Superior sulcus tumors (SSTs), or as otherwise known Pancoast tumors, make up a clinically unique and challenging subset of non-small cell carcinoma of the lung (NSCLC). Although the outcome of patients with this disease has traditionally been poor, recent developments have contributed to a significant improvement in prognosis of SST patients. The combination of severe and unrelenting shoulder and arm pain along the distribution of the eighth cervical and first and second thoracic nerve trunks, Horner’s syndrome (ptosis, miosis, and anhidrosis) and atrophy of the intrinsic hand muscles comprises a clinical entity named as ‘Pancoast-Tobias syndrome’. Apart NSCLC, other lesions may, although less frequently, result in Pancoast syndrome. In the current review we will present the main characteristics of the disease and focus on the preoperative assessment.

**ABSTRACT**

Superior sulcus tumors (SSTs), or as otherwise known Pancoast tumors, make up a clinically unique and challenging subset of non-small cell carcinoma of the lung (NSCLC). Although the outcome of patients with this disease has traditionally been poor, recent developments have contributed to a significant improvement in prognosis of SST patients. The combination of severe and unrelenting shoulder and arm pain along the distribution of the eighth cervical and first and second thoracic nerve trunks, Horner’s syndrome (ptosis, miosis, and anhidrosis) and atrophy of the intrinsic hand muscles comprises a clinical entity named as ‘Pancoast-Tobias syndrome’. Apart NSCLC, other lesions may, although less frequently, result in Pancoast syndrome. In the current review we will present the main characteristics of the disease and focus on the preoperative assessment.

**KEYWORDS**

Pancoast; lung cancer; surgery

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**Introduction**

Superior sulcus tumors (SSTs), or as otherwise known Pancoast tumors, make up a clinically unique and challenging subset of non-small cell carcinoma of the lung (NSCLC). Although the outcome of patients with this disease has traditionally been poor, recent developments have contributed to a significant improvement in prognosis of SST patients. SSTs are characterized by the infiltration of the thoracic inlet and may present with a constellation of symptoms depending on the invasion of specific structures. The combination of severe and unrelenting shoulder and arm pain along the distribution of the eighth cervical and first and second thoracic nerve trunks, Horner’s syndrome (ptosis, miosis, and anhidrosis) and atrophy of the intrinsic hand muscles comprises a clinical entity named as “Pancoast-Tobias syndrome”. Apart NSCLC, other lesions may, although less frequently, result in Pancoast syndrome.

**Definition, history, epidemiology and anatomic features of Pancoast tumors**

**Definition**

The name SSTs is associated with an anatomical groove present...
in the lung apex, formed by the subclavian artery as it passes over the lung at this point. Not all SSTs are associated with this precise anatomic location, but the term has come to signify any tumor that is identified in the apices of the lungs with the associated clinical symptoms that are the hallmark of this disease. These tumors are often referred to as Pancoast tumors, after the radiologist Henry Pancoast described these lesions, developing at the chest apex, as carcinomas of uncertain origin in 1924 and 1932 (1,2).

The following criteria must be met for characterizing a lesion as a Pancoast tumor; the tumor must invade the parietal pleura and cause pain, paresthesias or other neurological dysfunction; it is not sufficient only to have an apical lung tumor. These tumors may invade muscles, upper ribs, thoracic vertebral bodies, subclavian vessels, the inferior portion of the brachial plexus, and the upper end of the thoracic autonomic chain including the stellate ganglion. Invasion of the brachial plexus leads to the constellation of neurologic signs and symptoms known as the Pancoast syndrome, whereas destruction of the stellate ganglion by tumor causes Homer syndrome.

**Historical background**

The first recorded case of a Pancoast tumor was described by Hare in 1838 (3). This “tumor involving certain nerves”, was producing constant and characteristic pain in the shoulder and the arm. Almost ninety years later in 1924, Henry K. Pancoast, a radiologist from Philadelphia, reported several cases of chest tumors associated with characteristic radiographic findings of “small homogenous shadows at the extreme apex”, “more or less” rib destruction and often vertebral infiltration (1). These tumors were associated with a clinical syndrome of pain in the distribution of the eighth cervical and first and second thoracic trunks and Horner’s syndrome. Eight years later he published a second report (2) on his original work upon the syndrome, reporting on seven such patients. He stated that these tumors were “not subject to surgical removal”, were “refractory to radiation treatment” and were “rather rapidly fatal”.

In 1946, Herbert and Watson (4) reviewed all published cases until then and presented eight new cases of Pancoast tumors. They concluded that the disease without effective therapy was uniformly fatal. All patients that they observed died within ten months after initial diagnosis was made. It was not until 1954 that Haas and colleagues (5) described palliation of the severe and unrelenting arm pain troubling these patients; they reported dramatic pain relief after external beam radiation. One of those patients survived for almost three years after initiation of therapy.

Chardack and MacCallum (6) were the first to achieve long-term survival (>5 years) by means of combination therapy consisting in lobectomy followed by external beam radiation. This report was the basis for others to follow, suggesting that combined therapy might be appropriate for these patients. In 1961, Shaw and Paulson (7) presented a series of patients who were treated with radiotherapy preoperatively followed by surgical resection. However, these initial attempts at surgical resection were not widely accepted; reports of significant numbers of patients who received palliative therapy alone without surgery continued to appear in the literature (8). Nevertheless, combination therapy remained the mainstay of therapy for Pancoast tumors for over three decades. At the late 1990’s the introduction of concurrent chemo- and radiotherapy led to significant improvement in the outcome of the disease.

**Epidemiology**

Pancoast tumors represent 3% to 5% of all lung cancers, and are biologically similar to typical NSCLC with a predilection for distant metastasis (9). The major risk factor responsible for their development is cigarette smoking. The average age at presentation is the sixth decade of life, with men affected more frequently than women.

The most common cause of Pancoast syndrome is NSCLC of squamous cell origin (10) followed by adenocarcinoma and large cell carcinoma subtypes (11). However, in some studies adenocarcinoma has been reported to be more frequent than squamous cell subtype and since its incidence nowadays predominates in the developed countries, it may even overtake squamous cell carcinoma (12,13). The reasons underlying this shift have not been completely understood yet, but consumption of filtered cigarettes over the last decades has substantially contributed to this change. Small cell lung cancer is an infrequent cause of Pancoast tumor (14,15). Other primary apical neoplasms can also produce Pancoast syndrome; adenoid cystic carcinoma (16), carcinoid (17), hemangiopericytoma (18) and mesothelioma (19) have also been reported. Metastases to the lung from the larynx (19), thyroid (20), bladder (21) and cervix (22) have also been described. Hematologic malignancies such as plasmacytoma (23), non-Hodgkin lymphoma (24), and lymphomatoid granulomatosis (25) have also been listed as infrequent causes of Pancoast tumors. Finally pseudomalonal (26) and staphylococcal (27) infections, as well pulmonary actinomycosis (28), have also been incriminated in the pathogenesis of a Pancoast-like syndrome (29). Rarely, tuberculosis (30), aspergillosis (31), cryptococcosis (32) and allescheriasis (33) have also been reported as possible causes.
**Anatomic features of superior pulmonary sulcus tumors**

In 1932 Pancoast reported that these tumors arose in a residual fissure formed during the period of embryonic development of the right upper lobe and the migration of the azygos vein; he stated that the original cells were likely epithelial rests from the fifth brachial cleft (2). On the contrary, Tobias suggested that the site of origin of these tumors was "bronchial pulmonary tissue" (34).

Variations exist among efforts made to describe the superior pulmonary sulcus as a definite anatomic structure. These contradictions can be explained because there can be both a functional definition of these tumors based on the characteristic presentation of the Pancoast syndrome, as well as an anatomic one based on the location of these lesions in the upper thoracic cavity.

Even nowadays the precise definition of the anatomic space of the superior sulcus remains inaccurate since most anatomy textbooks do not include its description as a defined anatomic area. In the original description, Pancoast described the tumor location as within the "superior pulmonary sulcus", which later became well known as the "superior sulcus". The superior sulcus therefore is considered the most cephalad extent of the chest wall, particularly the apical costovertebral gutter. In Kubic’s Surgical Anatomy of the Thorax (35) it is described as the “backward curve of the ribs which produces a deep groove internally on either side of the vertebral column”.

The term “superior sulcus” is obscured even more by those considering it to be within the lung itself and formed by the subclavian artery as it crosses the pulmonary apex (36). Paulson (37) agreed with this belief suggesting that most apical lung neoplasms arose in close proximity to this sulcus. On the other hand, Seydel and colleagues (38) suggested that SSTs arise in the fissure formed by the migration of the azygos vein during the development of the right upper lobe; if this were true, left-sided Pancoast tumors would not exist.

Netter (39) supported that the superior pulmonary sulcus actually “does not correspond to any recognized anatomic location”. These tumors were considered as apical carcinomas that involve the parietal pleura, upper ribs, endothoracic fascia, brachial plexus, sympathetic chain, vertebral bodies, with the resultant clinical syndrome.

Exceptions exist among those who tried to define the superior sulcus as a single consistent groove in the lung. Tumors have been shown to reside in pulmonary impressions formed by the first rib, azygos vein, superior vena cava, esophagus and inferior vena cava on the right and by the first rib, aortic arch, and descending aorta on the left side (40). Apical cancers do not commonly originate from the subclavian artery or vein sulcus. If they did, invasion of those vessels would be far more frequent.

Thus, this inconsistency by many authors and the difficulty to agree in a standard term defining the superior pulmonary sulcus has led to the rejection of that term. An understanding of the symptoms that associate the invaded anatomical structures and their radiologic documentation is critical in therapeutic planning.

**Presentation, diagnostic workout, biology and staging of Pancoast tumors**

**Presentation**

Superior sulcus lesions of NSCLC origin account for less than 5% of all bronchogenic carcinomas (9,41). Because the thoracic inlet represents a narrow compartment, modest growth and direct extension produce characteristic symptoms. Therefore, symptoms such as cough, hemoptysis, and dyspnea are uncommon in the initial stages of the disease due to the peripheral location of these tumors (9,29). The same stands for hilar pulmonary infiltration and mediastinal structure invasion. On the other hand, involvement of supraclavicular lymph nodes is not unusual, and the physical findings are related to the local invasion of nervous, vascular and bony structures of the apex by the process producing the full blown Pancoast’s syndrome.

In the early stages, shoulder pain represents the most common symptom; common causes include invasion of the parietal pleura, upper ribs, brachial plexus, endothoracic fascia, or the adjacent vertebral bodies. The pain may radiate down the ipsilateral arm following the typical distribution of the ulnar nerve. Thus, clinical features depend upon the location and type of structures invaded at the thoracic inlet by the tumor (see Table 1).

Tumors of the anterior compartment usually invade the first intercostal nerve and upper ribs rather than the phrenic nerve or superior vena cava, and usually present with pain distributed to the upper anterior chest wall.

Tumors of the middle compartment present with signs related to the compression or infiltration of the middle and lower trunks of the brachial plexus, such as pain and paresthesias irradiating to the shoulder and upper limb.

Tumors lying posterior to the middle scalene muscles present with a painful or abnormal sensation in the axilla and medial aspect of the upper arm in the territory of the intercostobrachial nerve.

Irritation of the sympathetic chain by the adjacent tumor can produce ipsilateral flushing and even hyperhidrosis of the face way before its invasion. Additionally reflex sympathetic dystrophy can also been reported. Further invasion of the sympathetic chain by the tumor results in Horner’s syndrome.
associated with ipsilateral ptosis, miosis, and anhidrosis, a phenomenon observed in 40% of patients (42). In only five percent of cases the tumor may involve the intervertebral foramina at the initial presentation (29). Diagnostic and radiologic work-up is always essential at presentation in order to assess surgical resectability and proceed to preoperative staging of the tumor.

Preoperative assessment

Upon presentation of a patient referring symptoms associated with the existence of a Pancoast tumor the physician should undergo a thorough and detailed preoperative work-up to establish thoracic inlet invasion. These steps should define the preoperative stage, histologically confirm the diagnosis and assess tumor’s resectability.

The keystone in the beginning of every preoperative workout should always be patient’s history and physical examination. After examining and understanding of the patient’s complains additional exams will be necessary. Pancoast tumors are not easily detected on plain chest X-rays (CXR) in their early stages of the disease, since they represent small apical tumors hidden behind the clavicle and the first rib. As the disease progresses, a CXR may reveal asymmetry of the pulmonary apices or pleural thickening; frequent suspicious findings include unilateral apical cap of more than 5 mm in thickness or asymmetries of both apical caps more than 5 mm, bone destruction or even thoracic wall and spinal invasion according to the stage. Lordotic views and radiographs of the cervical and upper thoracic spine may also be helpful in the determination of the presence of tumor (43,44).

CT scanning is an important diagnostic tool to define the size of the process, detect peripheral or satellite lesions and assess the presence of enlarged lymph nodes that are undetectable on conventional radiographs. CT scanning may also reveal bony, spinal, mediastinal or brachial plexus invasion (42). Enhancement with intravenous contrast medium injection can provide useful information about blood vessel involvement by the process.

Magnetic resonance imaging (MRI) of the chest is a more accurate preoperative examination in identifying the extent of the tumorous process than CT scan. It should be routinely performed when tumors approach the intervertebral foramina in order to rule out invasion of the extradural space. Additionally, MRI angiography offers a better assessment of invasion through the pleura and subpleural fat and the involvement of the subclavian vessels (45), brachial plexus (46), and vertebral bodies than CT scanning (43). CT scans provide 60% sensitivity, 65% specificity, and 63% accuracy in defining the local extent of tumor, in contrast to MRI with a sensitivity of 88%, a specificity of 100%, and an accuracy of 94%. Therefore MRI has evolved as the imaging modality of choice in the assessment of the local extent of Pancoast tumors.

Bronchoscopy with the flexible fiberoptic bronchoscope may assist in determining invasion of the tracheal or bronchial cavities and set diagnosis in about 30% to 40% of cases, since the majority of Pancoast tumors tend to grow in the periphery of the lung parenchyma (47). On the other hand, Narayan and colleagues (48) contradicted such a high percentage, suggesting that this is effective only up to 20% of cases.

Although 90% of all patients suffering from Pancoast tumor can be diagnosed in the basis of clinical and conventional radiologic methods alone, biopsy is mandatory for histological confirmation, operability assessment and therapy planning. Moreover, the wide variety of diseases that can result in

<table>
<thead>
<tr>
<th>Compartments</th>
<th>Limits</th>
<th>Anatomical structures</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior</td>
<td>Between sternum and the anterior part of anterior scalene muscle</td>
<td>Platysma, sternocleidomastoid, omohyoid muscles, subclavian and jugular veins, scalene fat pad</td>
<td>Pain radiating to the upper anterior chest wall, venous thrombosis</td>
</tr>
<tr>
<td>Middle</td>
<td>Between anterior and middle scalene muscles</td>
<td>Anterior and middle scalene muscles, subclavian artery, phrenic nerve and trunks of brachial plexus</td>
<td>Pain and paresthesias radiating to the shoulder and upper limb, arterial thrombosis, paralysis of the diaphragm</td>
</tr>
<tr>
<td>Posterior</td>
<td>Behind middle scalene muscle</td>
<td>Posterior scalene muscle, posterior scapular, posterior part of subclavian and vertebral artery, stellate ganglion, sympathetic chain, long thoracic and accessory nerves, neural foramina, vertebral bodies</td>
<td>Pain in axillary region and medial part of upper arm, Horner’s syndrome</td>
</tr>
</tbody>
</table>

Table 1. Anatomic structures of thoracic inlet and clinical symptoms reproduced by tumor invasion of specific compartments.
Panagopoulos et al. Pancoast assessment

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Additional studies support this concept associated with vertebral body invasion. Furthermore, tumors invading the subclavian vessels are also staged as T4. Dartevelle et al. (58) reported a 30% 5-year survival in T4 patients. However, subclavian vessel involvement was a negative prognostic factor.

The poor 5-year survival of Pancoast patients with pN2 or pN3 involvement underlines the importance of identifying these patients preoperatively. Thus, lymph node status is a very important prognostic factor. Since positive mediastinal N2 lymph nodes occur in about 20% of Pancoast tumors (59) the incidence of unsuspected N2 disease suggests further assessment of the mediastinum by means of mediastinoscopy as previously mentioned or PET, even in those patients without radiological sings of lymph node infiltration. Although in the past, mediastinoscopy was not routinely performed in most studies, Paulson (60) underlined the importance of mediastinoscopy as a preoperative staging method, since SST patients exhibited poor prognosis if mediastinal or hilar lymph nodes were involved.

Invasion of ipsilateral supraclavicular lymph nodes by the tumor is classified as N3 disease. Some series show that patients with supraclavicular lymph node metastases had a better prognosis than patients with N2 disease. Evidence suggests that such involvement in patients with a Pancoast tumor may not prevent long-term survival since may have a prognostic significance similar to that of N1 disease. These nodes are in close vicinity of the tumor and therefore could have the characteristics of the biological behavior of local nodes. Ginsberg reported a 5-year survival of 14% in patients with N3 disease as opposed to 0% in patients with N2 disease (41). Nevertheless, with the introduction of chemo-radiotherapy and associated extensive resections, an argument can be made to pursue more aggressive extrathoracic staging even in those without symptoms of distant metastases.

In one of the largest studies published for SSTs at Memorial Sloan-Kettering Cancer Center (61) with patients treated according to the bimodality therapy (preoperative radiotherapy followed by en bloc resection) 5-year survival was 46% for stage IIB, 0% for stage IIIA, and 13% for stage IIIB tumors. Survival was influenced by T and N status and completeness of resection. However, resection was considered pathologically complete in only 64% of T3 N0 and 39% of T4 N0 tumors. Therefore accurate staging significantly influences survival.

Pancoast tumors are staged according to the 2009 IASLC/UICC AJCC TNM staging system for NSCLC (62) (see Table 2).

**Table 2. Staging of pancoast tumours.**

<table>
<thead>
<tr>
<th>TNM</th>
<th>Stage</th>
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<tbody>
<tr>
<td>T3, N0, M0</td>
<td>IIB</td>
</tr>
<tr>
<td>T3, N1-2, M0</td>
<td>IIIA</td>
</tr>
<tr>
<td>T4, any N, M0</td>
<td>IIB</td>
</tr>
<tr>
<td>Any T, N3, M0</td>
<td>IIIB</td>
</tr>
<tr>
<td>M1</td>
<td>IV</td>
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</table>

**Summary**

Pancoast (or superior sulcus) tumors represent 3% to 5% of all lung cancers, and are biologically similar to typical NSCLC. They are characterized by the infiltration of the thoracic inlet and may present with a constellation of symptoms depending on the invasion of specific structures. The combination of severe and unrelenting shoulder and arm pain along the distribution of the eighth cervical and first and second thoracic nerve trunks, Horner’s syndrome (ptosis, miosis, and anhidrosis) and atrophy of the intrinsic hand muscles comprises a clinical entity named as “Pancoast-Tobias syndrome”. Various other neoplasms or infectious diseases have been reported to be responsible for the reproduction of the Pancoast syndrome. Variations also existed over the past decades among efforts made to describe the superior pulmonary sulcus as a definite anatomic structure. An understanding of the symptoms that associate the invaded anatomical structures and their radiologic documentation is critical in therapeutic planning. Because these tumors by definition involve the chest wall, it is logical that these patients usually present with local rather than systemic manifestations of the disease. In the early stages, shoulder pain represents the most common symptom due to invasion of the parietal pleura, upper ribs, brachial plexus, endothoracic fascia, or the adjacent vertebral bodies. Clinical features depend upon the location and type of structures invaded at the thoracic inlet by the tumor.

Less than 50% of patients with Pancoast tumors are considered resectable lesions at presentation. The remaining is unresectable because of extensive vertebral body involvement, mediastinal nodal disease, or distant metastases. Therefore accurate staging is mandatory since it significantly influences survival.

Histological proof is mandatory upon presence of mediastinal lymph node enlargement on preoperative radiological examinations, since Pancoast lesions associated with mediastinal nodal metastases (positive N2 or N3 disease) have a poor prognosis. Mediastinoscopy and/or anterior mediastinotomy may be decisive in determining extend of the disease and should be strongly considered in these cases.

Invasion of ipsilateral supraclavicular lymph nodes by the tumor is classified as N3 disease. Studies showed that patients...
with supraclavicular lymph node metastases exhibited better outcome than patients with N2 disease. Evidence suggests that such involvement may have a prognostic significance similar to that of N1 disease. Additional evidence suggests that the biology of Pancoast tumors is indifferent than that of other NSCLC since survival is increased when resection of a Pancoast tumor involves a lobectomy rather than a wedge resection alone.

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