Management of Carcinoma of the Superior Pulmonary Sulcus

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Tumors of the superior pulmonary sulcus (Pancoast tumors) are bronchogenic carcinomas that occur at the thoracic inlet and typically involve, by direct extension, the lower trunks of the brachial plexus, the intercostal nerves, the stellate ganglion, and adjacent ribs and vertebrae. These tumors are rare, comprising 5% of all lung cancers. Treatment of Pancoast tumors has traditionally consisted of preoperative radiation to a dose of 3,000 to 4,500 cGy followed by surgical resection. Overall 5-year survival rates range from 30% to 50%. Even if treatment achieves local disease control, distant failure (brain or bone) is common. Recent treatment efforts have focused on the use of induction chemoradiation followed by surgery and further chemotherapy. This combined-modality approach may become the new treatment paradigm for Pancoast tumors. [ONCOLOGY 11(6):781-785, 1997]

Introduction

Tumors of the superior pulmonary sulcus were first recognized by Edwin Hare in 1848. It was not until 1932, however, that H. K. Pancoast defined tumors in this location and associated them with a distinct clinical syndrome.[1] A Pancoast tumor is a bronchogenic carcinoma that occurs at the thoracic inlet and typically involves, by direct extension, the lower trunks of the brachial plexus, the intercostal nerves, the stellate ganglion, and adjacent ribs and vertebrae (Figure 1). The Pancoast syndrome, as it is known today, is characterized by shoulder pain, with or without radiation to the arm, axilla, or scapula; Horner's syndrome; and atrophy of the muscles of the hand. Tumors of the superior pulmonary sulcus are rare, comprising less than 5% of all lung cancers. Similar to other lung cancers, smoking is the predominant risk factor for Pancoast tumors. The histology of these tumors varies from series to series, but approximately 50% are squamous cell carcinomas and 50% are adenocarcinomas or large cell carcinomas. Very few of these lesions are of small (oat) cell histology. Diagnostic and treatment modalities for these rare tumors are still evolving.

Diagnosis

The diagnosis of Pancoast tumor begins with the appropriate symptom complex and the suggestion of a mass at the apex of the lung field on a chest roentgenogram. A CT scan of the chest and/or an MRI scan (Figure 2) should then be obtained to determine the degree of tumor invasion into the surrounding structures. Controversy exists as to which of these modalities is superior. Several studies have demonstrated that MRI is no more accurate than CT scanning in staging lung cancers in general.[2,3] Heelan et al argue, however, that superior pulmonary sulcus tumors are unique. Since these tumors involve the apex of the lung and the nerves and blood vessels have a horizontal orientation at this point, coronal and sagittal MRI images display the relationships at the apex better than do CT scans. Their study showed that, overall, MRI was more accurate than CT in evaluating superior sulcus tumors (94% vs 63%).[4] Other groups have corroborated these findings.[5]

A tissue diagnosis should be obtained in patients with a suspected Pancoast tumor to rule out infectious causes of a mass in this location, which may produce the symptoms of the Pancoast syndrome. Sporadic cases have been reported in the literature of actinomycoses, aspergillosis, cryptococcoses, and Staphylococcus aureus infections causing symptoms characteristic of a superior pulmonary sulcus tumor.[6]

Obtaining a tissue diagnosis is also necessary to determine the histology of the tumor since there is a 2% to 10% incidence of small cell carcinoma in this setting.[7,8] Sputum cytology is rarely helpful in this regard (less than 15% of such specimens are positive). Bronchoscopic washings or biopsy also have a low yield due to the peripheral nature of these lesions.
Fine-needle aspiration (FNA) biopsy has become the method of choice for obtaining a tissue diagnosis. Traditionally, this has been performed under CT or fluoroscopic guidance. Yang et al have suggested that ultrasound can be used safely and accurately to guide FNA of Pancoast tumors. They were able to reach a diagnosis in over 90% of their patients.[9] If the findings of Heelan et al and Yang et al can be confirmed in larger numbers of patients, ultrasound and MRI may supplant CT scan/fluoroscopy in this group of patients.

The work-up of a patient with a Pancoast tumor would not be complete without obtaining MRI or CT scans of the brain and abdomen to rule out metastatic disease. A bone scan is also performed to rule out distant bone metastasis.

Staging

According to American Joint Committee on Cancer criteria,[10] T3 lesions are tumors of any size with chest wall involvement. Thus, by definition, Pancoast tumors are at least T3 lesions. If vertebral body involvement or invasion of the neural foramen or the major blood vessels is demonstrated, the tumor is upstaged to T4. Nodal metastasis is designated N1, N2, or N3, for involvement of the hilar, mediastinal, and supraclavicular nodes, respectively. Distant metastasis is designated M1. By stage grouping, Pancoast tumors are either stage IIIa, IIIb, or IV.

In order to accurately stage a patient with a superior pulmonary sulcus tumor, it is necessary to determine whether there is lymph node involvement. Mediastinoscopy or anterior mediastinotomy is, therefore, a key element of the staging process. Fine-needle aspiration of supraclavicular nodes should be performed if there is palpable adenopathy. Lymph node status is the most significant factor in determining the treatment paradigm and prognosis of the patient with Pancoast tumor.

Treatment

Combined-Modality Approach

When Pancoast reported seven cases of superior pulmonary sulcus tumors in 1932, radiation therapy was thought to be ineffective and surgical extirpation was considered impossible. It was not until the 1950s, when Chardack and MacCallum reported the first successful en bloc resection of a Pancoast tumor (combined with postoperative irradiation), that surgical resection became a reality. In 1961, Shaw, Paulson, and Kee described the successful surgical resection of Pancoast tumors following a short course of preoperative radiation therapy.

This treatment regimen was formulated arbitrarily as described by Shaw in a 1984 manuscript.[11] A patient was referred to him with what was thought to be an unresectable superior pulmonary sulcus tumor. A course of "palliative" radiation (to a total dose of 3,000 cGy) was administered. Three weeks after radiation therapy, a chest roentgenogram showed a dramatic decrease in the size of the tumor. Despite previous failures, Shaw proceeded to remove the tumor with portions of three ribs and performed an upper lobectomy. The patient was still alive 27 years after treatment. This combined-modality approach was implemented by this group and others over the next 20 years.

In 1975, Paulson reported on a series of patients with Pancoast tumors treated with preoperative radiation therapy and surgery.[12] Of the 92 patients eligible for treatment, 18 were eliminated on the basis of metastatic disease at presentation and another 9 developed metastases during the preoperative phase of treatment. Thus, 61 patients received 3,000 cGy of radiation over a 3-week period followed by surgery.

The scope of the surgical procedure included resection of the chest wall, portions of three ribs and the thoracic vertebrae, the intercostal nerves, the lower trunk of the brachial plexus (C8, T1), the stellate ganglion, and part of the sympathetic chain, along with either lobectomy or segmental lung resection. Survival at 5 years was estimated to be 34% and 10-year survival, 29%. Positive mediastinal or hilar lymph nodes predicted a poor prognosis.

Although the treatment paradigm outlined by Shaw, Paulson, and Kee represented significant progress in the treatment of patients with Pancoast tumors, the long-term survival statistics were less than impressive. Continuing research focused on determining: (1) the optimal dose and timing of radiation, (2) whether the addition of postoperative radiation or chemotherapy affords any further benefit, and (3) how to identify patients who would benefit most from combined-modality treatment. Questions were raised about the need for radiation (vs surgery alone) in select groups of patients and about the need for surgery in addition to radiation in other select groups of patients.

Due to the rarity of Pancoast tumors, no prospective randomized trials have been conducted to assess the benefit of surgery over radiation, or the efficacy of either of these modalities alone over combination therapy. The role of chemotherapy is even less clearly defined. The only available data...
Management of Carcinoma of the Superior Pulmonary Sulcus
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on which to base treatment decisions come from single institutions and are retrospective in nature. However, several universal themes emerge from the literature:

1. not all patients are candidates for surgery;
2. the role and optimal dose of radiation (neoadjuvant, adjuvant, sole treatment modality, or palliative) have yet to be defined;
3. palliation of pain is often a paramount issue;
4. even if local control can be obtained, distant failure is likely; and therefore,
5. better systemic treatment is needed.

Surgery
It is difficult to evaluate the role of surgery in the treatment of Pancoast tumors from the available data. Many of the early series lumped together patients with various disease stages. Some series included apical lung cancers that do not fit Paulson's strict definition of a superior pulmonary sulcus tumor.[12] In other series, patients received various combinations of surgery, radiation (preoperative and postoperative), and, rarely, chemotherapy.

Clearly, some patients do benefit from surgical resection. One of the largest surgical series is reported by Hilaris et al.[13] They performed thoracotomies on 129 patients with Pancoast tumor from 1960 through 1982.

Out of 129 patients, 82 received preoperative radiation to a dose of 4,000 cGy. A complete or partial resection was done in 82 patients. Interstitial intraoperative brachytherapy was given to 103 patients. Postoperative radiation therapy was given to 36 patients and postoperative chemotherapy was given to 28 patients in this group.

Univariate and multivariate analyses were performed. In the univariate analysis, survival was affected by the histology of the tumor (patients with adenocarcinoma did better), mediastinal node status, the use of preoperative radiation, and the completeness of resection. Of interest, patients with N0, N1, or N3 lymph node status fared better than did patients with N2 disease. In the multivariate analysis, survival was improved in patients with negative mediastinal lymph nodes and in those who received preoperative radiation.

Hilaris et al also concluded that patients with superior pulmonary sulcus tumors who have involvement of the vertebral body, a major vessel, or the upper rami of the brachial plexus (above C8) should not undergo surgical resection. Paulson defined similar contraindications to surgery in his earlier series. These recommendations were echoed in a series from Italy reported by Sartori et al. None of their patients with vertebral body or subclavian artery invasion survived more than 1 year.[14]

Whether surgical resection should be performed in patients with lymph node involvement is less clear from the literature. Paulson was unable to demonstrate an advantage to postoperative radiation in patients with N2 disease. Furthermore, he considered resection palliative in patients with N2 disease because few patients survive more than a year.[12] Hilaris et al found a median survival of only 9 months in patients with N2 disease.[13] Another series reported by Ginsberg et al failed to demonstrate any advantage to intraoperative brachytherapy or postoperative external-beam radiation in patients with incomplete resection or N2-N3 disease.[15] Shahian et al treated 14 patients with positive lymph nodes (including N2 disease) and/or positive margins with postoperative radiation. This series had a total of 18 patients and reported an overall 5-year survival of 56%.[16]

Whether wedge or segmental resection or lobectomy should be used to treat Pancoast tumors is also debated in the literature. Paulson, Hilaris et al, and Shahian et al reported no difference in local recurrence with wedge/segmental resection vs lobectomy as long as the tumor was completely removed.[12,13,16] Ginsberg et al found that 5-year survival was 60% in their patients who underwent lobectomy with en bloc chest resection, thus favoring lobectomy.[15]

Complications of Surgery--The complications reported for surgical resection in the various series are similar to those reported for routine pulmonary resections (eg, bronchopleural fistula, empyema, wound infection). Complications expected after surgery for Pancoast tumors are ulnar nerve deficits and Horner's syndrome, which confer significant morbidity. Meningitis, due to violation of the dura, is a rare complication of surgery for superior pulmonary sulcus tumors that requires vertebral body resection.

In summary, surgery plays a significant role in the treatment of patients with Pancoast tumors. Vertebral body invasion, invasion of the subclavian artery, and invasion of the upper rami of the brachial plexus are contraindications to resection. Involvement of the mediastinal lymph nodes (N2
Management of Carcinoma of the Superior Pulmonary Sulcus
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...disease) renders patients incurable, and, in such patients, surgery may be indicated for palliation of pain or within the context of a clinical trial. Proper preoperative staging (mediastinoscopy) should therefore be performed in all patients. N3 lymph node disease may not preclude long-term survival. Lobectomy is probably no better than wedge/segmental resection with an adequate margin. The best results are achieved in patients who receive preoperative radiation, who are node negative, and whose resection can be achieved with clear margins.

Radiation Therapy

The use of preoperative radiation in the treatment of Pancoast tumors seems to be well established. Hilaris et al retrospectively compared patients who were resected for Pancoast tumor who did (group I) and did not (group II) receive preoperative radiation. Resection was possible in 26% of patients in group I and only 9% of those in group II.[17] Selection bias in this study precludes any definitive conclusion. A 1991 retrospective study of 73 patients by Neal et al also addressed the question of radiation alone vs radiation and surgery. Preoperative radiation to a dose of 3,000 or 4,500 cGy was given followed by surgery. Definitive radiation to a dose of 6,500 to 7,000 cGy was given to patients who did not undergo surgery. No difference in survival was seen between the two groups. The local recurrence rate, however, was significantly higher in the radiation-alone group than in the radiation-surgery group (83% vs 63%).[18] Studies by Komaki et al and van Houtte et al also describe the results of definitive radiation therapy for Pancoast tumors.[19,20] Radiation doses ranged from 2,000 to 7,000 cGy. Symptomatic relief was achieved in the majority of patients. The overall 5-year survival rates in the two studies were 23% and 18%, respectively. Selected groups with less advanced disease had survival rates in the 40% range. Complications of definitive radiation therapy were few but included suprachlavicular skin fibrosis with shoulder limitation, obstruction of the subclavian vein, and Lhermitte syndrome.

In another study, Komaki et al attempted to better define the role of radiation and surgery in the treatment of Pancoast tumor.[7] This series included 85 patients treated with various combinations of surgery, radiation, and chemotherapy. Half of the patients were stage IIla and half were stage IIlb. Fifty-two percent of the patients who received surgery as part of their treatment survived for more than 2 years, as opposed to 22% of those who did not undergo surgery. Among the patients who received radiation as part of their treatment, 32% survived for 2 years. In unresectable patients, a radiation dose greater than 6,500 cGy achieved a better local control rate than did lower doses (69% vs 38%). This study is retrospective, and selection bias may account for some of the findings. The authors concluded, however, that surgical resection should be used whenever possible for superior pulmonary sulcus tumors.

Chemotherapy

The effect of chemotherapy on the outcome of patients with Pancoast tumors is unknown. Ginsberg et al treated 10 patients in their series with platinum-based induction chemotherapy, and reported no long-term disease-free survivors.[15] There is some evidence that induction chemotherapy may be beneficial in patients with stage IIIa or IIIb lung cancers. In a Southwest Oncology Group (SWOG) trial reported in 1993 by Rusch et al, 75 patients with stage IIIa or IIIb disease received cisplatin (Platinol; 50 mg/m²), etoposide (VePesid; 50 mg/m²), and concurrent radiation to a dose of 4,500 cGy. Of the 75 patients, 68 then underwent thoracotomy, 55 of whom had a complete resection. Survival at 2 years was 40%.[21] In 1995, Albain et al reported on longer follow-up of the same study. The survival of the patients at 3 years was 26%.[22] A second study by Yashar et al treated 36 stage IIIa patients with cisplatin and concurrent radiation to 5,500 cGy, and 31 patients then underwent complete resection. The 3-year survival rate was 61% in those patients whose tumors were resected.[23] These studies establish a firm basis for performing phase III trials of induction chemoradiation followed by surgery in patients with stage IIIa and perhaps IIIb disease. The benefit of induction chemoradiation in treating Pancoast tumors is currently being studied.

Fox Chase Cancer Center Approach

Patients with Pancoast tumors who are evaluated at our institution are encouraged to participate in Eastern Cooperative Oncology Group (ECOG) S9416, a phase II trial testing the feasibility and toxicity of a regimen of cisplatin (50 mg/m²), etoposide (50 mg/m²), and concurrent radiation to a dose of 4,500 cGy. Patients are seen by a thoracic, radiation, and medical oncologist. A tissue diagnosis is...
obtained, an MRI is obtained for staging, and a metastatic work-up is conducted. Mediastinoscopy is performed in all patients.

Patients who have T3-T4, N0-N1 disease are eligible for the study. Two cycles of chemotherapy are given with concurrent radiation in twenty-five 180-cGy fractions. Patients are then reevaluated for extent of disease 2 to 4 weeks after induction therapy.

If no disease progression is evident, the patient undergoes surgery. Surgical resection includes the chest wall, portions of the involved ribs, intercostal nerves and vessels, the lower trunk of the brachial plexus (if involved), the stellate ganglion and part of the sympathetic trunk (if involved), and the upper lobe of the involved lung. Two additional cycles of chemotherapy are administered after surgery. If patients are not candidates for surgery or experience disease progression, they receive the two final cycles of chemotherapy.

Any patient with a superior pulmonary sulcus tumor who is not a candidate for the ECOG protocol is offered another protocol involving chemotherapy and radiation.

**Summary**

Pancoast tumors are rare, comprising 5% of all lung cancers. Treatment has traditionally involved preoperative radiation to a dose of 3,000 to 4,500 cGy followed by surgical resection. Overall 5-year survival ranges from 30% to 50%. Even if treatment achieves local disease control, failure at a distant site (brain or bone) is probable.

Recent efforts in the treatment of superior pulmonary sulcus tumors have focused on induction chemoradiation followed by surgery and further chemotherapy. This combined-modality approach has the potential to become the new treatment paradigm for Pancoast tumors.

**References:**


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