

ETIOLOGY AND OUTCOME OF SUPERIOR VENA CAVA (SVC) OBSTRUCTION IN ADULTS

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Abstract. Between 1997 and 2002, 107 patients with symptoms of superior vena cava (SVC) obstruction presented at a university hospital in Northeast Thailand. Age averaged 50.7 years (range, 1 to 84). The male to female ratio was 5.7:1. Duration of symptoms before diagnosis was 29.4 days (range, 2 to 240), including facial swelling, cough, and chest discomfort. About 20% of cases developed respiratory failure and 11.2% died shortly after admission. The mean hospital stay was 23.7 days. Anteroposterior and lateral chest radiographs and computed chest tomography helped locate the lesion. Transbronchial biopsy through bronchoscopy, transthoracic needle biopsy under computed tomography, lymph node biopsy, pleural fluid cytology and/or biopsy were used for histopathologic sampling. High levels of α -fetoprotein and β -HCG indicated an anterior mediastinal mass. The most common etiology of SVC obstruction was bronchogenic carcinoma (51.8%), followed by an anterior mediastinal mass (14.5%), lymphoma (13.6% – with an LDH of 262 to 1459 U/l), metastatic cancer (9.1%), and acute lymphoblastic leukemia (1.8%). Benign SVC thrombosis was found in four patients with Behcet's disease or some other idiopathy. Mediastinal fibrosis from melioidosis occurred in three patients, which is rare, has not been previously reported. Most patients (63.6%) received a combination of radiotherapy and corticosteroid and this helped 55.2% improve.

INTRODUCTION

Superior vena cava (SVC) obstruction syndrome is a common complication of mediastinal conditions. It causes severe discomfort and distress, and requires rapid diagnosis and treatment. William Hunter (1757) first reported this syndrome as a complication of a syphilitic aortic aneurysm. Today, most patients with SVC syndrome have bronchogenic carcinoma, lymphoma, or metastatic cancer (Parish *et al*, 1981). Increasingly, SVC obstruction occurs as a result of venous thrombosis caused by central venous catheterization and benign etiologies such as Behcet's disease or systemic lupus erythematosus (van den Brink *et al*, 1990; Greenberg *et al*, 1991; Roguin *et al*, 1997).

Some say emergency radiotherapy is needed to assess and alleviate the airway obstruction, cerebral venous hypertension, and symptoms secondary to mediastinal compression (Schraufnagel *et al*, 1981; Baker *et al*, 1992), while others suggest treatment should wait diagnosis (Wudel and Nesbitt, 2001), since the treatment chosen de-

pends on the cause of the obstruction. Rapid histologic diagnosis can be achieved by ultrasound-guided transthoracic needle aspiration biopsy (Ko *et al*, 1994), computed tomographic guided transthoracic needle biopsy (Alder *et al*, 1983), mediastinoscopy with biopsy (Jahangiri and Goldstraw, 1995), bronchoscopy with biopsy (Yellin *et al*, 1990), and lymph node biopsy.

Our objective was to evaluate the etiology, treatment and outcomes of SVC obstruction syndrome in our hospital.

MATERIALS AND METHODS

A cross-sectional study was conducted between January 1, 1997 and December 31, 2002 at Srinagarind University Hospital, Northeast Thailand. Patients 15 years or older with SVC obstruction were included. All charts were retrieved and pertinent data reviewed. We collected demographic data, initial clinical symptoms and signs, smoking habits, chest radiographs and computed chest tomographic findings, final diagnosis, treatments and outcomes. Etiologic diagnosis was made by cytology and/or histology of lymph node tissue, transbronchial biopsy, transthoracic needle biopsy and pleural fluid or tissue. In benign cases,

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diagnosis depended on the results of a culture, computed chest tomography and the criteria used to diagnose collagen vascular diseases.

Ethics

The Ethics Committee of the Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, scrutinized and approved the research protocols for the study.

Statistical analysis

Descriptive statistics were used: means and standard deviations were calculated for continuous data, and number and percentage for categorical data.

RESULTS

Over six years, 107 patients (91 men and 16 women) averaging 50.7 years of age (range, 15 to 84) were diagnosed with SVC obstruction. Over two-thirds (68.2%) had smoked more than 20 pack-years. Farming was the most common occupation (45%). Some (31) had a known underlying disease: lymphoma (5.6%), bronchogenic carcinoma (4.7%), and diabetes mellitus (3.7%) (Table 1).

The mean duration of symptoms was 29.4 days (range, 2 to 240). The most common clinical symptoms were facial swelling (89.7%), cough (57.0%) usually producing mucoid sputum but sometimes dry, and chest discomfort (41.1%). The common clinical signs at initial presentation (Table 2) were swelling of the upper extremities and face (93.5%), and dilatation of superficial veins (63.6%). Lymphadenopathy, hoarseness, and Horner's syndrome presented in 34.9, 28.0 and 2.8% of patients, respectively.

Bronchogenic carcinoma was the most common established cause of SVC obstruction (51.8%). The most common cell type was adenocarcinoma followed by squamous cell carcinoma. Small cell lung cancer was confirmed in five cases. Other etiologies included anterior mediastinal mass (14.5%), lymphoma (13.6%), metastatic carcinoma (9.1%), SVC thrombosis (6.4%), melioidosis (2.7%) and acute lymphoblastic leukemia (1.8%). The common sites of metastatic cancer were the gastrointestinal system, breast and cervix. Thromboses of the SVC of these seven cases were idiopathic (3), bronchogenic cancer (2), cholangiocarcinoma (1) and

Table 1
Patient characteristics.

Patient characteristics	N = 107
Age, years (mean, SD)	50.7 (14.2)
Male:female ratio	91 : 16
Smoking (n, %)	73 (68.2)
Occupation	
Farmer	45 (42.0)
Government employee	12 (11.2)
Underlying diseases (n, %)	
Lymphoma	6 (5.6)
Bronchogenic carcinoma	5 (4.7)
Diabetes mellitus	4 (3.7)
Anterior mediastinal mass	3 (2.8)
Old pulmonary tuberculosis	2 (1.9)
Chronic obstructive pulmonary disease	2 (1.9)
Asthma	2 (1.9)
Other ^a	7 (6.5)

^aSeven other cases include a case each of ischemic heart disease, mitral stenosis, Behcet's disease, acute lymphoblastic leukemia, thalassemia, CA cervix and CA breast.

Table 2
Clinical symptoms and signs of SVC obstruction.

Symptoms and signs	N = 107
Duration of symptoms, days (mean, range)	29.4 (2-240)
Symptoms (n, %)	
Facial swelling	96 (89.7)
Cough	61 (57.0)
Chest discomfort	44 (41.1)
Dyspnea	41 (38.7)
Fever	32 (29.9)
Weight loss	26 (24.3)
Signs (n, %)	
Swelling of upper extremities and face	100 (93.5)
Superficial vein dilatation	68 (63.6)
Lymphadenopathy	37 (34.9)
Hoarseness	30 (28.0)
Horner's syndrome	3 (2.8)

Behcet's disease (1). In the three cases of melioidosis, two cases of SVC obstruction were from mediastinal fibrosis and another from an anterior mediastinal mass (Table 3).

Two chest radiographs, one anteroposterior and the other lateral, were used to locate the mass.

Table 3
Etiology of SVC obstruction.

Etiology	N	%
1. Bronchogenic carcinoma	57	51.8
2. Anterior mediastinal mass	16	14.5
3. Lymphoma	15	13.6
4. Metastatic CA	10	9.1
5. SVC thrombosis	7	6.4
6. Melioidosis	3	2.7
7. Acute lymphoblastic leukemia	2	1.8
	110	100

Note: Two patients had bronchogenic carcinoma with SVC thrombosis and one had an anterior mediastinal mass with melioidosis.

Table 4
The management of SVC obstruction.

Management	N	%
Corticosteroid alone	11	10.3
Radiotherapy alone	12	11.2
Chemotherapy alone	0	0
Heparin alone	2	1.9
Combined corticosteroid and radiotherapy	68	63.6
Combined corticosteroid and chemotherapy	4	3.7
Combined corticosteroid and heparin	4	3.7
Combined radiotherapy and chemotherapy	2	1.9
Combined corticosteroid, radiotherapy, and chemotherapy	2	1.9
Combined corticosteroid, radiotherapy, and heparin	2	1.9
	107	100

When the location was uncertain, or no mass was observed on radiographs, computed tomography of the chest was used. For an intrapulmonary mass, bronchoscopy with transbronchial biopsy was useful. Transthoracic needle aspiration biopsy under ultrasound or computed tomography guide was preferred for assessing an anterior mediastinal mass. Cytology and histopathology from the lymph node(s) and pleural fluid or pleural tissue were also used.

Serum tumor markers can help diagnose certain diseases. A serum LDH level ranging between

Table 5
Outcome of management.

Outcome	N = 107
Hospital stay (mean, SD)	23.7 (18.0)
Outcome (%)	
Improvement	55.2
No improvement	33.6
Death	11.2
Complication (%)	
Respiratory failure	19.6
Hospital-acquired pneumonia	14.9

262 and 1,459 U/l (median 700 U/l) occurred in 10 of the 15 cases of lymphoma. Of the 16 cases of anterior mediastinal mass, three had high α -fetoprotein and one high β -HCG, which histopathologically demonstrated germ cell choriocarcinoma.

In most cases of SVC obstruction, patients received combined radiotherapy and corticosteroids (63.6%). Eleven patients (10.3%) received only corticosteroids, and twelve (11.2%) only radiotherapy. Corticosteroid was given to 72% of patients within 48 hours, and radiotherapy to 42% within 48 hours, of diagnosis. A few patients had chemotherapy with corticosteroid and/or radiotherapy (Table 4).

The mean hospital stay was 23.7 days (SD 18): half (55.2%) the patients improved but one-third (33.6%) did not and transferred home. Twelve patients (11.2%) died: seven from bronchogenic carcinoma, two from metastatic cancer, and one each from lymphoma, acute lymphoblastic leukemia, and anterior mediastinal mass. Acute respiratory failure and hospital-acquired pneumonia were common complications (Table 5).

DISCUSSION

Of 86 cases of SVC obstruction reported by Parish *et al* (1981), 67 (78%) were due to malignancy and 19 (22%) to benign causes. Bronchogenic carcinoma was the most common etiology in the malignancy group followed by lymphoma and breast cancer. Squamous cell, small cell, and adenocarcinoma were the common cell types of bronchogenic carcinoma. In the benign group, mediastinal fibrosis and venous thrombo-

sis were the common etiologies. In our series of 107 cases of SVC obstruction, 101 (94.4%) were due to malignancy, of which bronchogenic carcinoma was also the most common etiology. The common cell type among these were adenocarcinoma and squamous cell carcinoma. Small cell lung cancer was rare. The second and third most common etiology in our report were anterior mediastinal mass and lymphoma.

Benign SVC thrombosis and melioidosis accounted for a rare benign etiology. These patients responded well to heparin and antimicrobial agents (ceftazidime plus cotrimoxazole), respectively. The exception was melioidosis plus an anterior mediastinal mass, where the response to treatment depended on the nature of the mass. A key indicator for melioidosis was underlying diabetes mellitus and fever. In SVC thrombosis, diagnosis was made by computed tomography of the chest. Thrombolytic drugs (Gray *et al*, 1991; Meister *et al*, 1989) and/or bypass surgery (Marlier *et al*, 1996) were also well documented. SVC obstruction from infection is rare but includes pulmonary tuberculosis (Jena *et al*, 1996) and histoplasmosis (Zufferey *et al*, 1990). To our knowledge, there has been no report of pulmonary melioidosis in these condition, so our report represents a first.

Invasive investigation was needed to identify the etiology of SVC obstruction. Tissue diagnosis was obtained by bronchoscopy with biopsy, transthoracic needle biopsy, lymph node biopsy, or pleural biopsy. Ultrasound-guided transthoracic needle aspiration biopsy proved a useful and safe diagnostic tool for mediastinal lesions. Ko *et al* (1994) reported its diagnostic yield at 83.3%. Mediastinoscopy with tissue biopsy has been suggested by some authors (Jahangiri *et al*, 1995), but it was not used often in our series.

High levels of serum tumor markers were diagnostic, especially for germ cell tumors (Cameron *et al*, 2001), although normal serum tumor marker levels did not exclude these conditions. In our series, one patient had high serum β -HCG and was positive for urine pregnancy test. Indeed, tissue diagnosis proved to be a germ cell tumor (choriocarcinoma); thus, a urine pregnancy test in a young male can be another effective rapid screening test (Tsai *et al*, 2002).

Management of SVC obstruction depended on duration of symptoms and acute deterioration

of symptoms. Some authors advocate the use of emergency radiotherapy without tissue diagnosis, because of the risk of a life-threatening airway obstruction and cerebral edema (Nissenblatt, 1979). However, pre-biopsy irradiation causes significant tissue alteration, making subsequent histologic diagnosis difficult (Loeffler *et al*, 1986). Effective chemotherapy has replaced radiotherapy as the treatment of choice for small cell lung cancer (Urban *et al*, 1993) and lymphoma (Nomori *et al*, 1998). In our situation, even though these invasive diagnostic procedures were done as soon as possible, the histopathological assessment was time-consuming. During the wait, palliative radiotherapy has a role for patients with progressive dyspnea and deteriorating symptoms (Egelmeers *et al*, 1996). Subsequent chemotherapy, according to the etiology of the obstruction, should prevent recurrence. Emergency radiotherapy, however, is not available in every hospital. In our study, 42% of the patients received radiotherapy in the first 48 hours. For this limitation, earlier treatment with corticosteroid, followed by combined radiotherapy with corticosteroid, may be of benefit.

Bronchogenic carcinoma was the most common etiology of SVC obstruction in our series. The recommended treatment is a combination of chemo- and radio-therapy (Rowell and Gluson, 2001): in small cell lung cancer, the response rate was 77%, and in non-small cell lung cancer, 60%. Non-small cell lung cancers, especially adenocarcinoma cell types, were more common in this study, which may explain the poor response to therapy. Although the majority of patients was treated with combined radiotherapy and corticosteroid, the overall response to our treatments for SVC obstruction was 55.2%, which is comparable to other studies (Parish *et al*, 1981; Fincher, 1987). After histopathological diagnosis, specific chemotherapy was given. Some patients could not be followed-up, so recurrence and deterioration of symptoms may have occurred.

Conclusion

The presentation of SVC obstruction requires urgent diagnosis and management. Invasive procedures for definite diagnosis should be done as soon as possible since treatment and response depend on the underlying cause. Benign conditions occurred rarely in our series but benign SVC thrombosis and melioidosis responded

well to treatment. If patients waiting for diagnosis are run-down, combined radio-corticosteroid therapy should be given. In special malignancies (small cell CA lung, lymphoma, and germ cell tumor), if rapid diagnosis is made, combined chemo- and radio-therapy is the most effective treatment.

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