

# The Superior Vena Cava Syndrome: A Review of the History and the Present Prospects of Target Therapy

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## Abstract

**Background:** Knowledge of the superior vena cava syndrome has been dated back to the 1757 work of William Hunter in the field of syphilis.

**Method:** The present paper deals with the history of the syndrome from 1833 to 1892 with reference to lung cancer.

**Results:** The old authorities provided such detailed data that lines for future research are derivable. Thus, much as expectations from the theory of lung cancer spread are those of superabundant secondaries, the reality is that particular cases exhibit secondaries which are merely adjacent to the main tumor.

**Conclusion:** It is hypothesized that, as this is Nature's own model, translational laboratories should explore employing it as a human model.

**Keywords:** Superior vena cava syndrome; Lung cancer; History; Future prospects

## Introduction

The superior vena cava syndrome (SVCS) was defined in a review [1] in terms of when "Patients with superior vena cava obstruction present complaining of face, neck, and arm swelling; shortness of breath; orthopnea; and cough." Concerning its historical angle, that review only mentioned that William Hunter described the first patient with the syndrome in 1757. This historic date was accepted by Ahmann [2].

Therefore, this paper dwells on history with particular reference to cancerous diseases of the lungs. However, concerning lung cancer, Davies [3] did warn, as far back as 1835, in terms of "of their greater rarity, of their signs being scarcely known, and their mode of treatment being very imperfectly understood."

### Historical Parameters.

By 1837, William Stokes [4], physician to the Meath Hospital in Dublin, made the point that lung cancer may be diagnosed when "we have a mass producing compression, displacement, and obliteration of organs." He illustrated with two cases. In one case, "The face and neck became oedematous, and the swelling was observed to be greater on the right side." The malignant mass in the chest weighed more than 6 pounds and "filled completely the right cavity," whereas the left lung was "perfectly healthy." By 1842, when he became the Regius Professor of Physic in the University of Dublin, Stokes [5] reemphasized the problem of "a mass producing compression" with the "vena innominata (being) obliterated."

Some years earlier, John Sims [6] published cases of malignant tumors with special reference to the heart and lungs. His second case manifested increased swelling of the face and headache. Concerning the autopsy, he wrote: "The tumours of the right lung occupied about two thirds of the capacity of the entire thorax." The other lung, he noted, was "quite free from the morbid growth." His description of the superior vena cava, which passed through the tumor, was thorough thus: on laying open three or four inches of it, it appears to have identified itself with the diseased mass, and in some parts small flattened tubercles with long peduncles, of a very soft texture, grow from its sides. The structure of the vein was so much altered in this part, as to present the appearance of the channel being continued through the tumour, and the venous tissue absorbed.

In this particular case, there were no extrathoracic deposits, although the interior of the left auricle exhibited unevenly surfaced secondaries. Incidentally, note should be made of the author's use of the word "tubercles." As I expounded elsewhere [7], in the olden days, tuberculosis and cancer were often discussed with this same word.

Samuel Wilks [8] documented a massive right lung growth which did not spread outside the chest even though it "had pierced the auricles of the organ (heart) itself." He provided remarkable details:

The superior vena cava was at first not to be found, being apparently, destroyed in the malignant growth. By tracing it up, however, from the heart, remains of the anterior wall were found. The posterior wall was quite destroyed.

A case report that appeared in 1872 [9] was of additional interest in that (a) the lung and heart were invaded, (b) the other organs were not invaded, and (c) there was microscopical confirmation of malignancy on examining the venous and cardiac lesions. The following fine details were provided:

Right auricle especially distended and found to contain a large nearly spherical mass about two inches in diameter which all but filled it; this was covered with delicate membrane and had some pendulous highly vascular processes attached to it. Tracing this upward it was found to obstruct the entrance of superior vena cava, greater part of this being filled with some new growth, and branches of it, as innominate and commencement of right jugular, seemed perfectly blocked up.

In the 14th case of Vincent Harris [10], he reported thus: The masses at the root of the lung were continuous with a large mass in the anterior mediastinum, completely filling it and being adherent to the sternum. In it were enveloped the large vessels, the carotids, and subclavian arteries and innominate veins and superior cava.

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In a wide ranging lecture on primary cancer of the lung in 1869, Hyde Salter [11] reminded his listeners to learn from rare cases as “you may probably pass the rest of your student’s life without seeing another example of it.” As to the patient’s remarkable presentation, Salter said: “His face looks like that of a man with well-developed renal dropsy – the eyes prominent, the eyelids baggy, the whole face puffed and bloated.” He added that the veins were prominent, varicose, and tortuous to a remarkable degree. As he argued, this revealed “the establishment of a collateral venous circulation; and this as clearly points to the obliteration (partial or complete) of the original channel.” At autopsy, the right lung was found to be converted into massive cancer while the left lung was found “quite unaffected with the disease.” The appearances of the growths were described as follows:

It was found completely to have surrounded the superior cava, the right vena innominata, the windpipe at, and a little above, its bifurcation, and the right bronchus. It had completely obliterated the cava, for on cutting into the right auricle, and attempting to thrust the finger into the upper orifice, it was found to be blind – completely occluded... No cancer was found in any other organ of the body.

He concluded that primary cancer of the lung generally affects only one lung “in strict conformity with the laws of the disease.” Regarding such laws, Fagge [12] was crystal clear in his 1886 textbook in the following words:

But when there is a mediastinal new growth venous obstruction is a very frequent result. Sometimes the growth penetrates the coats of the vena cava, and fungates within it as a soft smooth mass which may be as large as a thumb. Sometimes it surrounds that vessel or one of the innominate veins, and causes extreme narrowing or even complete obliteration of the blood-channel.

## Discussion

Clearly, the old masters documented their cases very well. In particular, two patterns of considerable interest in terms of the current theories of cancer metastasis were revealed by them thus:

(i) Venous blood channels were blocked because of cancer cells entering and occluding them. However, beyond these veins, careful autopsy did not reveal deposits formed by these same locally aggressive cells.

(ii) Moreover, despite the ravages going on in the one lung, the lung just across the midline usually remained unaffected.

There is continuing interest in SVC naturally. The latest paper is from Landete’s associates as regards seminoma with bronchial involvement [13]. Much earlier, in 1969, Salsali and Clifton [14] provided autopsy records. It is noteworthy that the more recent papers, according to the extensive review of Nieto and Doty [1], show that over 90% of SVC are due to some form of malignant disease. In their opinion, surgical intervention has led to long survival. No doubt, the successes are because the extrathoracic spread is usually limited [15].

As Nogueira, Mincer and Botstein concluded [16], “Aggressive therapy with irradiation seems to provide better palliation and may occasionally be associated with remarkably long survivals in this normally highly lethal disease.” Or, as Ahmann [2] put it happily, “achieving symptomatic improvement was remarkable.”

## Future Prospects

In sum, from the period of 1833 to 1892, history taught that in every case of SVCS, Nature prodigiously piled up cancer cells which occluded the lumens of neighboring veins. Yet, there was frank freedom from attack beyond them. Consequently, each patient presenting in this way

can be viewed in terms of Nature’s handwork. Perhaps, this natural order points to the need to look for possible solution. For example, as Foster [17] advised way back in 1870, “The experiments which nature is everywhere making on so grand a scale may be interpreted by means of comparison, with almost the same precision as experiments in a laboratory.” Therefore, whatever occurs peculiarly in SVCS can be viewed as such experiments.

## Conclusion

The possible role of experimental models based on autopsy models should be investigated. Elsewhere [18], I have documented a dozen such models. Therefore, it is hypothesized here that a model based on SVCS should be employed to hasten the quest for target therapy. This is because it was owing to the commingling of red cells and cancer cells that I inferred that there must be an underlying protective “Erythrocyte Associated Necrosis Factor” [19] within the thoracic duct’s microenvironment. Now, consider that these same erythrocytes are also commingled with cancer cells in SVCS. Therefore, this is a natural subset worthy of rigorous research in the field of translational medicine.

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