Palliative Medicine Doctors Meeting

A CLINICAL AUDIT ON THE MANAGEMENT OF SUPERIOR VENA CAVA OBSTRUCTION IN THE DEPARTMENT OF CLINICAL ONCOLOGY QUEEN ELIZABETH HOSPITAL

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BACKGROUND

Etiology of SVCO

Superior Vena Cava Obstruction (SVCO) was first described by William Hunter in 1757 (1). This particular case was caused by syphilitic aortic aneurysm. In the early decades of this century, benign causes accounted for over half of the cases. Nowadays over 80% of the SVCO cases result from neoplastic causes, with lung cancers being the commonest etiology followed by lymphoma (2 - 5).

SVCO is present at diagnosis in 1.7% of patients with non-small cell lung cancer (NSCLC). Its occurrence in small cell lung cancer (SCLC) is much higher, ranging from 8.6 to 12% (6, 16,). SCLC is the commonest histological subtype of lung cancer associated with SVCO, followed by squamous cell carcinoma, adenocarcinoma and large cell carcinoma. Lung cancer on the right side is 4-fold more frequent as the cause of SVCO than its left-side counterpart.

In the study by Perez-Soler R et al. on non-Hodgkin's lymphoma (NHL), 36 out of 915 patients (4%) developed SVCO. Twenty-three out of thirty-six patients suffered diffuse large cell lymphoma, 12/36 lymphoblastic lymphoma and 1/36 follicular large cell lymphoma. Lazzarino M et al. found that 57% of primary mediastinal B-cell lymphoma with sclerosis developed SVCO (7). SVCO rarely occurs in Hodgkin's disease.

Superior Vena Cava Syndrome

SVCO clinically manifests as the distressful Superior Vena Cava Syndrome (SVCS) with characteristic symptoms and signs. Dyspnoea is present in 50-80% of patients. Other common presenting complaints are orthopnoea, chest pain, cough and hoarseness. Swelling of face, neck and upper limbs, venous engorgement of neck, chest and upper arms are tell-tale signs of SVCO (1, 2).

Application of formal scoring system to grade SVCO severity is rare in the literature. Nicholson et al. (8) assessed treatment response using a SVC Obstruction Scoring System based on selected symptoms and signs of the SVCS (Table 1).

Arm/head/extremity swelling.	Cough.	Tinnitus.
Neck veins/chest veins distension.	Headache.	Dyspnea/tachypnea
Conjunctival edema/blurred vision.	Dizziness.	Plethora.
Cyanosis/Horners syndrome/vocal cord paralysis.		
Note: one point for each: maximum is 10 points.		

Table 1. SVC Obstruction Scoring System.

Evolution of management philosophy

The management philosophy of SVCO has changed significantly in recent decades. In the past, SVCO was reckoned an oncological emergency and immediate radiotherapy was commenced even before attainment of histological diagnosis. In addition, invasive diagnostic procedures, such as mediastinoscopy, thoracotomy, etc., were deemed hazardous in the presence of SVCO.

For the majority of patients, it is now believed that SVCO is not an emergency. Ahmann reviewed 1986 SVCO patients and identified only 1 death directly related to SVCO (9). Besides, the outcome of SVCO was found to be unrelated to the duration of symptoms (3, 10).

Without histological diagnosis, immediate radiotherapy jeopardizes the therapeutic outcomes of patients who actually have underlying SCLC and NHL in which combination chemotherapy (+/- radiotherapy) produces significant survival benefit.

Actually a significant proportion of SVCO patients, if treated by immediate radiotherapy without histological diagnosis, would be deprived of appropriate treatment. Porte H et al. recruited in a study 88 SVCO patients after less invasive diagnostic procedures (including FOB) failing to attain histological diagnosis. With the use of more invasive tools, such as mediastinoscopy, CAT guided biopsy, thoracoscopy, pericardioscopy, etc., definitive histological diagnosis was eventually established in all these patients. Out of the 88 patients, 36 patients had NHL and 25 patients SCLC (11).

Attempt to obtain histological diagnosis after radiotherapy is often unsuccessful. Loeffler et al. found that mediastinal irradiation before biopsy precluded proper interpretation of the specimen in almost half of the cases (12).

With the advance in diagnostic procedures and general anaesthesia, more invasive diagnostic investigations are no longer reckoned dangerous. Ahmann studied 843 invasive & semi-invasive diagnostic procedures for SVCO (including venography, thoracotomy, bronchoscopy, mediastinoscopy, nodal biopsy, etc.) and found 10 cases of complications. No mortality was noted (9).

Treatment of SVCO

Treatment includes general measures for symptomatic relief of SVCS and definitive treatment targeted at the underlying cause. Sitting up posture alleviates the pressure sensation inside the head. Oxygen supplement relieves shortness of breath. Systemic steroid is generally used in conjunction with radiotherapy because of concern about radiation-induced oedema. Diuretic has been used with anecdotal reports of benefit. Benzodiazepine and morphine are also effective means for symptomatic control (13).

Radiotherapy is the definitive treatment of choice for SVCO in NSCLC. 3 patterns of radiotherapy are commonly practiced: 1) conventional daily fractionation throughout (1.8-2Gy daily fraction), 2) large initial fractions of 4Gy for the first few days followed by conventional daily fractionation till the desired total dose is reached, 3) hypofractionation throughout. It is unclear which regimen is the best. Some authors believe that large dose fractions produces faster relief of symptoms.

Chemotherapy is the initial definitive treatment of choice for patients with SCLC. Sculier et al. demonstrated that symptomatic relief of SVCO was achieved in 73% of patients initially treated with chemotherapy and in 43% of patients initially treated with radiation (16).

For NHL, the standard of care is chemotherapy because it provides both local and systemic therapeutic activity. The choice of regimen depends on the grade, stage and histological subtype.

It is generally accepted that metallic expandable stents should be considered for persistent or recurrent SVCO after failing chemotherapy or radiotherapy. Some authors advocate performance of stenting earlier in the course of the disease, especially in cases when general measures fail to control SVCS (15). Nicholson et al. (8) compared the relative therapeutic efficacy of metal stents vs radiotherapy and found that stents-containing groups (stents +/- radiotherapy) were superior to radiotherapy alone group in terms of higher response rate, faster relief of SVCS, greater improvement of SVC obstruction score and longer asymptomatic survival. However, this procedure is expensive and time-consuming, particularly when thrombolysis is required.

Rowell and Gleeson conducted a systemic review on the management of SVCO in lung cancers (6). In SCLC, chemotherapy +/- radiotherapy relieved SVCO in 77% and 17% of those treated suffered a relapse of SVCO. 60% of NSCLC patients had relief of SVCO by chemotherapy +/- radiotherapy and recurrent SVCO occurred in 19% cases. Percutaneous placement of metallic expandable stents

relieved SVCO in 95% of cases. 11% of those treated had SVCO relapse. Recanalization rate was high resulting in a long-term patency rate of 92% (6).

THE AUDIT

Objectives of the Audit

In light of the change in management philosophy of SVCO and that appropriate management is essential for rapid symptomatic relief, I conducted a clinical audit in Nov 2001 on the management of SVCO in the Department of Clinical Oncology QEH. The objectives of the audit were:

1. To study the current practice and therapeutic efficacy of the management of superior vena cava obstruction in the Department of Clinical Oncology in Queen Elizabeth Hospital of Hong Kong.
2. To determine how our current practice and therapeutic efficacy conformed with published standard of care and therapeutic efficacy.
3. To identify areas for improvement.

Setting standard

The standard of management of SVCO is set according to the management strategies published in international journals & standard textbooks (13, 15 & 17) and other experts' opinions.

The acceptable standard for the ***process*** of management of SVCO is defined as follows:

- Full clinical assessment of symptoms and signs of SVCO is mandatory.
- Imaging study should be performed for the investigation of SVCO. Options are chest radiography, CAT scan of thorax and bilateral arm venography.
- Histological diagnosis should be attained before definitive treatment. Options of diagnostic procedures to attain histology are:
    - Sputum cytology.
    - Bronchoscopy + biopsy.
    - Percutaneous transthoracic guided FNAc of lung or mediastinal lesion.
    - Mediastinoscopy + biopsy.
    - Nodal FNAc or biopsy.
- Treatment of malignant SVCO
    1. General measures include sitting the patients up, oxygen supplement and systemic steroids +/- diuretic +/- morphine +/- benzodiazepine.
    2. Initial definitive treatment depends on the underlying histology. In patients with SVCO secondary to NSCLC, radiotherapy is the treatment of choice. In patients with SVCO complicating SCLC, chemotherapy is the treatment of choice. For SVCO in NHL, chemotherapy is the preferred treatment modality. In case of other pathology, radiotherapy is recommended.
    3. Placement of expandable stents should be considered for persistent or progressive SVCO after initial definitive treatment.

The acceptable standard of ***therapeutic efficacy*** is defined as follows:

- Response rate to radiotherapy for SVCO in NSCLC is 64% (6).
- Response rate to chemotherapy for SCLC is 84% (6).

Sampling and procedure of auditing

The discharge summary of patients admitted to the Department of Clinical Oncology in Queen Elizabeth Hospital of Hong Kong during the time period of 1st Jun 2001 to 7th Nov 2001 were retrospectively reviewed. Patients admitted for the management of superior vena cava obstruction or developed superior vena cava obstruction during hospital stay was identified. Their hospital records and RT folders were then reviewed. Clinical and pathological characteristics, imaging studies, treatment and outcomes were evaluated. An audit sheet was completed for each case. Statistical analysis was performed using SPSS software.

RESULTS

Clinical and pathological characteristics of patients

21 patients were identified with M:F = 19:2. The median age at the diagnosis of SVCO was 68 (range, 40-84). Their histological diagnosis was summarized in Table 2.

Histological diagnosis	Number of patients
Non-small cell lung cancer	6
Small cell lung cancer	7
Lymphoma	1
Anaplastic thyroid cancer	1
Nasopharyngeal carcinoma with lung and mediastinal metastasis	1
Rectal adenocarcinoma with lung metastasis	1
No definitive histological diagnosis	4

Table 2. Histological diagnosis of SVCO patients.

Compliance rates of the management process to the standard (Table 3)

Practice standards	Standard fulfilled				
	Yes	No	NA	VR	Compliance rate (%)
Performance of clinical assessment of symptoms and signs of SVCO.	21	0	0	21	100
Performance of imaging studies for the investigation of SVCO	21	0	0	21	100
Attainment of histological diagnosis of the underlying lesion	17	4	0	21	81
Use of oxygen supplement	19	0	2	19	100
Use of dexamethasone	19	2	0	21	90.5
Radiotherapy is used as initial definitive treatment for SVCO in NSCLC	6	0	15	6	100
Chemotherapy is used as initial definitive treatment for SVCO in SCLC	7	0	14	7	100
Chemotherapy is used as initial definitive treatment for SVCO in NHL	0	1	20	1	0
Radiotherapy is used as initial definitive treatment for SVCO due to other pathology	3	0	18	3	100
Placement of stents for patients who fail initial definitive treatment.	0	3	18	3	0
Overall score	113	10	87	123	92

Table 3. Compliance rates of the practice to the standard.

Treatment response

Symptomatic relief was noted in 18 out of 21 patients. Persistent or progressive disease was found in 3 out of 21 patients. The 3 non-responding cases are: 1 anaplastic thyroid cancer, 1 non-small cell lung cancer and 1 clinical lung cancer.

For the 6 patients with NSCLC, 5 patients (83.3%) responded to irradiation treatment. All 7 patients with SCLC were treated by chemotherapy using Carboplatin and Etoposide. Seven out of 7 patients responded to the chemotherapy. These response rates were comparable with the standard.

Discussion and areas for improvement.

For the selection of initial definitive treatment, 100% compliance rate was noted in case of SVCO in NSCLC, SCLC and other pathology. For the one patient with NHL, his disease was resistant to multiple courses of chemotherapy. Hence radiotherapy was used instead of chemotherapy for the

progressive disease with SVCO.

The compliance rate of attainment of histological diagnosis before definitive initial treatment was suboptimal (81%). 4 patients did not have definitive histological diagnosis: 1 patient with atypical cells after pleural cytology, 1 patient with atypical cells after sputum cytology and bronchoscopic biopsy, 1 patient had sputum cytology showing no malignant cells, and the last patient had sputum cytology and bronchoscopic biopsy showing suspicion of malignancy. Attainment of histological diagnosis should be further promoted. This has survival impact to the treatment outcomes of SVCO, especially in case of chemotherapy-sensitive tumours like SCLC and NHL.

For the 3 patients with progressive or persistent SVCO after initial definitive treatment, none received stents insertion. This was likely due to the concern about the short life expectancy of non-responding patients and the cost-effectiveness of the procedures. However, in cases of non-responders with reasonably good general condition, stents insertion is worthwhile for effective palliation of distressful symptoms.

Conclusion

High compliance rates were noted in most areas of the management process (90.5-100%). Response rates to radiotherapy in NSCLC and to chemotherapy in SCLC were comparable with international standard. Attainment of histological diagnosis should be further promoted. This has survival impact to the treatment outcomes of SVCO, especially in case of chemotherapy-sensitive tumours like small cell carcinoma and lymphoma. Placement of stents should be considered for patients failing initial definitive treatment.

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