CHAPTER 2

TREATMENT AND PROGNOSIS OF SUPERIOR SULCUS TUMORS

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SUMMARY

- Superior sulcus tumors, also known as Pancoast tumors, are non-small-cell lung carcinomas with a specific clinical presentation and management due to their localization in the lung apex.
- This type of tumors is rarely detected at an early stage due to the low incidence and the late occurrence of symptoms.
- Shoulder pain, with or without radiation to the ipsilateral arm or hand, and Horner’s syndrome are often the first symptoms.
- Currently, standard treatment consists of concurrent chemoradiotherapy followed by en-bloc resection of the tumor and involved structures; this treatment results in 5-year survival rates of over 50%.
- Local invasion, mediastinal lymph metastasis and, in a selected group of patients, distant metastasis are not necessarily a contra-indication for surgery.
- Patients that underwent a complete resection or have a complete pathological response after induction treatment, have significantly higher survival rates.
- Treatment of patients with a superior sulcus tumor should take place in a multidisciplinary team; due to the complexity of treatment it is recommended to refer patients to specialized centers.
INTRODUCTION

Non small-cell lung cancer (NSCLC) is the number one cause of tumor-related mortality in the Netherlands (source: www.cijfersoverkanker.nl). Superior sulcus tumors, or Pancoast tumors, are a subtype of NSCLC. They are distinguished by their location at the pulmonary apex and invasion of surrounding structures. Superior sulcus tumors account for less than 5% of all NSCLC. In this paper we will discuss the clinical presentation, diagnosis, treatment and prognosis of this type of lung cancer, in accordance to the recent literature.

BACKGROUND

In 1932 Henry Pancoast, a radiologist at the Hospital of the University of Pennsylvania, described a tumor in the pulmonary apex associated with pain, Horner’s syndrome, bone destruction and atrophy of the hand musculature. This typical combination of symptoms was later known as the Pancoast syndrome. The term superior sulcus tumor is derived from the typical location of these tumors in the upper part of the pulmonary sulcus. This is the costo-vertebral gutter extending from the first rib to the diaphragm.

In clinical practice the term superior sulcus tumor is used for upper lobe tumors invading the chest wall above the level of the second rib. They can be subdivided based on their anatomical position relative to the scalene muscles. Tumors in the anterior, middle and posterior compartment cause different symptoms, depending on the involved surrounding structures. The histological type of superior sulcus tumor is usually squamous cell- or adenocarcinoma. Small-cell carcinoma’s are rare and require a different therapeutic approach.

CLINICAL PRESENTATION

Superior sulcus tumors are generally diagnosed in a late stage. Early detection is impeded for two reasons. First, the incidence of superior sulcus tumors is low. In 2009, almost 11.000 new patients with lung cancer were diagnosed, of which only an estimated 5% were superior sulcus tumors (source: www.cijfersoverkanker.nl). There are approximately 9000 general practitioners working in The Netherlands. This means that an average general practitioner, working for 35 years, will only see one or two patients with this type of tumor in his whole
career. A second reason for late detection is the peripheral localization of this tumor. Due to this localization there are almost no pulmonary symptoms, such as hemoptysis, dyspnea or coughing.\(^1,4\) Also, a post obstructive pneumonia is unlikely to develop.\(^1,4\) As a result, patients frequently consult their general practitioner because of pain. Shoulder pain, sometimes radiating to the arm (C8,T1 or T2 dermatome), is the most frequent occurring symptom in superior sulcus tumor patients.\(^1,7\) Together with atrophy of the hand musculature, this is caused by invasion of the brachial plexus.\(^7\) Often, patients are treated with physical therapy for some time because of shoulder pain before they are diagnosed with a superior sulcus tumor. Another, frequently occurring symptom is Horner’s Syndrome, due to invasion of the stellate ganglion of the sympathetic cord.\(^1,4,7\) This syndrome is a combination of ipsilateral ptosis, miosis and anhidrosis.\(^7\) Weight loss is a non-specific symptom but can be present in non-small-cell lung cancer patients.\(^4\) Other symptoms, such as supraclavicular lymphadenopathy or superior vena cava syndrome are rare.\(^4\) As with all non-small-cell lung cancers, smoking is the most important risk factor for developing a superior sulcus tumor.\(^8\) In patients with risk factors (advanced age, smoking) and unexplained shoulder pain, with or without radiation to the arm, that is not responding to physical therapy or pain killers, further investigation is warranted.

**DIAGNOSIS & STAGING**

Superior sulcus tumors are staged using the 7th edition of the TNM classification.\(^9\) Superior sulcus tumors can be identified on a plain chest radiograph where they appear as a unilateral apical cap (Figure 1, page 23). A contrast enhanced computed tomography (CT) scan of the chest (including the cervicothoracic junction and the upper abdomen) can be used to confirm the lesion. The size of the tumor and loco regional invasion, as well as mediastinal and hilar lymphadenopathy and the presence of distant metastasis (i.e. liver and adrenals) can be assessed.\(^2\) A fluordeoxyglucose-positron emission computed tomography (FDG-PET/CT) scan is part of the standard work-up for detection of metastases to the lymph nodes or distant organs.\(^2\) Brain metastases, the most common localization for distant metastasis in NSCLC, should be ruled out using magnetic resonance imaging (MRI) of the brain.\(^2\) MRI of the thoracic outlet can yield additional information about invasion of the brachial plexus, subclavian artery and vein and spinal column and can be considered in individual cases.
Figure 1. A posteroanterior plain chest radiograph demonstrating an increased density in the apex of the right upper lobe, the so-called “apical cap”, characteristic for a superior sulcus tumor. The 2nd rib is destructed by the tumor and partially not visible anymore.

Figure 2. Axial slide of a chest CT-scan demonstrating a superior sulcus tumor in the right upper lobe with invasion of the thoracic spine. The vertebral body and the 2nd rib are partially destructed by the tumor.
Histological confirmation of the diagnosis can be obtained by performing CT- or ultrasound-guided aspiration. Due to the peripheral localization of the tumor, bronchoscopy is less frequently successful in obtaining tissue for histopathology. In case of suspected mediastinal lymph nodes found on the CT- or FDG-PET/CT-scan, tissue for cytology or histology can be obtained through endobronchial ultrasound (EBUS), transesophageal ultrasound (EUS) or mediastinoscopy.²

Invasion of structures such as the spinal column, subclavian vessels or brachial plexus is not a contra-indication for resection (Figure 2, page 23). Mediastinal lymph node metastases and solitary metastases to the brain, adrenals or the bones are no absolute contra-indications for surgery. An important reason for this is the relatively favorable prognosis of this group of patients compared to the overall group of NSCLC patients. Another reason is the importance of local control of the primary tumor, because invasion of the brachial plexus, spine and chest wall can lead to severe pain that can hardly be palliated.² Of all superior sulcus tumor patients without distant metastasis approximately one third is eligible for surgery.¹⁰ The majority of patients is not considered for resection due to tumor progression or distant metastases during chemoradiotherapy or a poor general condition. Assessment of resectability of the tumor should be performed by an experienced team in a multidisciplinary approach involving a pulmonary physician, surgeon, radiologist, specialist in nuclear medicine, radiotherapist and sometimes a neurosurgeon or orthopedic surgeon. Therefore, referral of patients to a center with broad experience with the treatment of superior sulcus tumors is recommended.²

The physical condition of the patient is assessed based on general condition, comorbidity and testing of lung function and exercise tolerance. After this assessment it is decided whether the patient is capable of undergoing the planned trimodality treatment with an acceptable risk for morbidity and mortality.²¹¹

**TREATMENT & PROGNOSIS**

There is only limited evidence available for the optimal treatment of superior sulcus tumors, based on retrospective cohort studies and a few phase 2 studies. Randomized trials are lacking. Since their first description in 1932, much has changed in the management of superior sulcus tumors. Until the early 1950s these tumors were considered unresectable and uniformly fatal. Shaw and his co-workers introduced radiotherapy as neo-adjuvant therapy followed by resection.¹² Results of this strategy were promising although 5-year survival
figures did not exceed 47% (T3 tumors) and 13% (T4 tumors) and 40% of patients developed a local recurrence. Surgical techniques were refined and in the early 1990s preoperative chemotherapy was added to the treatment strategy. Concurrent chemoradiotherapy instead of sequential chemoradiotherapy offered improved survival rates, mainly due to improved local control. Local recurrence rates decreased (12% instead of the 40% reported before) and 5-years survival rates exceeding 50% in case of a complete resection were reported. A complete resection can be obtained in 76 - 97% of patients and a complete pathological response is found in 16 - 45%.

For patients undergoing treatment with a curative intention, distant metastases, especially to the brain, remain a major problem. Whether prophylactic irradiation of the brain leads to improved survival in NSCLC patients is currently investigated.

Nowadays, standard therapy for superior sulcus tumors is concurrent chemoradiotherapy followed by surgery. Several schedules for induction chemoradiotherapy are reported. Usually, schedules consist of at least 2 cycles of platinum based chemotherapy combined with concurrent radiotherapy to a total dose of at least 45 Gy. Patients with tumors considered to be unresectable receive a high dose (for example 66 Gy) of radiotherapy for palliation. If the general condition of the patient does not allow combined chemoradiotherapy, application of radiotherapy only can be considered.

In selected patients with limited metastasis, usually a solitary metastasis in the brain, adrenals or bone, chemoradiotherapy followed by resection with a curative intent can still be chosen. This should then be combined with radical treatment of the metastasis with stereotactic radiotherapy or resection.

To assess resectability and to exclude metastases, restaging is performed using a CT- or FDG-PET/CT-scan. Resection of the tumor is planned approximately 6 weeks after administration of the last fraction of radiotherapy and consists of en-bloc resection of the tumor and involved structures, usually 1 or more ribs and the T1 nerve root of the brachial plexus. Mediastinal lymph node dissection is part of the standard treatment. Postoperative pain management, for example epidural analgesia, and physical therapy including breathing exercises are essential for preventing postoperative complications, especially atelectasis and pneumonia. Post-radiation fibrosis can hamper resection of vascular (hilar) structures in particular and, additionally, can give rise to disturbed wound healing. The combined treatment of chemoradiotherapy followed by resection is associated with a mortality of 3 to 7% and considerable morbidity.

Patients not eligible for curative treatment can be treated with palliative radiotherapy with or without chemotherapy, depending on tumor stage and the general condition of
the patient. Molecular analysis of the tumor can sometimes help to select tumor-directed palliative chemotherapy.

For all patients adequate symptomatic treatment, including painkillers, is needed. A specialist in pain management should be part of the treating team. During chemoradiotherapy and before surgery the nutritional status of the patient is evaluated and optimized with the help of a dietitian. Additionally, smoking cessation should be pursued.

Not much is known about the quality of life after resection of a superior sulcus tumor. The extensive resection of lung tissue, chest wall and parts of the brachial plexus might lead to impairments (pulmonary function, shoulder & arm function), pain and complaints of cosmetic nature. In the literature, it is stated that resection of the T1 nerve root of the brachial plexus is usually well tolerated, while resection of the C8 nerve root leads to loss of strength and diminished arm function and fine motor function of the hand. However, this is based on observations in only a few patients. In our experience, the arm function in patients with a superior sulcus tumor is mainly impaired by invasion of the tumor before the start of the treatment and to a less extent by the treatment itself. At this moment a prospective study to assess the arm function and quality of life in this group of patients is performed in our center.

Follow-up after trimodality treatment for a superior sulcus tumor is provided by a pulmonary physician and consists of a history, physical examination and a chest radiograph or chest CT-scan. If indicated, additional imaging studies, such as an FDG-PET/CT-scan, can be performed. Follow-up visits take place every 3 months in the first year, once every 6 months in the second year and thereafter once a year during at least 5 years. Following thoracotomy, some patients develop a chronic pain syndrome. In these cases referral to a specialist in pain management is recommended.

While superior sulcus tumors initially were uniformly untreatable, following the addition of radiotherapy, chemotherapy and later concomitant chemoradiotherapy, a curative treatment became possible with 5-years survival rates of more than 50%. Both a complete resection and a pathological complete response following induction chemoradiotherapy are associated with favorable prognosis. Following a microscopic or macroscopic irradical resection survival rates are worse and comparable with that of patients that did not underwent resection. A complete pathological response is obtained in approximately one third of patients. The development of diagnostic modalities that can identify a complete pathological response preoperatively could possibly prevent an unnecessary resection in these patients.

The most important factor for treatment failure is the development of distant metastasis,
mainly to the brain. For the future, better chemotherapeutical regimes might offer some improvement. At the moment some studies are evaluating whether prophylactic cranial irradiation offers any survival benefit.\textsuperscript{14}

**CONCLUSION**

Of all non-small-cell lung carcinoma’s, only 5% are superior sulcus tumors. Therapy resistant arm or shoulder pain in patients with increased risk (high age, smoking) is a reason for further investigation. Treatment of superior sulcus tumor patients requires a multidisciplinary approach and preferably takes place in a specialized center. Current standard treatment is concomitant chemoradiotherapy followed by resection. Invasion of vital structures, such as the subclavian vessels, brachial plexus and vertebra, is not necessarily a contra-indication for surgery, neither are metastases to the mediastinal lymph nodes or limited, often solitary, metastases to the brain, adrenals or bones.
REFERENCES


