductions are required to limit normal tissue reactions. In patients with lung cancer the adjacent lung tissue is the most important limiting factor. Radiotherapy also leads to widespread vascular changes. In small and medium sized arteries acute radiation lesions are uncommonly observed, although delayed injury after more than six months is fairly common. Irradiation causes accelerated development of atherosclerosis in exposed large arteries. Following mediastinal or thoracic wall irradiation the risk of coronary artery disease is significantly increased after follow up for more than 10 years. Following radiotherapy of head and neck tumours a 3–4-fold increase in carotid artery stenosis is observed, most clinically symptomatic stenoses being observed about eight years after irradiation.¹ Three patients have recently been described who developed chronic arterial insufficiency in the lower extremities and pelvis 20 years after radiotherapy treatment for gynaecological malignancies.² The pathogenesis of radiation induced injury in large vessels is not fully understood. It is hypothesised that changes in large vessels are caused by the effects of radiation on the vasa vasorum of the large vessel wall and the cells in the tunica intima layer. Radiation may directly stimulate proliferation of the intimal cells and formation of a generalised thickening or focal plaque in the tunica intima. The vasa vasorum is the microvasculature that nourishes the walls of large blood vessels. Radiation induced loss of some of the vasa vasorum may create hypoxic conditions which could also stimulate intimal proliferation.³ The chronic hypoxia caused by disruption of the vasa vasorum may increase the probability of late vascular damage such as vascular spasm and occlusions. Vascular spasm may also be caused by increased release of neurotransmitters in the damaged regions. Alternatively, obstruction of the large vessels after radiation may be due to severe fibrosis of

the muscles and surrounding tissue that could entrap the vessel contributing to the obstruction or loss of some vasa vasorum nourishment.

Case reports have described patients with thrombosis of the subclavian or axillary veins several years after radiotherapy.^{4,5} However, the appearance of obstruction of the greater veins in the chest due to local radiation induced fibrosis of the vascular wall without thrombosis is rare. In a series of publications on treatment of SVCS with stents we found only one case with SVCS due to radiation fibrosis.^{6–10} Veins are apparently less prone to developing radiation induced fibrosis, probably because their walls are less cellular. The two patients described here developed venous obstruction of the superior mediastinum due to local radiation fibrosis of the vein five and seven years after radiotherapy.

SVCS is usually not life threatening and diagnostic and invasive procedures can safely be performed to confirm a diagnosis. Obstruction of venous return in the mediastinum and thoracic inlet several years after radiotherapy is not always caused by a relapse of the previous malignancy, as we have shown. Also, a mediastinal shift caused by prior surgery or radiotherapy may cause venous obstruction.

In cases of non-malignant SVCS, implantation of an intravenous stent should be considered, although experience with stents in non-malignant SVCS is very limited. In 84 patients, predominantly with malignancies, in whom stenting of the SVC was performed, 92% experienced relief of symptoms.^{6–10} In some cases the SVC may be reconstructed with a surgical bypass. Any patient with SVCS can be considered to have a final thrombotic occlusion, but the usefulness of treatment with oral anticoagulation has not been properly documented. In our first patient the symptoms of SVCS rapidly disappeared after placement of the stent. In our second patient the placement of a stent and a surgical bypass procedure were not possible. The patient's symptoms gradually disappeared, probably as a result of collateral circulation development.

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