Long Survival in Patients with Bronchogenic Carcinoma Complicated by Superior Vena Caval Obstruction*

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When superior vena caval obstruction complicates cancer of the lung; the prognosis is grave; 1 percent of such patients survive for one year. Improved palliation is reported from many radiation therapy centers using higher initial dose fractions and tumorcidal doses. We now report the findings in three patients with histologically confirmed bronchogenic carcinoma who had superior vena caval obstruction and who survived for nine years (two patients) and seven years (one patient). Aggressive therapy with irradiation seems to provide better palliation and may occasionally be associated with remarkably long survivals in this normally highly lethal disease.

Obstruction of the superior vena cava produces a dramatic syndrome consisting of edema and plethora of the face, neck, and arms, engorgement of the veins in the neck, and the appearance of dilated, tortuous, superficial collateral veins on the arms, neck, and upper torso.1,4 The patient may also suffer from dyspnea and disturbance of the sensorium, both often worse in the recumbent position, and from stridor, hoarseness, visual disturbance, convulsions, suffusion of the conjunctiva, and propotis.1,4 Venous pressures in the neck and arms are always increased and are greater than the pressures in the legs or right atrium and may be paradoxically increased with inspiration.1,2,6,7

The most common cause of the superior vena cava syndrome is bronchogenic carcinoma, accounting for 75 to 90 percent of all cases.4,8 A second common cause is lymphoma.4 Other neoplastic diseases cause most of the remaining cases,4 although the list of possible causes is long. Uncommon causes of the superior vena cava syndrome include metastatic cancer,4 aortic aneurysm (atherosclerotic or syphilitic),5,10 retrosternal goiter,7,11 mediastinitis (idiopathic, tuberculotic, histplasmotic, actinomycotic, syphilitic, or pyogenic),4,7,12-14 and iatrogenic causes (central venous catheter, wire of pacemaker, irradiation-induced pneumonitis, ven-triculioatrial shunt, or surgical bypass in congenital heart disease).7,15,16 Rare causes of the superior vena cava syndrome include thymoma,7,17 teratoma,15 vasculitis,7 bronchogenic cyst,7,18 pericarditis,7 sarcooidosis,7 atrial myxoma,7,17 trauma,7,17 congenital aneurysm or arteriovenous fistula, bilateral clavicular osteomyelitis,7 mitral stenosis,7 pneumothorax,7,18 and idiopathic thrombosis.7

The superior vena cava syndrome complicates about 5 percent of all cases of bronchogenic carcinoma.6,19,20 and its presence suggests a large, centrally located primary tumor, particularly of the proximal right main bronchus, or metastatic cancer in the mediastinal lymph nodes.2,4,20 The combination of bronchogenic carcinoma and superior vena caval obstruction is particularly lethal.2,4,6,20

We now report three unusual cases of superior vena caval obstruction complicating histologically proven bronchogenic carcinoma. Two men died of their carcinomas seven and nine years after they had superior vena caval obstruction, and a woman is alive and free of disease nine years after diagnosis.

Case Reports

Case 1

A 63-year-old Maltese man developed signs of superior vena caval obstruction in August 1966. A chest roentgenogram revealed a right hilar mass, and phlebographic studies revealed constriction of the superior vena cava just below the junction of the innominate veins and complete occlusion of the right innominate vein. A lymph node biopsy obtained via a mediastinoscopic procedure revealed squamous cell carcinoma. The patient was treated with radiotherapy to a wide upper mediastinal and right hilar field, to a total midline dose of 4,500 rads over five weeks. There was prompt clinical improvement, and the patient was well until August 1973,
Three years later, in 1969, dyspnea developed, and a left pleural effusion was found. Cytologic examination of the pleural fluid and a pleural biopsy failed to reveal cancer. The protein content of the fluid was 2.0 gm/100 ml. Repeated thoracenteses were required because of rapid reaccumulation of pleural fluid, until "moving-strip" radiotherapy to the entire left lung prevented further accumulation. The patient, now 81 years old, was discharged feeling well and vacationed in Florida. His chest roentgenogram at this time was similar to his original films (Fig 2).

In 1970, the superior vena cava syndrome and the pleural effusions recurred, and the patient was treated with diuretic drugs and repeated thoracenteses. He died in 1971, and an autopsy revealed poorly differentiated squamous cell carcinoma of the right lung, originating in the right main bronchus 1 cm from the carina, infiltrating and invading the superior vena cava, the esophagus, the pericardium, the left upper lobe, and all three lobes of the right lung. A "frozen mediastinum" was described. There were metastases in the liver and gastric mucosa. Right ventricular hypertrophy and chronic passive congestion of the liver were also found.

Case 3

A 56-year-old nurse smoked nearly three packages of cigarettes per day until May 1969, when her cough worsened and dyspnea developed. A chest roentgenogram revealed widening of the superior mediastinum, and a right scalene node biopsy revealed small cell anaplastic carcinoma. The patient was not treated initially, but within one month the superior vena cava syndrome rapidly developed. She was given 4,500 rads of teletherapy with radioactive cobalt to the mediastinum and both supraclavicular areas over four weeks via anterior ports. Both the superior vena cava syndrome and the mediastinal mass resolved.

In June 1970, abdominal pain developed, and a pelvic mass was palpated. Exploratory laparotomy revealed a 15-cm mass in the left ovary, which was examined histologically and was found to be metastatic small cell anaplastic carcinoma. A comparison of the scalene node biopsy and the ovarian mass revealed the histologic findings to be very similar, both compatible with primary bronchogenic small cell anaplastic carcinoma.

After surgery a wide pelvic field was treated with 4,000
Table 1—Previously Reported Cases of Histologically Proven Bronchogenic Carcinoma with Superior Vena Cava Obstruction and Long Survivals

<table>
<thead>
<tr>
<th>Case</th>
<th>Reference</th>
<th>Histologic Type</th>
<th>Length of Survival, mo</th>
<th>Radiotherapy, Total Rads/Days</th>
<th>Other Therapy</th>
<th>Final Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Holmes10</td>
<td>Anaplastic</td>
<td>44</td>
<td>3,600/40</td>
<td>None</td>
<td>Alive and well</td>
</tr>
<tr>
<td>2</td>
<td>Holmes10</td>
<td>Abnormal cytologic findings for sputum</td>
<td>78</td>
<td>3,000/19</td>
<td>None</td>
<td>Alive and well</td>
</tr>
<tr>
<td>3</td>
<td>Pate and Hammon11</td>
<td>Undifferentiated</td>
<td>80</td>
<td>3,000/7</td>
<td>Single dose of mechloretamine (nitrogen mustard)</td>
<td>Died of cerebrovascular accident</td>
</tr>
<tr>
<td>4</td>
<td>Banker and Maddison;10 Fox and Scadding;24 Howard10</td>
<td>Carcinoma, unspecified</td>
<td>120</td>
<td>3,765/7</td>
<td>Single dose of mechloretamine (nitrogen mustard)</td>
<td>Alive and well</td>
</tr>
<tr>
<td>5</td>
<td>Banker and Maddison;10 Fox and Scadding;24 Howard10</td>
<td>Carcinoma, unspecified</td>
<td>48</td>
<td>Unspecified</td>
<td>Fibrolysin</td>
<td>Died of primary brain tumor</td>
</tr>
<tr>
<td>6</td>
<td>Stewart et al25</td>
<td>Anaplastic</td>
<td>120</td>
<td>Unspecified</td>
<td>None</td>
<td>Alive and well</td>
</tr>
</tbody>
</table>

rads via anterior and posterior ports. At the present time, nine years after diagnosis, the patient is without any detectable cancer and continues to work full time.

**Discussion**

Prolonged survival in bronchogenic carcinoma complicated by superior vena caval obstruction has been very rare; in four large series that reported mortality, only 70 of 759 patients (less than 1 percent) survived for one year after diagnosis.20-23 We were able to find descriptions of only six patients with histologically proven bronchogenic carcinoma, superior vena cava obstruction, and survival for three years or more (Table 1).10,18,22,24-26 All of these patients received radiotherapy; and, in addition, one received a single dose of mechloretamine (nitrogen mustard), and one was treated with fibrinolysin.2,5,6,20,21,23

Our two male patients had squamous cell carcinoma, and both died of their cancers, one seven and the other nine years after diagnosis. For patient 1, a severe superior vena cava syndrome was relieved during an aggressive initial course of radiotherapy (4,500 rads in five weeks). Six years later, at a time when his symptoms were mild and stable, a repeat venacavagram revealed exactly the same degree and location of the obstruction as had been reported on his initial cavagram (Fig 1). The palliation therefore was associated with shrinkage of the tumor and the formation of collateral vessels, but not with relief of the superior vena cava obstruction. This is consistent with the finding in the series from Memorial Hospital, ie, that most patients examined at autopsy continue to have superior vena cava obstruction, even though clinical relief may have occurred after radiotherapy.8

Patient 2 underwent repeat irradiation for recurrent, severe superior vena cava syndrome, to a total mediastinal dose of 8,200 rads. Although he died with extensive epidermoid carcinoma in the mediastinum, obstructing the superior vena cava, he experienced good clinical improvement after each course of mediastinal irradiation. At autopsy, there was only minimal evidence of irradiation-induced fibrosis.

The dangers of repeat irradiation of the mediastinum to high total doses are well known;26 however, in lung cancer, repeat irradiation of the chest for recurrent distressing symptoms (such as atelectasis, hemoptysis, and superior vena cava obstruction) has been recommended because immediate relief is the goal, and survival long enough to develop symptomatic irradiation-induced fibrosis is unlikely.27 For patient 2, in retrospect, repeat irradiation seemed to provide considerable clinical benefit with minimal toxic effects.

Patient 3 is unique because she has had a long survival and an apparent cure of a small cell anaplastic carcinoma with histologically proven metastasis to a supraclavicular node and an ovary, as well as superior vena cava obstruction. Long survivals and apparent cures in patients with unresected "early" small cell carcinomas treated with radiotherapy alone are infrequent but well documented.24

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Long survivals in other histologic types of bronchogenic carcinoma (unresected) are also noted in several series of irradiated patients.28

Although there are no prospective controlled studies, the palliative effects of radiotherapy in the superior vena cava syndrome due to bronchogenic carcinoma have been described in many large series of patients.2  Fears of irradiation-induced edema and acute exacerbation of the superior vena cava syndrome with high individual dose fractions and high total doses seem unfounded.1,7 Indeed, retrospective studies suggest better palliation with more aggressive treatment.1,4,15,22,25

Since long survivals have been reported in irradiated patients2,13,22,26 and since there is some evidence that more aggressive treatment results in better palliation, we believe that in the superior vena cava syndrome complicating bronchogenic carcinoma, therapy with a tumoricidal dose of about 4,500 rads in fractions of 200 rads or more should be begun promptly.

When the carcinoma is confined to the thorax, fields of treatment should be wide enough to include all of the tumor and the supraclavicular fields as well, if involvement there is suspected.

A variety of ancillary measures, including therapy with diuretics,1,19 corticosteroids,19 anticoagulants,2,21 and fibrinolytic agents,2,5 have been recommended, but their efficacy is uncertain. We administer diuretics and corticosteroids in moderate to severe cases. Since there is postmortem evidence that thrombosis is a major factor in many cases of carcinomatous superior vena cava obstruction,2,5,21 the role of therapy with anticoagulant drugs and thrombolytic agents deserves further evaluation.

The addition of chemotherapy with only mechlorethamine (nitrogen mustard) does not confer any added benefit, and in one small, prospective randomized study, the patients given mechlorethamine and cautious radiotherapy had fewer responses and shorter survivals than the group given only radiotherapy (but in higher initial and total doses).2,3,29 Various surgical bypass procedures have been reported for the palliation of superior vena caval obstruction.5,5,6,50,81 They have little, if any, role in superior vena caval obstruction due to bronchogenic carcinoma. In fact, the dangers of uncontrolled bleeding and respiratory distress have been said to attend even diagnostic procedures such as thoracotomy, mediastinoscopic examination, lymph node biopsy, and bronchoscopic procedures;1,2,4,29,50 and it may be advisable to omit such diagnostic procedures in patients with severe superior vena cava syndromes and promptly begin treatment.1,4

We believe that in bronchogenic carcinoma the presence of the superior vena cava syndrome is best treated by radiotherapy that is begun promptly and delivered in potentially curative doses to fields of adequate size to encompass all of the known tumor. Aggressive radiotherapy is well tolerated, affords good palliation, and is occasionally associated with prolonged survival.

REFERENCES


§References 1, 3, 10, 20, 22, 23, 25, and 27.
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