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Profile of SVCS Presenting to Radiation Oncology Department at a Tertiary Cancer Centre

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ABSTRACT

Background: Superior venacaval syndrome(SVCS) is a potentially life threatening condition presenting as a collection of symptoms and signs of oncological emergency needing immediate attention. Bronchogenic carcinoma is the commonest cause of SVC syndrome, amongst which small cell carcinoma is the commonest histological subtype. The primary treatment options for SVCS depend on underlying conditions and include radiation, chemotherapy, thrombolytic therapy, anticoagulation, stents and balloon angioplasty, and surgery. **Methodology:** All adult cases presenting with SVCS to the Radiation Oncology Department in a tertiary care setting during a time period of 18 months from 1st January 2017 to 30th June 2018 were included. All those patients who had completed their prescribed treatment and had an Eastern Cooperative Oncology Group (ECOG) performance score of 0-3 were enrolled. The records of these patients were analyzed completely for diagnosis, clinical features, histopathological results, radiotherapy details and response shown. **Results:** 30 patients with SVCS presenting to the department of Radiation Oncology during the designated time period were eligible for the study. 26 out of 30 cases (86.6%) were due to a malignant etiology with Lung cancer contributing to 20 cases. Out of the 20 lung cancers, squamous cell cancer was commonest in 8(40%) cases. 10(33.3%) cases were taken up for emergency radiotherapy without any biopsy. Of the 30 patients, 28 were managed with upfront radiotherapy whereas 2 patients; one with small cell lung cancer and other with Lymphoma were given chemotherapy and responded to same, Of the 28 patients treated with radiotherapy, 21 were given Hypo fractionation protocol with 20 Gy/ 5Fr while as 7 patients were treated with conventional fractionation. 22 out of these 28 (78.5%) patients had some kind of symptomatic improvement with radiotherapy; 19 (67.8%) had partial and 3(10.7%) had complete improvement in their symptoms at completion of radiotherapy. 6(21.4%) patients failed to show any kind of response. The improvement in symptoms was poorer in older age groups, non-ambulatory and in those receiving conventional radiotherapy fractionation, although the association was found to be insignificant. **Conclusions:** Radiotherapy effectively relieves symptoms of SVCS to a great extent but overall poor outcome associated with SVCS is due to lack of proper diagnostic workup, late presentation of patients and advanced nature of the primary etiological condition. This can be improved by multimodality approach and endeavor should be to find out primary cause of SVCS rather than going for urgent radiotherapy without proper evaluation.

Keywords: SVCS, Hypofractionation, Radiotherapy.

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INTRODUCTION

Superior venacaval syndrome (SVCS) is a constellation of clinical symptoms & signs that unless managed in time can be life threatening. Superior vena cava, a thin walled vessel, is vulnerable to obstruction or compression due to intrinsic & extrinsic factors as a result of either thrombosis or direct invasion by the disease process. The resultant elevated venous pressure in head, neck, upper extremities & upper thorax leads to the subsequent symptoms collectively known as SVC Syndrome or SVC obstruction. Nowadays malignancy, in particular Lung cancer, is the commonest underlying cause for SVCS responsible for more than 70% cases, unlike in the pre-antibiotic era when infective conditions like Tuberculosis, Syphilis would be the causative agents for SVCS.[1] Amongst Lung cancer, small cell subtype contributes to most number of SVCS cases. Iatrogenic causes can also be related to thrombus formation (intrinsic compression) in the presence of pacemaker wires & indwelling central lines.[2]

The diagnosis of SVCS is made mainly on clinical examination and imaging modalities like chest x-ray, CECT chest, Doppler chest and histopathological diagnosis.

The primary treatment options include radiation, chemotherapy, thrombolytic therapy,

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anticoagulation, stents and balloon angioplasty, and surgery. Unlike in the past, when initiating urgent mediastinal irradiation at the outset without proper evaluation was done, it is now reserved for rare circumstances like inaccessible site for biopsy, life threatening situations like stridor, cerebral edema, coma.[3]

Objective

- To describe the demographic data and underlying disease conditions of patients presenting with SVCO to department of Radiation Oncology.
- To determine the response rate in SVCO cases after receiving palliative radiotherapy.

MATERIALS & METHODS

Descriptive Study.

Time Period: 18 months from 1st January 2017 to 30th June 2018 in the Radiation Oncology Department.

Inclusion criteria:

1. All adult cases presenting with SVCS to the department of Radiation Oncology SKIMS, a tertiary care hospital, during the mentioned time period were enrolled.
2. Patients with Eastern Cooperative Oncology Group (ECOG) performance status of 0-3.
3. Only patients who had completed prescribed treatment.

The medical records of these patients were retrieved, summarized and analyzed; specifically for diagnosis, symptom(s), duration of presenting symptom, histopathological results, symptomatic relief, and Radiotherapy dosage (dose/fraction, number of fractions, total dose, and overall treatment time). Information thus collected was analyzed using descriptive statistics. Percentages were used to describe and compare the distribution of patients. Qualitative data was illustrated using tables and figures. Chi square with Yates correction was used to obtain 'P' value for statistical association.

Response was calculated as significant regression of symptoms or > 50% reduction in size of the mass lesion as seen on imaging.

RESULTS

The total number of cancer patients registered at regional cancer center of SKIMS during the designated time period was 7007 and the number of lung cancer patients during that time was 729 (10.40%). 30 patients with SVC syndrome were eligible for the study. Of these 24 (80%) patients were males & 6(20.0%) were females. Majority of the patients were above 50 years of age with 29.9% in the age group of 51-60 years, followed by 26.6% in age group of 61-70 years and 23.3% in age group of 41-50 years with mean age of 56.55 years [Table 1].

Breathlessness was the commonest symptom in 83.3% of cases followed by cough in 66.6% cases. On clinical examination, upper limb/neck edema was seen in 66.6% and engorged neck veins were seen in 63.3% cases [Figure 1].

Table 1: Patient characteristics

		Number (n=30)	%
Age groups (years)	< 30	2	6.6
	31-40	2	6.6
	41-50	7	23.3
	51-60	9	30.0
	61-70	8	26.6
	> 71	2	6.6
Gender	Males	24	80.0
	Females	6	20.0

Table 2: Radiotherapy Protocol and Response to Radiotherapy

			No (n=28)	%
Radiotherapy Fractionation		Hypofractionated	21	75
		Conventional	7	25
Response	Improvement seen (n=22/78.5%)	Complete Improvement seen	3	10.7
		Partial Improvement seen	19	67.8
	No improvement		6	21.4

Table 3: Correlation of Response Seen

		Improvement seen n=12				NO improvement n-6	%	Remarks
		N	Complete Improvement N=3	Partial improvement N=19	%			
ECOG P.S	0	4	2	2	100.0	0	0.0	p= 0.64 N.S
	1	8	1	5	75.0	2	25.0	
	2	12	0	10	83.3	2	16.6	
	3	4	0	2	50.0	2	50.0	
Radiotherapy Fractionation	Hypo	21	2	15	80.9	4	19.0	p= 0.93 N.S
	Conven	7	1	4	71.4	2	28.5	

Age (years)	< 30	2	1	1	100.0	0	0.0	p= 0.94 N.S
	31-40	1	1	0	100.0	0	0.0	
	41-50	6	1	4	83.3	1	16.6	
	51-60	9	0	8	88.8	1	11.1	
	61-70	8	0	5	62.5	3	37.5	
	> 71	2	0	1	50.0	1	50.0	

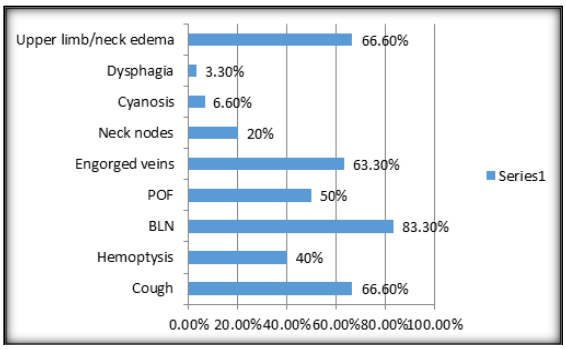

Figure 1: Presenting Symptoms of Patients with SVCO

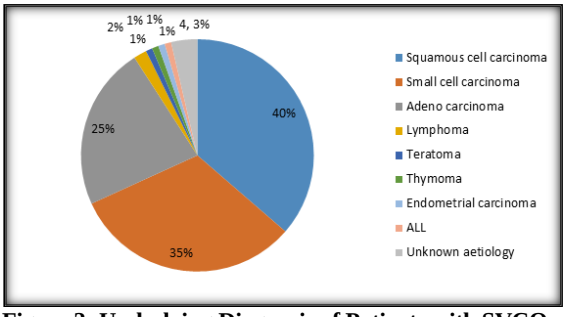

Figure 2: Underlying Diagnosis of Patients with SVCO.

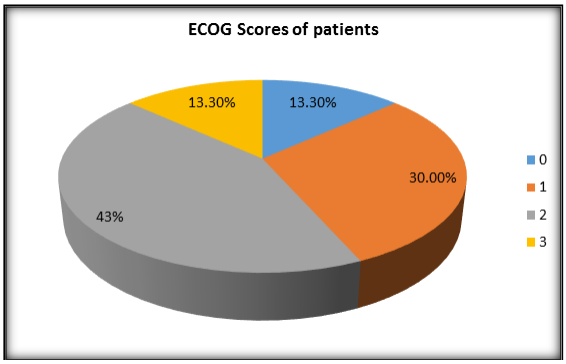

Figure 3: ECOG P.S of Patients

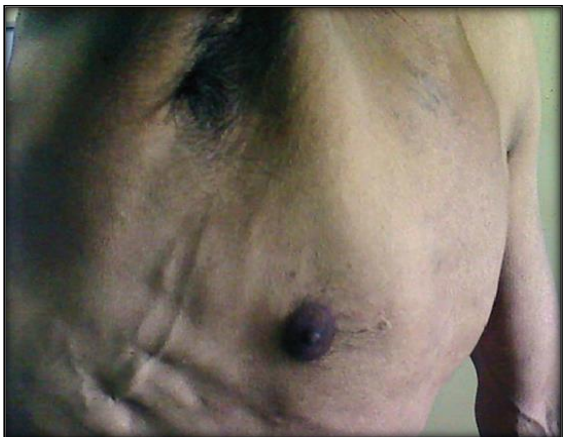

Image 1: Formation of Collateral Veins in Patient of SVCS

Malignancy was the commonest etiological factor seen in 26(86.6%) cases, with Lung cancer in 20 cases. In these 20 lung cancers cases, squamous cell cancer was commonest histological subtype in 8(40%) cases followed by small cell carcinoma 7(35%) and adenocarcinoma 5(25%) patients. The other underlying cancers leading to SVCS were Lymphoma (2 cases of NHL with mediastinal lymphadenopathy), Thyroid cancer, Malignant Thymoma, ALL and Endometrial carcinoma with Lung metastases, each contributing 1 case. [Figure 2]. Among the Lung cancer cases, right sided lung cancer was seen in 13(65%) and left sided in 7(35%) cases. Most of the patients had ECOG performance score of 2 (43%) followed by score of 1(30%) [Figure 3].

20(66.6%) patients in our study had biopsy guided diagnosis available at the time of presentation whereas 10(33.3%) cases were without any histopathological evidence of malignancy. These 10 cases were taken up for emergency radiotherapy in view of respiratory distress. At completion of palliative short course radiotherapy, the latent diagnostic work up showed that 6(60%) of these 10 cases were having Lung cancer. In the remaining 4 cases primary etiology couldn't be established due to poor follow. All the 30 patients had a CT scan of chest/Abdomen done as well as Doppler USG neck which rvealed concomitant thrombus in jugular veins in 4 cases.

Of the 30 patients presenting with SVCS, 28 were managed with Radiotherapy after reporting to our department whereas 2 patients were given chemotherapy, one of them had small cell lung cancer and other had Lymphoma. Treatment was started within the first week of presenting to the department in all the patients.

All 28 patients who received radiotherapy were treated by 4MV photon by telecobalt 60 source using opposing anteroposterior and posteroanterior fields, with the borders of the radiation field dependent on the extent of the mass as seen on CT-simulator at the time of planning. 21 of these were irradiated with Hypo fractionation protocol, with the intent of prompt relief of symptoms, with 20 Gy/5 Fr @ 4 Gy/Fr while as 7 patients were treated with conventional fractionation [Table 2]. Out of these 7 patients 6 were Lung cancer cases; 3 small cell and 3 squamous cell lung cancer. They received initially 45 Gy/22 Fr @2Gy/Fr which was followed by dose escalation up to 60Gy with reduced portals in order to spare the spinal cord. The remaining patient was a case of Lymphoma and was treated with 35 Gy @ 2Gy/Fr.

22 out of 28 (78.5%) patients had some kind of symptomatic improvement with radiotherapy; 19 (67.8%) had partial and 3(10.7%) had complete improvement in their symptoms at completion of radiotherapy. 6(21.4%) patients failed to show any kind of response [Table 2]. In majority of cases, the first symptom to be relieved was breathlessness followed by decreased facial edema and flushing. None of the patients received concurrent chemotherapy.

The response to radiotherapy was correlated with age group of the patients, radiotherapy fractionation schedule and ECOG performance score. It was observed that patients with ECOG PS 0, 1 showed better response than ECOG score of 3. Similarly, patients of younger age groups reported better response to radiotherapy than older age groups. Patients who had received radiation with short fractionation schedule showed slightly better response rates than those with conventional fractionation schedule. However, the findings were statistically insignificant. [Table 3].

DISCUSSION

SVCO can present as an oncological emergency requiring immediate intervention. The primary focus of this study was to determine the demographic and clinical profile of patients with SVCO presenting to the department of radiation oncology and outcome of treatment modality employed for relief of their symptoms. The studied patients were a heterogeneous group with multiple underlying causes.

In the pre antibiotic era, majority of cases of SVC were caused by infective processes but in the present times 85% to 90% of all cases have a malignant etiology.[4] Iatrogenic causes have also emerged as an important cause for the same due to various interventional procedures especially in cardiac diseases.[5] The current study also showed that malignancy was the main cause of SVCO, responsible for 26(86.6%) of cases, with Lung cancer being the etiological agent in 20 cases.

The total number of cancer patients registered at regional cancer centre of SKIMS during the time period of 18 months from 1st January 2017 to 30th June 2018 was 7007 and the number of lung cancer patients during that time was 729. Out of these, 20 patients developed SVCS, thereby resulting in case prevalence of 2.74% in lung cancers which is comparable to 3% as seen by Sculier et al.[6] Approximately 5% to 15% of patients with bronchogenic carcinoma develop SVCS, Majority of cases are seen on right side due to location of SVC.[7] This was consistent with our study, with 13 (65%) out of the 20 lung cancer patients being right sided tumors.

Majority of the patients in our study were in the 5th to 7th decade of life with (29.97%) patients in 51-60 years age group, followed by 26.64 % in 61-70 years and 23.33% in age group of 41-50 years. The average age recorded was 56.55 years. This was comparable to study done by De Gregorio et al.[8]

SVCS mainly manifests as dyspnoea (54%), cough (54%), hoarseness (17%) facial edema (82%), arm edema (46%) distended neck veins (63%), facial plethora (20%). In rare cases patient may present with severe respiratory distress; stridor (4%) or features of cerebral edema; syncope (10%) headache (9%), dizziness (6%), confusion (4%).[9] This was consistent with our study as well with patients presenting with Breathlessness (83.3%) cough (66.6%), upper limb/neck edema (66.6%), engorged veins (63.3%) and facial puffiness in 50(%) cases.

The diagnosis of SVCS is mainly done on basis of clinical signs and symptoms which is further augmented by radiological imaging to find out the extent of the obstruction as well as etiological process. These include chest x-ray, CECT chest, Doppler chest. Contrast enhanced CT scan of chest is the commonest modality used in SVCS. Previously radionuclide venography was frequently used for detection of SVCS, but since the advent of non-invasive modality like CT scan, its use has diminished. Other diagnostic modalities used include Sputum cytology, Bronchoscopy, Mediastnoscopy, Lymph node biopsy, Thoracotomy, Digital subtraction angiography, Echocardiography, etc. Nowadays Endobronchial Ultrasound-guided Transbronchial needle aspiration (EBUS-TBNA) is safely used in SVCS patients to collect sample for histopathological diagnosis.[10] In our study all patients underwent CECT before starting any treatment. 20(66.6%) patients in our study had biopsy guided diagnosis available at the time of presentation whereas 10(33.3%) cases were taken up for emergency radiotherapy. Once their condition improved they were evaluated and the diagnostic work up showed that 6(60%) of these cases were having lung cancer. In 4 cases primary etiology couldn't be established due to poor follow up.

For long periods of time SVCS presenting due to malignant etiology or even unknown etiology was managed as an emergency with urgent radiotherapy without proper evaluation.[11] However multiple studies concluded that SVCO does not constitute a radiotherapeutic emergency because there is little shown evidence that venous obstruction caused life-threatening situations (i.e., cerebral or laryngeal edema) and that mortality in these cases was the direct result of SVCO.[12]

Treatment of SVCS is usually dictated by the underlying cause and the stage of the primary disease. Aim of the treatment is to relieve symptoms and at the same time treat the underlying cause.[13] Treatment options for SVCO due to malignant tumors include chemotherapy, radiation therapy, thrombolysis, stent placement and surgery.

However Radiotherapy remains the commonest modality of treatment in this syndrome due to

tumoricidal activity in all malignant & some non-malignant causes of SVCS as well. Moreover patients often present late with poor general condition when chemotherapy or any surgical procedure may not be possible and associated with increased toxicities.

Till any specific treatment was administered we treated patients in our study with various supportive measures in the form of Oxygen Inhalation, parenteral and inhalational steroids, diuretics, antibiotics, etc. The role of steroids and diuretics isn't established in SVCS,[14] but they have shown reasonable success in clinical practice. Diuretics potentially act by decreasing venous return to heart and steroids act by their anti-inflammatory action. In the 4 patients with concomitant thrombus in jugular venous system, parenteral low molecular weight heparin was given in therapeutic doses.

Attempts should be made to find out the underlying cause of SVCS, especially obtaining histopathological diagnosis before initiation of specific treatment. Nowadays with improved techniques it is safer to obtain biopsy specimen for pre-treatment diagnosis.[15] Certain conditions like small cell lung carcinoma and lymphoma respond dramatically to chemotherapy and it also provides systemic treatment for overall control of disease. Whereas thrombosis from a central line catheter does not respond to this treatment. Nevertheless, in a set up with limited resources like ours, patients present late with advanced symptoms of SVCS and are usually taken for upfront radiation.

In our study 28 out of 30 patients received radiotherapy after presenting with SVCS. Two patients had less severe symptoms so that chemotherapy was started in them at the outset. One had small cell lung cancer and other had NHL. Both of them showed good clinical response and hence were continued with routine chemotherapy protocol.

Radiotherapy was seen as the mainstay of treatment for SVCO showing improvement in 78.9 % patients in our study. Although complete disappearance of symptoms was seen in only 3 patients but 19 more patients had partial but significant reduction in their symptoms. Relief of symptoms in small cell lung cancer is reported to be 81%.[16] In another study by Lee et al 68% patients of SVCS achieved subjective relief from the obstruction at the completion of palliative radiation therapy.[17]

At our centre also, hypofractionation schedule is preferred for SVCS patients in view of quicker response seen. 21 out of 28 patients (75.0%) were treated with 20Gy in 5 fractions. 7 patients who received radiotherapy at conventional fractionation had milder symptoms and were started at 2Gy/Fr. The study by Lee also preferred 4 Gy per fraction in 11 (62%) cases of SVCS, like our study. Another study has shown that a total dose of 20 Gy in five fractions or 30 Gy in 10 fractions is usually adequate for palliation.[18]

After the palliative hypofractionation was completed, further management was determined by the response, status of primary disease as well as general condition of the patient. In case of Lung cancer being underlying cause, treatment portal was enhanced to include the whole of primary lesion along with 2 cm margin after initial high dose per fraction and subsequent radiation was given at conventional fractionation.

On correlation of response to radiotherapy with some variables, it was observed that patients who were non ambulatory (with higher ECOG score) showed poorer clinical response to radiotherapy. Similarly patients of age group more than 60 also didn't respond as well to radiotherapy as did the younger patients, although these results were not statistically significant. These results have also been reported by Maddox, et al, who reported that non-ambulatory performance score and age more than 65 years were among the poor prognostic factors in SVCS contributing most to mortality.[19] We also documented that patients who were irradiated with hypofractionation schedule showed slightly better results than patients treated with conventional fractionation radiotherapy.

Studies have shown that the presence of SVCO does not imply a poor prognosis in itself. The major factor determining survival is the underlying disease, not the presence of the syndrome, which can be corrected with therapy. To improve the outcome, SVCS needs to be identified at early stage and multidisciplinary approach should be deployed right from the onset of symptoms, diagnostic methods and treatment modality used. The need is to have randomized controlled trials to establish treatment protocols of SVCS.[20] Moreover at completion of initial radiotherapy, treatment of primary disease should be completed as far as possible. Adjuvant chemotherapy may be considered in good performance patients.

CONCLUSION

Malignancy, in particular Lung cancer, is the commonest etiology leading to Superior Venacava Syndrome. Radiotherapy effectively relieves symptoms of SVCS to a great extent but lack of diagnostic workup, late presentation of patients and advanced nature of the primary disease can affect the outcome. This can be improved with multimodality approach. Endeavour should be to find out primary disease responsible for SVCS rather than going for urgent radiotherapy without proper evaluation.

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