

Pancoast tumour: current therapeutic options

V. D. Palumbo^{1,2}, S. Fazzotta¹, F. Fatica¹, B. D'Orazio¹, F. P. Caronia³, M. Cajozzo¹, G. Damiano¹, A. Maffongelli¹, B. M. Cudia¹, M. Messina⁴, A. I. Lo Monte¹

¹Department of Surgical, Oncological and Stomatological Disciplines, University of Palermo; ²Euro-Mediterranean Institute of Science and Technology (IEMEST), Palermo; ³Mediterranean Oncological Institute (IOM), Viagrande; ⁴School of Medicine, University of Palermo, Italy

Abstract

Background. Pancoast's syndrome is caused by malignant neoplasm of superior sulcus of the lung which produces destructive lesions of thoracic inlet and comes along with the involvement of brachial plexus and stellate ganglion. Computed tomography (CT) or magnetic resonance imaging (MRI) scans can detect early lesions otherwise missed by routine radiographs and can also define the local extent or metastatic progression of the disease. Protocols involving combinations of irradiation, chemotherapy, and surgery are currently being under investigation to determine the best management.

Aims. This work reviewed the current diagnostic and therapeutic approaches to Pancoast's tumors.

Discussion. Patients with lung superior sulcus carcinoma should be considered for surgery only after an appropriate diagnostic assessment. The perfect candidate for surgery should have a confined to the chest disease with T3N0M0 staging. Inoperable patient with severe pain after irradiation therapy may benefit from palliative surgical resection. Medical therapy plays only a secondary role in lung cancers, patients with disseminated lung cancer might require palliative treatment and medical management of paraneoplastic syndrome symptoms. Following surgery, radiation and chemotherapy may improve local and systemic control by addressing individual adverse findings.

Conclusions. The cooperation of surgeons, clinicians and radiologists represents the gold standard today and a multidisciplinary approach is essential to achieve the best outcome possible.

Further studies are advisable in order to define the best surgical approach and the real advantage of mini-invasive surgery by comparison with open surgery. *Clin Ter 2019; 170(4):e291-294. doi: 10.7417/CT.2019.2150*

Key words: Lung superior sulcus carcinoma, lung tumor, thoracoscopy, video-assisted thoracic surgery

Introduction

Pancoast's syndrome is caused by malignant neoplasm of superior sulcus of the lung which produces destructive lesions of thoracic inlet and comes along with the involvement of brachial plexus and stellate ganglion (1-3), causing

severe pain of the shoulder radiating toward axilla and scapula to the ulnar aspect of the hand muscles; so that it leads to complete atrophy of the hand and arm muscles, Horner's syndrome and generalized oedema.

Most of the tumours that causes Pancoast's disease are squamous cell carcinomas (SCCs) or adenocarcinomas; only 3-5% are small cell carcinomas.

Computed tomography (CT) or magnetic resonance imaging (MRI) scans can detect early lesions otherwise missed by routine radiographs and can also define the local extent or metastatic progression of the disease. Diagnosis can be reached throughout several techniques such as: CT-guided supraclavicular fine needle aspiration (FNA) biopsy (positivity of 90-95%); bronchoscopy; linear or radial Endobronchial Ultrasound (EBUS); open chest biopsy throughout thoracotomy access or video-assisted thoracic surgery (VATS) biopsy.

Histological and cytological samples are important not only to confirm the diagnosis but also to provide molecular profiling, as a matter of fact new targeting therapies for non-squamous and squamous cell carcinomas are available (EGFR-VEGF) (4).

Careful assessment and appropriate staging should be performed before surgery; moreover selected patients may undergo preoperative irradiation of 30 Gy over 2 weeks and after an interval of 2-4 weeks could benefit from surgical resection of the chest wall, lower brachial plexus and en bloc lung resection with a 5-year survival rate of 30%. Contraindications to surgery include the following: extension of the tumour into the neck or vertebrae, presence of substantial mediastinal lymph nodes, peripheral tumour progression.

Protocols involving combinations of irradiation, chemotherapy, and surgery are currently being under investigation to determine the best management.

Overall Pancoast tumours are much less common than other lung cancers, accounting for fewer than 5% of all lung cancers (1-3% in various previous series) (5,6). Originally deemed as universally fatal, Pancoast tumours might be now fought with effective and curative treatments thanks to improvements in combined management. Nevertheless prognosis for Pancoast's syndrome is stage-dependent and

Correspondence: Dr. Vincenzo Davide Palumbo, Department of Surgical, Oncological and Stomatological Disciplines, University of Palermo Via Del Vespro, 129 – 90127 – Palermo, Italy. Tel.: +393273694514. E-mail: vincenzodavide.palumbo@unipa.it

adverse prognostic factors include the presence of Horner syndrome, involvement of mediastinal lymph nodes, incomplete resection, involvement of supraclavicular lymph nodes and vertebral body invasion. Up to present no patient with the first 3 prognostic factors has survived till 5 years. Distant progression of disease limits as well the survival, brain is the most frequent site of metastatic progression causing failure of treatment, so that a careful surveillance for brain metastasis during and after therapeutic management is recommended. Attar et al reported a median survival of 36.8 months in patients with T3 lesions undergoing combined treatment; median survival was only 6.4 months in the patient with T4 disease (7).

Overall survival data were summarized by Detterbeck, who reported 5-year survival rates around 15% and 56%. (8) Attar and coworkers treated 104 patients, among these ~7% were 5-year survivors and ~3% were 10-year survivors. (7) Further studies demonstrated a surgical morbidity rate of 7-38%, with mortality rate from 5% to 10% (9).

More generally predictors of 5-year survival for Pancoast disease include weight loss, supraclavicular fossa or vertebral body involvement, disease stage and feasibility of surgical treatment. A study by MD Anderson group reported the following findings (10):

- among patients with stage IIB disease, the 5-year survival rate was 47%, whereas for those with stage IIIA and IIIB disease, it was respectively 14% and 16%;
- among patients with stage IIB disease, surgical treatment and weight loss were significant independent predictors of 5-year survival;
- among patients with stage IIIA disease, the only predictor of survival was the Karnofsky performance score;
- among patients with stage IIIB disease, the only independent predictor of survival was a right superior sulcus location, which was associated to a worse 5-year survival rate by comparison with a left superior sulcus location;
- patients with adenocarcinoma more frequently had cerebral metastases within 5 years than patients with squamous cell tumours.

Local relapse is common despite preoperative or postoperative radiation therapy, Muscolino et al found local recurrence in 60% of patients undergone a combined approach; in two thirds of patients who underwent complete resection, local recurrences were the first site of relapse (5).

This local distribution of relapses has been reported from several studies reviewed by Detterbeck, many of which involving patients undergone preoperative radiation therapy. (8) In Memorial Sloan-Kettering experience, additional postoperative brachytherapy was administered to achieve the best local control, nevertheless local and distant relapses were common. (5) The aim of this brief review is to clarify diagnostic modalities and therapeutic approaches for Pancoast's tumour. The selection of relevant literature was based on Medline queries using the following key words: "Pancoast's tumour", "superior sulcus carcinoma", "Pancoast treatment", "Pancoast diagnosis", "surgery in Pancoast's tumour". The article follows INCA guidelines for narrative reviews (11).

Treatment

Patients with lung superior sulcus carcinoma should be considered for surgery only after an appropriate diagnostic assessment. The perfect candidate for surgery should have a confined to the chest disease with T3N0M0 staging. A rare exception is made for a right upper-lobe lesion with intranodal mediastinal metastases and T3N2M0 staging. However, surgery alone is not the prevalent treatment. Inoperable patient with severe pain after irradiation therapy may benefit from palliative surgical resection. Contraindications to surgery include extensive invasion of neck, brachial plexus, or vertebrae; perinodal mediastinal extension and peripheral metastases (extrathoracic metastatic disease and positive mediastinal nodes); complete upper and lower brachial plexus invasion is a relative contraindication while vertebral body involvement should not be considered a contraindication unless involvement of the cortex is reported.

Medical therapy plays only a secondary role in lung cancers, patients with disseminated lung cancer might require palliative treatment and medical management of paraneoplastic syndrome symptoms. In the last few years Japanese researchers reported that patients with Pancoast tumours may take advantage from preoperative chemo-radiotherapy. (12) Nevertheless, data indicate that the best survival rate is reached throughout preoperative chemo-radiotherapy followed by surgical resection in carefully selected patients (13,14), even if preoperative radiotherapy followed by surgery is a reasonable alternative in some patients. A few centres obtained satisfying survival rate after surgery, by developing better surgical approaches to subclavian vessels and vertebral column even though the involvement of these structures is overall associated with poor survival (15).

Up to now, no data recommend an appropriate management of unresectable disease, even if radiotherapy offers good palliation for pain.

Filis embraces a combined triple-modality treatment based on chemo-radiotherapy and surgical resection, as described by the Southwest Oncology Group (SWOG), with 5-year survival rates markedly improved ($\geq 55\%$ with complete resection).

However, protocols have changed in time, as well as the management of Pancoast tumours (16).

Ultrasound-guided cervical nerve roots ablation can be considered for patients with intractable neuropathic pain, anecdotal studies have shown an excellent pain relief as well as an improvement in quality of sleep.

Surgical approach

Resection of Pancoast tumours is made of two elements: surgical incision of the chest wall at the thoracic inlet and upper lobe lobectomy with hilar and mediastinal lymph node dissection. Pancoast tumours are difficult to deal with because of the location of the apex in a small and rigid area and the need to approach the hilar lymph nodes.

Current practice in most centres is based on a specific planned treatment for each single patient. Frequently the therapeutic plan is developed by a multidisciplinary team with particular attention to adverse prognostic factors.

All patients with Pancoast tumours involving parietal pleura and chest wall should undergo surgery, provided that the following conditions are satisfied:

- Absence of distant metastases
- Good cardiopulmonary status of the patients allowing surgery
- Absence of preoperative evidence of extensive mediastinal adenopathy.

Involvement of mediastinal nodes is always associated with poor outcome after resection. At the time of surgery, a complete resection of all involved structures is recommended.

In most patients the surgical treatment of choice is a complete removal of the tumour by en bloc chest wall resection combined with lobectomy and node staging (5). Depending on the extent of local invasion, surgical treatment may require resection of paravertebral sympathetic chain, stellate ganglion, lower trunks of the brachial plexus, subclavian artery or portions of thoracic vertebrae. For tumours invading the brachial plexus and/or the spine, a combined thoracic-neurosurgical approach is recommended. For patients with apical tumours apparently not attached to the chest wall at computed tomography (CT) scan, evidence suggests that thoracoscopy can be used to assess for chest wall invasion avoiding unnecessary neoadjuvant treatment and futile thoracotomy (17,18). Moreover, a study by Caronia et al revealed that video-assisted thoracic surgery (VATS) can be used to manage Pancoast tumours, this technique allows a reduction of the magnitude of resection, by sparing the patient a useless thoracotomy or by optimizing the site of the thoracotomy. It may also have a significant educational role. (19,20) As a matter of fact, VATS provides several theoretical edges: rib retractors, known as a source of pain, are not used; lobectomy is performed through well-known accesses avoiding the uncommon transmanubrial approach for lobar dissection; Grunenwald contra-incision is shortened; unnecessary resection of thoracic wall is avoided. The so called “VATS observation first” philosophy has the advantage to exclude previously undetected pleural dissemination and to precisely define the tumour location (21). From a surgical standpoint, superior sulcus tumours not invading the thoracic inlet are completely resectable through the classical posterior Shaw-Paulson, even if this approach does not allow a direct and safe visualization, manipulation and complete oncological clearance of all anatomical structures in the thoracic inlet, so that this restricted access may be one of the reasons of incomplete resections and high surgical morbidity and mortality related to this approach.

The anterior transcervical approach appears to be the optimal method to access anterior lung apex or first rib lesions, this for, according to Nikolaos, every apical tumour without invasion of the thoracic inlet can be completely resected through the posterior Shaw-Paulson approach alone. Highly suspicious lesions for invasion of the thoracic inlet should be first explored by an anterior transclavicular approach and may be followed by the Shaw-Paulson approach (22) Kaway and colleagues described a novel technique based on a combined approach consisting of a partitioned thoracoscopic incision and the employment of LigaSure vessel-sealing system (Valleylab, Boulder, CO, USA) for chest wall resection, this technique allows to perform chest

wall resection under direct vision from a limited posterior incision without special devices to retract the specimen, moreover Ligasure can easily hold the layer of muscle to be dissected with a reliable haemostatic effect without damages of surrounding tissues. Besides chest wall resection at the thoracic inlet, the video-assisted thoracoscopic lobectomy was performed using usual method. This combined approach to resect Pancoast tumours is feasible and guarantee good access to both apical and hilar sites in a less invasive way (23). Following surgery, radiation and chemotherapy may improve local and systemic control by addressing individual adverse findings. In many centres, neoadjuvant or induction chemo-radiotherapy is administered to patients with potentially resectable tumours (see above). Important predictive factors include T category, nodal status, presence of Horner syndrome, and completeness of resection (5-9,24).

The most severe complication related to Pancoast tumours surgical treatment is cerebrospinal fluid leaks which usually appears as a pulmonary air leakage leading to meningitis experienced as a severe headache, moreover additionally resection of the stellate ganglion and the root of C8 may lead to Horner syndrome (4). Although the T1 nerve root is not the main contributor to the hand muscles' function, its involvement and consequent sacrifice, in case of involvement of the first rib, brings to a functional impairment leading to the paresis of the ipsilateral hand (15).

Finally we can state that surgery for Pancoast's tumours remains a challenge.

Conclusions

Pancoast's tumours were historically thought to have a fatal prognosis. Despite the significant improvements in understanding the biology and treatment of these tumours, as they represent a small percentage of lung cancer population, additional studies are required. The cooperation of surgeons, clinicians and radiologists represents the gold standard today and a multidisciplinary approach is essential to achieve the best outcome possible.

For what concerns therapy the combined triple-modality treatment consisting in chemo-radiotherapy followed by surgical resection seems to be the best approach to improve survival rate. Further studies are advisable in order to define the best surgical approach and the real advantage of minimally-invasive surgery by comparison with open surgery.

References

1. Pancoast HK. Importance of careful roentgen ray investigations of apical chest tumors. *JAMA* 1924; 83:1407-11
2. Pancoast HK. Superior pulmonary sulcus tumor: tumor characterized by pain, Horner's syndrome, destruction of bone and atrophy of hand muscles. *JAMA* 1932; 99:1391-6
3. Hare ES. Tumor involving certain nerves. *Lond Med Gaz* 1838; 1:16-8
4. Zarogoulidis K, Porpodis K, Domvri K et al. Diagnosing and treating pancoast tumors. *Expert Rev Respir Med*. 2016 Dec; 10(12):1255-1258. Epub 2016 Oct 27
5. Ginsberg RJ, Martini N, Zaman M et al. Influence of surgical

- resection and brachytherapy in the management of superior sulcus tumor. *Ann Thorac Surg* 1994; 57:1440-5
6. Johnson DE, Goldberg M. Management of carcinoma of the superior pulmonary sulcus. *Oncology (Huntingt)*. 1997; 11:781-6
 7. Attar S, Krasna MJ, Sonett JR et al. Superior sulcus (Pancoast) tumor: experience with 105 patients. *Ann Thorac Surg* 1998; 66:193-8
 8. Detterbeck FC. Pancoast (superior sulcus) tumors. *Ann Thorac Surg* 1997; 63:1810-8
 9. Arcasoy SM, Jett JR. Superior pulmonary sulcus tumors and Pancoast's syndrome. *N Engl J Med* 1997; 337:1370-6
 10. Komaki R, Roth JA, Walsh GL et al. Outcome predictors for 143 patients with superior sulcus tumors treated by multidisciplinary approach at the University of Texas M. D. Anderson Cancer Center. *Int J Radiat Oncol Biol Phys* 2000; 48:347-54
 11. La Torre G, Backhaus I, Mannocci A. Rating for narrative reviews: concept and development of the International Narrative Systematic Assessment tool. *Senses Sci* 2015; 2:31-5
 12. Uchino K, Tauchi S, Tanaka Y, et al. Treatment of superior sulcus tumor. *Kyobu Geka* 2010; 63:18-22
 13. Anderson TM, Moy PM, Holmes EC. Factors affecting survival in superior sulcus tumors. *J Clin Oncol* 1986; 4:1598-603
 14. Detterbeck FC, Jones DR, Kernstine KH, Naunheim KS. Lung cancer. Special treatment issues. *Chest* 2003; 123:244S-258S
 15. Hilaris BS, Martini N, Wong GY, Nori D. Treatment of superior sulcus tumor (Pancoast tumor). *Surg Clin North Am* 1987; 67:965-77
 16. Filis AK, Robinson LA, Vrionis FD, Resection of the First Rib With Preservation of the T1 Nerve Root in Pancoast Tumors of the Lung. *Cancer Control*. 2016 Jul;23(3):295-301
 17. Stanford W, Barnes RP, Tucker AR. Influence of staging in superior sulcus (Pancoast) tumors of the lung. *Ann Thorac Surg* 1980;29:406-409.
 18. Hubbard MO, Schroeder C, Linden PA. Routine use of staging thoracoscopy for pancoast tumors without overt radiographic chest wall invasion. *Surg Laparosc Endosc Percutan Tech* 2011; 21:111-5
 19. Caronia FP, Ruffini E, Lo Monte AI. The use of video-assisted thoracic surgery in the management of Pancoast tumors. *Interact Cardiovasc Thorac Surg* 2010; 11:721-726
 20. Caronia FP, Fiorelli A, Ruffini E, et al. A comparative analysis of Pancoast tumour resection performed via video-assisted thoracic surgery versus standard open approaches. *Interact Cardiovasc Thorac Surg* 2014; 19:426-435
 21. Rosso L, Palleschi A, Mendogni P, et al. Video-assisted pulmonary lobectomy combined with transmanubrial approach for anterior Pancoasttumor resection: case report. *J Cardiothorac Surg* 2016;11:65
 22. Nikolaos P, Vasilios L, Efstratios K et al. Therapeutic modalities for Pancoast tumors. *J Thorac Dis* 2014; 6:S180-193
 23. Kawai N, Kawaguchi T, Yasukawa M, et al. Less Invasive Approach to Pancoast Tumor in a Partitioned Incision. *Ann Thorac Cardiovasc Surg* 2017; 9
 24. Muscolino G, Valente M, Andreani S. Pancoast tumours: clinical assessment and long-term results of combined radiosurgical treatment. *Thorax* 1997; 52:284-6