Review Article

Current Concepts

Superior Pulmonary Sulcus Tumors and Pancoast's Syndrome

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PANCOAST'S syndrome is a constellation of characteristic symptoms and signs that includes shoulder and arm pain along the distribution of the eighth cervical nerve trunk and first and second thoracic nerve trunks, Horner's syndrome, and weakness and atrophy of the muscles of the hand, most commonly caused by local extension of an apical lung tumor at the superior thoracic inlet.[1-3] These tumors are called superior pulmonary sulcus tumors or Pancoast's tumors. Nearly 90 years after the first documented case,[4] Pancoast described the clinical and radiologic findings of thoracic-inlet tumors. Pancoast mistakenly believed that these tumors emanated from epithelial rests of the fifth branchial cleft; Tobias, who identified the syndrome at the same time as Pancoast, correctly recognized their site of origin as bronchopulmonary tissue.[5] Although Pancoast's syndrome may be the result of diverse neoplastic, inflammatory, and infectious diseases, the focus of this review will be on primary bronchogenic carcinoma, which causes the vast majority of cases.

PRESENTATION

The most common initial symptom is shoulder pain, produced by neoplastic involvement of the brachial plexus, parietal pleura, endothoracic fascia, vertebral bodies, and first, second, and third ribs[6,7] (Fig. 1). Pain can radiate up to the head and neck or down to the medial aspect of the scapula, axilla, anterior part of the chest, or ipsilateral arm, often along the distribution of the ulnar nerve.[6] Treatment for presumed cervical osteoarthritis or bursitis of the shoulder is not uncommon, and in many series, a delay of 5 to 10 months in the correct diagnosis has been reported.[8-10]

Horner's syndrome, which consists of ipsilateral ptosis, miosis, and anhidrosis, is caused by invasion of the paravertebral sympathetic chain and the inferior cervical (stellate) ganglion (Fig. 1). It has been reported in 14 to 50 percent of patients with Pancoast's syndrome, and up to 83 percent in one series.[6,8,11] Ipsilateral flushing and hyperhydrosis of the face may occur before the development of Horner's syndrome, presumably from irritation of the sympathetic chain.[8,9] Rarely, contralateral facial flushing and sweating due to an excessive response by the intact sympathetic pathway as well as ipsilateral reflex sympathetic dystrophy may occur.[12,13]

Weakness and atrophy of the intrinsic muscles of the hand are not uncommon, along with pain and paresthesia of the medial aspect of the arm, forearm, and fourth and fifth digits along the distribution of the ulnar nerve, caused by extension of the tumor to C8 and T1 nerve roots.[6] With further extension through the intervertebral foramina in 5 percent of the patients initially, but as many as 25 percent later in the course of the disease, compression of the spinal cord and paraplegia may result.[6,9,14] Abnormal sensation and pain in the axilla and medial aspect of the upper arm in the territory of the intercostobrachial (T2) nerve have been reported as early signs of Pancoast's syndrome.[15]

Less common manifestations of Pancoast's tumors include involvement of the phrenic nerve and recurrent laryngeal-nerve involvement[14,16] and superior vena cava syndrome.[6,14] Enlargement of the supraclavicular lymph nodes may also occur.[8,14] Because of the peripheral location of the tumor, pulmonary symptoms such as cough, hemoptysis, and dyspnea are uncommon in the initial stages of the disease, but may occur later in the majority of patients.[6]

CAUSE

The majority of cases of Pancoast's syndrome are caused by non–small-cell bronchogenic carcinoma, most commonly squamous, followed by adenocarcinoma and large-cell carcinoma,[3,17,18] although in several series, adenocarcinoma was the most frequent histologic type.[10,16,19] Small-cell carcinoma is only rarely associated with this syndrome.[20-22] Although bronchogenic carcinoma is the usual cause of superior sulcus tumors, these tumors account for less than 5 percent of all bronchogenic carcinomas.[9,21,23]

The differential diagnosis of Pancoast's syndrome includes other primary thoracic neoplasms,[24-26] met-

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astatic[26-29] and hematologic[30-32] conditions, infectious diseases,[33-40] neurogenic thoracic outlet syndromes[41] (such as the cervical rib syndrome), and pulmonary amyloid nodules[42] (Table 1). Although in the past a histologic diagnosis was not considered necessary before therapy was initiated,[3,43,44] the wide variety of diseases that can result in Pancoast's syndrome now mandates a conclusive diagnosis before definitive treatment is begun.

RADIOLOGIC FINDINGS

Findings of superior sulcus tumors on plain chest radiographs include a unilateral apical cap of more than 5 mm, asymmetry of both apical caps of more than 5 mm, an apical mass, and bone destruction[14,44,45] (Fig. 2). Lordotic chest views and radiographs of the upper thoracic and lower cervical spine may also be of some assistance in the detection of the tumor.[7]

Computed tomography (CT) of the chest usually provides additional information about the extent of superior sulcus tumors and is especially helpful in the identification of other pulmonary nodules, parenchymal diseases, chest-wall involvement, and mediastinal lymphadenopathy.[6] Magnetic resonance imaging (MRI) is as effective as CT in its ability to detect mediastinal lymph-node involvement, appears to be more accurate in the identification of chest-wall invasion, and is superior to CT with respect to the detection of tumor extension to the brachial plexus, subclavian vessels, vertebral bodies, and spinal canal.[45-48]

DIAGNOSIS

The diagnostic yield of cytologic analysis of expectorated sputum is generally around 11 to 20 percent.[8,10,49,50] The use of fiberoptic bronchoscopy with cytologic analysis and biopsy will yield a diagnosis in 30 to 40 percent of cases.[10,44,50] Moreover, unexpected endobronchial tumors may occasionally be detected by bronchoscopy, seriously affecting the approach to therapy.[50] Nevertheless, the most sensitive procedure for the diagnosis of superior sulcus tumors is percutaneous transthoracic needle biopsy, which can be performed with a posterior or cervical approach with the use of fluoroscopy, ultrasonography, or CT for localization.[49,51,52] With this procedure, a diagnostic yield of 95 percent can be achieved.[10,49,51,53] Finally, video-assisted thoracoscopy or thoracotomy can be performed to obtain a histologic diagnosis if less invasive techniques are not diagnostic and to evaluate the extent of the tumor.

STAGING AND PREOPERATIVE ASSESSMENT

Because of their unique location and their involvement of the chest wall, superior sulcus tumors are generally defined as T3 lesions.[54] Invasion of the brachial plexus, mediastinal structures, or vertebral

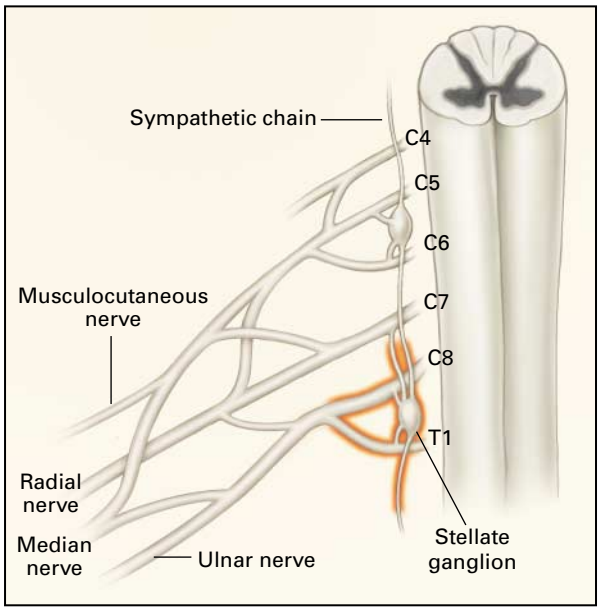
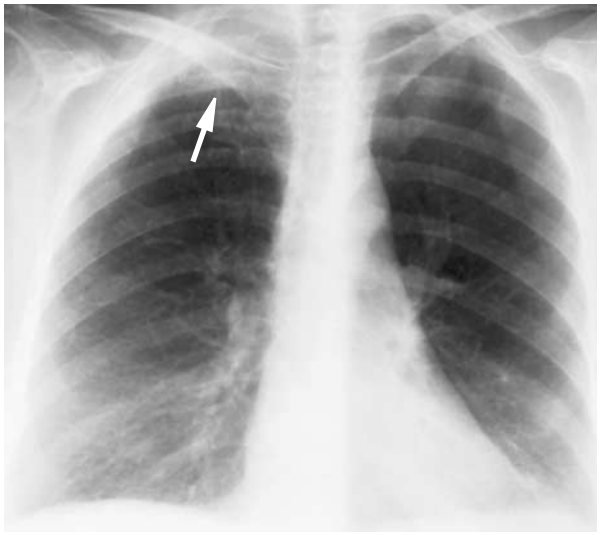


Figure 1. The Major Nerve Trunks and Branches of the Brachial Plexus, Paravertebral Sympathetic Chain, and Stellate Ganglion. The area highlighted in red may be involved by superior sulcus tumors.

TABLE 1. CAUSES OF PANCOAST'S SYNDROME.

Neoplasms
Primary bronchogenic carcinoma[3]
Other primary thoracic neoplasms
Adenoid cystic carcinoma,[24] hemangiopericytoma,[25] mesothelioma[26]
Metastatic neoplasms
Carcinoma of the larynx,[26] cervix,[27] urinary bladder,[28] and thyroid gland[29]
Hematologic neoplasms
Plasmacytoma,[30] lymphomatoid granulomatosis,[31] lymphoma[32]
Infectious processes
Bacterial
Staphylococcal[33] and pseudomonal pneumonia,[34] thoracic actinomycosis[35]
Fungal
Aspergillosis,[36] allescheriasis,[37] cryptococcosis[38]
Tuberculosis[39]
Parasitic
Hydatid cyst[40]
Miscellaneous causes
Cervical rib syndrome[41]
Pulmonary amyloidoma[42]



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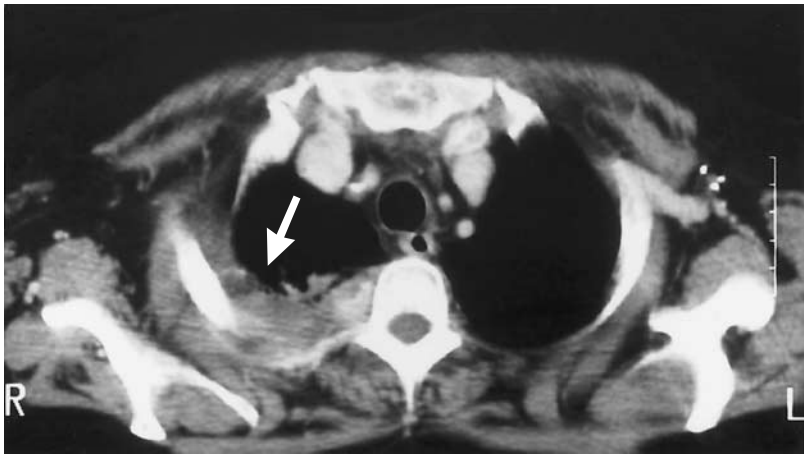

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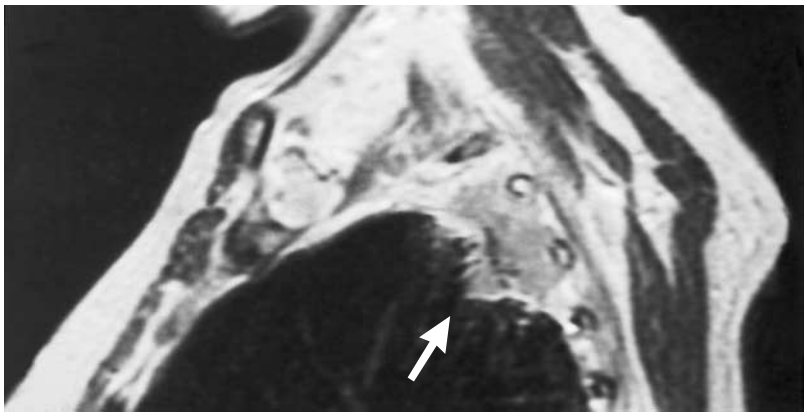

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Figure 2. Posteroanterior Plain Chest Radiograph (Panel A), Computed Tomographic Image (Panel B), and Sagittal T_1-Weighted Magnetic Resonance Image (Panel C) of the Chest of a Patient with a Right-Sided Superior Sulcus Tumor.

The arrow in Panel A indicates the abnormal opacity in the apex of the right lung. The tumor is located in the posterior aspect of this apex (arrows in Panels B and C), encasing the upper ribs and abutting the subscapularis muscle; however, there is no invasion of the brachial plexus or major vascular structures in the axilla (Panel C).

bodies is characteristic of a T4 lesion.[54] The staging of lymph-node involvement and distant metastasis is the same as for non–small-cell carcinoma elsewhere in the lungs. Therefore, by definition, superior sulcus tumors are either stage IIb or stage III (a or b) in the absence of distant metastasis.[54]

Noninvasive preoperative evaluation of the mediastinum by CT or MRI has been recommended; however, these radiographic studies are limited by substantial numbers of false positive and false negative results — up to 30 to 40 percent in some series, depending on the criteria used to define enlarged lymph nodes and the patient population.[46,55,56] Therefore, surgical assessment of the mediastinum with lymph-node sampling should be strongly considered before curative surgery is attempted.[16,53]

Distant metastatic spread should be sought by analysis of the patient's history, physical examination, and blood tests. CT of the chest and upper abdomen, including the liver and adrenal glands, and bone scanning as indicated by symptoms should be performed to evaluate common sites of metastatic disease. CT or MRI of the head must be part of the metastatic workup, because of the high incidence of brain metastasis with bronchogenic carcinoma in this location. Pulmonary-function tests and appropriate cardiac evaluation are recommended for patients who are being considered for surgical treatment.

TREATMENT

Radiotherapy and Surgery

The first successful treatment of a superior sulcus tumor by surgery and postoperative radiotherapy was reported by Chardack and MacCallum.[57] In 1961, the results of the first combined use of preoperative irradiation and surgery in 18 patients were published.[43] Since that time, different treatments that include radiation or surgery, alone or in combination, have been used, but there have been no prospective, randomized studies.

Preoperative radiotherapy followed by extended surgical resection has been the most common treatment of superior sulcus tumors.[3] In published series, the dose of radiation delivered to the tumor and its margins has ranged from 2000 to 6500 cGy[3,17,18]; however, no clear correlation between the dose of radiation and survival has been established.[17] Surgery is usually performed two to four weeks after the completion of radiotherapy.[3,17,43] The potential benefits of preoperative radiotherapy include a decrease in the size of the tumor, with improved resectability, and a reduction in the number of viable tumor cells, which theoretically prevents dissemination and implantation of the tumor during surgery.[3,43,58] However, there is no conclusive scientific evidence to recommend the standard use of preoperative radiotherapy in superior sulcus tumors, especially in view of a recent report, which suggests that the natural history and prognosis of these tumors are similar to those of other locally invasive non–small-cell lung cancers[59] for which preoperative radiotherapy is not beneficial.

Surgical treatment of superior sulcus tumors is usually performed by en bloc resection of the tumor and the chest wall, which may also be accompanied by resection of the involved paravertebral sympathetic chain, stellate ganglion, lower trunks of the brachial plexus, and in some cases, the subclavian artery and portions of the thoracic vertebrae. Tumor resection is generally performed by lobectomy or segmentectomy. Although limited lung resection has not been shown to affect the outcome adversely in several studies,[19,22,60] lobectomy remains the treatment of choice for bronchogenic carcinoma and has been found to decrease the rate of local recurrence and improve survival in some studies of superior sulcus tumors.[17,23] There are two major surgical techniques. The classic posterior approach is performed through a parascapular incision along the medial edge of the scapula, extending underneath its inferior tip and ending at the anterior axillary line.[3,43,61] The anterior transcervical approach involves an L-shaped incision that extends from the mandibular angle along the anterior border of the sternocleidomastoid muscle down to the suprasternal notch, and laterally under the medial half of the clavicle.[61,62] This approach is generally used for tumors located anteriorly at the thoracic inlet, particularly for those invading the subclavian vessels.[61,62] In patients with tumors involving the brachial plexus and the spine, a combined thoracic and neurosurgical approach can improve resectability and local control.[11] The reported surgical morbidity ranges from 7 to 38 percent,[10,17,44,60] with surgical mortality generally around 5 to 10 percent.[10,17,63]

Contraindications to surgical treatment include extensive involvement of the brachial plexus and paraspinal region, especially the intervertebral foramina, bodies, and laminae of the vertebrae; mediastinal perinodal involvement; invasion of the soft tissues at the base of the neck; venous obstruction; distant metastases; and clinically significant cardiopulmonary disease.[3,7,10] Involvement of the subclavian artery is a relative contraindication, but successful surgical resection in this circumstance has been reported.[53,62]

Radiotherapy can be used alone as a primary treatment, especially for inoperable superior sulcus tumors, palliating pain in up to 90 percent of the patients.[64-66] In most series, doses of 2000 to 8000 cGy have been used[21]; however, a dose of at least 6000 cGy is recommended for primary radiotherapy.[7,63,67] Intraoperative or interstitial radiotherapy and postoperative radiotherapy have been used for patients who have tumors that are not amenable to complete surgical resection, with some studies reporting survival rates similar to those for complete resection.[19,68] Despite these reports, other studies have failed to show

TABLE 2. RESULTS OF VARIOUS TREATMENTS IN PATIENTS WITH SUPERIOR SULCUS TUMORS.*

TREATMENT AND STUDY (DATE)	TOTAL NO. OF PATIENTS	NO. ASSIGNED TO TREATMENT	MEDIAN SURVIVAL	5-YR SURVIVAL
			mo	%
Preoperative radiotherapy and surgery with or without postoperative or intraoperative radiotherapy				
Hilaris et al.[58] (1974)	116	27	—	22
Ahmad et al.[66] (1984)	63	13	—	8
Paulson[3] (1985)	131	78	—	31
Beyer et al.[70] (1986)	28	15	31	48
Hilaris et al.[17] (1987)	129	82	23	29
Neal et al.[63] (1991)	73	29	—	21
Maggi et al.[22] (1994)	60	60	7–19	17.4
Ginsberg et al.[23] (1994)	124	124	17	26
Surgery and intraoperative or interstitial radiotherapy or postoperative radiotherapy				
Hilaris et al.[58] (1974)	116	57	—	15
Hilaris et al.[17] (1987)	129	46	14	20
Primary radiotherapy				
Hilaris et al.[58] (1974)	116	29	—	3.5
Ahmad et al.[66] (1984)	63	48	—	21†
Neal et al.[63] (1991)	73	32	—	22
Preoperative chemotherapy, radiotherapy, and surgery and intraoperative radiotherapy				
Martinez-Monge et al.[69] (1994)	18	18	—	56‡

*The studies cited represent some of the larger ones available. Several studies included patients who were treated with different treatments, such as primary radiotherapy and combined radiotherapy and surgery; therefore, these studies are listed more than once.

†The rate was for the 26 patients who received more than 5000 cGy.

‡The four-year survival rate is given.

any beneficial effects in terms of survival, especially after complete resection.[16,22] Thus, the role of intraoperative and postoperative radiotherapy is unclear at this time, and they should be used mainly in patients who are found to have unresectable tumors after a surgical attempt.[18,23,58]

Chemotherapy

Despite the recent interest in the use of induction chemotherapy in the initial treatment (neoadjuvant) of locally advanced bronchogenic carcinoma, its efficacy in the treatment of superior sulcus tumors has not been studied prospectively. In a study of 18 patients with stage IIIa or IIIb superior sulcus tumors who were treated with preoperative chemotherapy and irradiation followed by surgery and intraoperative radiotherapy, the rates of local control and survival at four years were 91 and 56 percent, respectively.[69] In contrast, in another study of 124 patients with superior sulcus tumors, there were no long-term disease-free survivors in a subgroup of 10 patients who were treated with preoperative platinum-based chemotherapy.[23] A phase 2 intergroup oncology trial of induction chemotherapy and radiotherapy followed by surgical resection of superior sulcus tumors with a nodal stage of 0 or 1 has been initiated to determine the feasibility and toxicity of treatment and to assess the objective response and resectability rates of these tumors.

SURVIVAL AND PROGNOSIS

The overall five-year survival rate after combined preoperative radiotherapy and extended surgical resection is generally around 20 to 35 percent, with a median survival of 7 to 31 months in various series[3,22,23] (Table 2). With radiotherapy alone, overall five-year survival rates range from 0 to 29 percent[10,63,64,71] (Table 2). Although the absence of involvement of mediastinal lymph nodes and bone and the achievement of local control in these series were associated with a five-year survival rate of up to 40 percent,[21,64] many studies of primary radiotherapy have reported survival rates of 0 to 10 percent.[14,58] This difference most likely reflects the inclusion of patients with unfavorable prognostic factors and unresectable tumors, making comparisons of primary radiotherapy with combined radiotherapy and surgery difficult.[14,16,67] Nonetheless, several more recent studies have found similar five-year survival rates of 18 to 23 percent among patients treated with primary radiotherapy and radiotherapy combined with surgery[21,63,64,66] (Table 2).

Relapse in the form of local or regional recurrence or distant metastasis is common after the treatment of superior sulcus tumors.[10,63,64,67] Brain metastasis is one of the most common forms of relapse, especially in patients with poorly differentiated large-cell carcinoma and adenocarcinoma.[17,23,64] Hence, some recommend prophylactic cranial irradiation for these patients.[17,64]

The prognosis of patients with superior sulcus tumors is related to several clinical factors. Factors that are associated with a poor prognosis in most series include extension of the tumor into the base of the neck; involvement of mediastinal lymph nodes, vertebral bodies, or great vessels; the presence of Horner's syndrome; and longer duration of symptoms.[3,10,16] The value of histologic findings as a prognostic indicator for survival is controversial.[3,10,17,64] Clinical factors associated with improved survival include good performance status, a weight loss of less than 5 percent of total body weight, and achievement of local control and pain relief after treatment.[10,21,67]

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