ELSEVIER

European Journal of Cardio-thoracic Surgery 36 (2009) 747—753

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

www.elsevier.com/locate/ejcts

Review

Current treatment paradigms of superior sulcus tumours

Masaya Tamura, Mir Alireza Hoda, Walter Klepetko *

Department of Cardiothoracic Surgery, Medical University of Vienna, Vienna, Austria

Received 28 November 2008; received in revised form 23 March 2009; accepted 14 April 2009; Available online 20 August 2009

Summary

Pancoast or superior pulmonary sulcus tumours are a rare subset of non-small-cell lung carcinomas (NSCLCs) which occur with an incidence of less than 5% of all lung cancers. Today, induction chemoradiation followed by surgical resection has become the established standard treatment approach for patients with sulcus superior tumours in the absence of other contraindications. This review focusses on the historical change of the treatment strategy, the evolution of surgical and multimodality management of this disease and the most recent published clinical outcome data of patients suffering from superior pulmonary sulcus carcinoma.

Keywords: Pancoast tumour; Sulcus superior tumour; Induction therapy; Radiotherapy; Surgery

1. Introduction

It has been nearly 85 years since Dr Henry Pancoast, a radiologist, for the first time, in 1924, described the clinical and radiographic features of special lung tumours located in the superior sulcus, which later on were named after the author [1]. Pancoast tumours are a rare but a unique subset of non-small-cell lung carcinomas (NSCLCs), which occur with an incidence of less than 5% of all lung cancers. Their treatment is inherent with particular challenges because of their special anatomical location and their late detection. Although, for a considerable period of time, the majority of these tumours were thought to be inoperable [2] and only patients with earlier disease IIB (i.e., T3, N0) were operated. However, the development of special approaches and new techniques now allows for surgical resection of structures that were previously considered unresectable. Together with the impressive progress that has been made with multimodality treatment protocols in the recent years, this resulted in dramatic improvements of results. This review focusses on the historical change of the treatment strategy, the evolution of surgical and multimodality management of this disease and the most recent published clinical outcome data of patients suffering from sulcus superior tumours.

2. Clinical presentation and diagnosis

The full clinical picture of the Pancoast—Tobias syndrome consists of a constellation of characteristic symptoms, including pain down the arm, eventually with weakness and numbness along the distribution of C8/Th1—2, Horner's syndrome and radiographic evidence of destruction of the first thoracic rib or vertebral body [3]. In many reports however, any patients with a tumour in the typical location of the apex of the lung and infiltration of the first rib is included under the term Pancoast tumour, regardless of whether Horner's syndrome or pain radiating down the arm is present [4—12].

On the other hand, the clinical diagnosis of a Pancoast tumour must not necessarily imply the presence of NSCLC. Patients suffering from other entities such as lymphoma, tuberculosis or primary chest wall tumours can present with an apical mass and chest wall involvement, which result in precisely the same clinical picture [2].

NSCLCs of the superior sulcus belong to the most challenging thoracic malignant diseases to treat because of their frequent invasion not only of the first rib but also of other adjacent vital structures, including the brachial plexus, subclavian vessels and the spine [13]. Patients with Pancoast tumours differ from other patients with NSCLC in as far as the usual symptoms, such as cough, dyspnoea and haemoptysis, do occur less frequently [14]. Instead, the leading symptom in this entity is the aforementioned pain in the shoulder and the arm, and therefore, the correct diagnosis is often delayed, because the origin of the problem is frequently believed to be of orthopaedic or rheumatologic nature [14].

Computed tomography usually leads to the correct diagnosis; however, it has a limited ability to determine the extent of invasion of the primary tumour into adjacent structures [15]. The latter is better performed with magnetic resonance imaging (MRI) [16] and magnetic resonance

* Corresponding author. Address: Waehringer Guertel 18-20, 1090 Vienna, Austria. Tel.: +43 1 40400 5644; fax: +43 1 40400 5642.
E-mail address: walter.klepetko@meduniwien.ac.at (W. Klepetko).

1010-7940/$ — see front matter
doi:10.1016/j.ejcts.2009.04.036

angiography (MRA) [17], both of which are able to provide more detailed information about the involvement of neural and vascular structures.

A tissue diagnosis can be established by bronchoscopy, however, due to the peripheral location of Pancoast tumours; this is only effective in about 10–20% of cases [15]. Instead, computed tomography-guided biopsy is the most preferred method to obtain tissue for histology.

The further staging of patients does not differ very much from that of patients suffering from other forms of NSCLC.

The specific value of PET is not clearly defined in Pancoast tumours, but has been found to improve staging of lymph nodes [18] and detection of occult metastatic disease in patients with NSCLC [19] in general. Since positive mediastinal N2 lymph nodes do occur in approximately 20% of Pancoast tumour cases [20], confirmation of the mediastinal lymph node status by mediastinoscopy and the endoscopic ultrasound-guided fine-needle aspiration [21,22] should be performed on a routine basis.

A specific problem represents supraclavicular lymph nodes, which can be involved in these patients more frequently than in standard NSCLC cases [4]. However, there is ongoing discussion whether such positive supraclavicular nodes should be classified as N3 or still should be considered to belong to local lymph node areas, in view of the special location of the tumour.

3. Treatment

3.1. Historical development

The special growing features of Pancoast tumours explain why radiotherapy, surgery or a combination of both have ever been an integral part of treatment, with the aim to achieve the best possible local tumour control.

Evolutions in the management of Pancoast tumours during the last 85 years can be classified into four eras.

During the first era (1930s–1950s), the tumours became recognised as a special growing form of primary lung carcinomas, but were thought to be inoperable and incurable. Treatment with radiotherapy, mainly with a palliative intention, became the standard of care of these patients, but necessarily was without long-term success. In the second era (1950s–1980s), initial attempts with surgical resection mainly in combination with radiotherapy were performed. In 1956, Chardack and MacCallum [23] reported the first successful treatment of a superior sulcus tumour using surgical resection, followed by postoperative radiation. The treated patient was alive and disease free 5 years later. In 1956, Shaw reported a patient with typical Pancoast syndrome who initially underwent radiotherapy with a palliative intention, which resulted in resolution of pain and decrease in tumour size, and therefore was followed by a radical resection. Shaw [24] tested this treatment strategy further, and reported improved local control and longer-than-anticipated survival. As a result, induction radiotherapy (30 Gy over 2 weeks) and *en-bloc* resection through an extended posterolateral thoracotomy became a clear alternative to radiotherapy alone for the treatment of superior sulcus tumours.

However, surgical resection remained limited to tumours invading the ribs only, and any further involvement of vascular or neural structures was still considered to remain a contraindication for an operation.

This only changed in the third era (1980s–1990s) when novel surgical approaches for the resection of tumours involving the spine and subclavian vessels were introduced. Dartevelle et al. [25] were the first to develop an anterior transcervical approach for cancers infiltrating the subclavian vessels, and, later on, several other modifications of this technique were reported [26,27]. However, overall survival at 5 years still remained about 30% and remarkable improvement in survival was not yet achieved. One of the reasons for this was based on the fact that more advanced cases were treated compared to earlier periods and that, besides systemic relapse, local recurrence still occurred in about 40% of patients [28].

These results emphasised the need for new treatment strategies in order to improve both local as well as systemic controls. With this intention, in the fourth era (1990s to present), induction chemoradiotherapy followed by radical surgical resection was introduced as a new treatment standard for superior sulcus tumours, which resulted in impressively improved outcome [29–39].

3.2. Radiotherapy as single-treatment modality

Results of radiotherapy as single-treatment modality for superior sulcus tumours are available from historic series [40,41] and from otherwise inoperable patients only. Therefore it is impossible to compare them with results obtained with the combination of radiotherapy and surgery, or with multimodality induction therapy followed by radical resection. Usually the applied doses of radiation ranged between 45 and 70 Gy. Van Houtte et al. suggested a dose–response relationship with improved results for doses in excess of 50 Gy [42]. However, there exists no randomised controlled trial that compared high-dose and low-dose radiation treatment. High doses (50 Gy or more) usually resulted in high morbidity and mortality rates [43,44].

Usually, radiotherapy alone has been reported to result in satisfying pain relief; however, in most studies, long-term survival was not achieved. From a total of 18 reports about treatment of Pancoast tumours with radiotherapy alone, eight reported 0% 5-year survival and the remaining 10 studies reported a rate of 5–23% (mean 6.25%) [6,11,30,37,42,44–56].

3.3. Radiotherapy combined with surgery

In 1956, Chardack and MacCallum reported the first successful treatment of a Pancoast tumour, managed by *en-bloc* resection and followed by postoperative radiation [23]. Since the 1960s, improved survival rates were reported with preoperative radiotherapy [57–59] and especially improved local control, reflected by marked radio-necrosis in the resected surgical specimens, was emphasised by some authors [60].

In a total of 23 reports about combined radio-surgical treatment of Pancoast tumours, a mean 5-year survival rate of 36.5 ± 12.7% (mean ± SD) was described [4,6,8,9,11,12,30,31,47,49,51,53,55–57,59–61,46,63–65], which was much better than the results reported for radiation treatment alone. However, since no randomised trial comparing radiotherapy alone vs the combination of radiotherapy and surgical resection exists until now [30], the available evidence that the chance of long-term survival is better with combined radiation therapy and operation than with high-dose radiotherapy alone [62] still remains conflicting.

With regard to the applied doses of preoperative radiotherapy, no standard exists as well. Attar and Miller initially have used preoperative doses of 40–60 Gy [42,57], but later lowered the dose to 30 Gy because of the remarkable postoperative morbidity and mortality observed. Fuller and Chambers [11] reported the feasibility of high doses (55–65 Gy) of preoperative irradiation, but were unable to demonstrate any survival advantage. On the other hand, low-dose preoperative radiation (30 Gy within 2 weeks) has been advocated by Paulson et al. and has resulted in a 5-year survival rate of 35% in 64 patients [61].

In another recent report, Martinod et al. [12] reported that preoperative radiotherapy significantly improved the 5-year survival for stage IIB–IIIA, while postoperative radiotherapy and chemotherapy did not significantly alter survival.

3.4. Trimodality treatment: induction chemoradiotherapy followed by surgical resection

The changing paradigms in treatment of NSCLC since the late 1990s resulted in the introduction of induction chemoradiotherapy (induction CT/RT), followed by radical surgical resection in the treatment plan of superior sulcus tumours.

Improvements in completeness of resection (Fig. 1), and clinical as well as pathological response rates, were the immediate results of such a therapy, which were followed by clearly improved long-term (5-year) survival rates (Table 1, Fig. 2). However, it is a well-known phenomenon of induction chemotherapy (CT)/radiotherapy (RT) that the assessment of

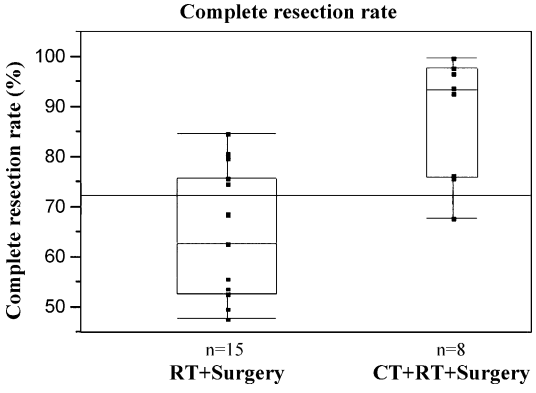

Fig. 1. Completeness of resection according to different modes of treatment. Results of publications are pooled and mean values with standard deviation are given.

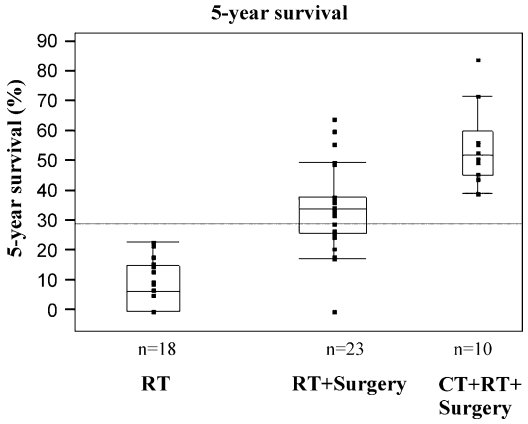

Fig. 2. Five-year survival rates according to different modes of treatment. Results of publications are pooled and mean values with standard deviation are given.

response is difficult. Complete pathological response can only be identified after surgical resection. For this reason, no prospective comparison between different treatment regimens can be performed.

The Essener group [36] operated on 31 patients (81% T3, 19% T4 tumours) with 29% with involvement of N2/3 lymph nodes, who were treated with an induction combination of three cycles of cisplatin (60 mg m^{-2}) and etoposide 150 mg m^{-2} or paclitaxel 175 mg m^{-2}. This was followed by concurrent chemoradiotherapy (one course cisplatin 50 mg m^{-2} and etoposide 100 mg m^{-2} combined with 45 Gy hyperfractionated accelerated radiotherapy). This resulted in 69% showing a complete or near-to-complete response and surgical resection resulting in 100% completeness of resection, with a postoperative mortality of 6.4%. Actuarial survival for all patients at 5 years was 46% with significantly better results in responders and patients with N0–1 disease only.

The largest of the available multimodality studies was performed by the Southwestern Oncology Group (SWOG 9416 trial), which tested a less-aggressive induction regimen of concurrent CT/RT (two cycles of induction chemotherapy (cisplatin 50 mg m^{-2} with etoposide 50 mg m^{-2}) together with 45 Gy of radiotherapy), which was followed by surgery and postoperative boost chemotherapy with two cycles of cisplatin–etoposide [35]. In this study, 110 patients were included, however, with a very conservative selection of N0/1 patients only. The authors reported that therapy was associated with acceptable morbidity and mortality. Complete or near-complete response was achieved in 61% and completeness of resection was 94%. Actuarial 5 years' survival for all patients was 44% and 54% after complete response. Questions about the study were raised that the large number of participating institutions might have negatively impacted overall results, because of a potentially considerable variability in the surgical part of the treatment.

A much more aggressive approach towards both patient selection and intensity of induction therapy was taken by the group of Krasna and colleagues [34], who accepted even patients with N3 lymph nodes and solitary brain metastasis (14%) for a combination therapy of two cycles platinum-based chemotherapy concurrent with 45-Gy large-field

Table 1
Results of trimodality treatment of superior sulcus tumours.

Author	Published	*n*	Stage			Treatment			Chemotherapy regimen		Radiation	Complete	p-CR	Survival		Median months
	Year										Dose (Gy)	Resection (%)	Ratio (%)	Two-year (%)	Five-year (%)	
Martinez-Monge [29]	1994	18		IIIA	IIIB	inc N2	CT/RT+S+IORT	CDDP	MMC	VDSor CBDCA	46–50	76.4	70.5	NR	56.2 (4 year)	NR
Attar [30]	1998	11			IIIB	IV	CT/RT+S		PTX	CBDCA	60	NR	NR	NR	72	NR
Wright [31]	2002	15				exc N2	CT/RT+S	CDDP	VP-16		51	93	87	93	84	NR
Barnes [32]	2002	8	IIB	IIIA	IIIB	exc N2	CT/RT+S	CDDP	VP-16		50	NR	NR	85.7	NR	NR
Miyoshi [33]	2004	11		NR			CT/RT+S	CDDP-based			40–56	NR	NR	73	53	NR
Kwong [34]	2005	36	IIB	IIIA	IIIB	IV	inc N2	CT/RT+S	CDDP-based		56.9	97	40.5	58	50	31
Rusch [35]	2007	88	IIB	IIIA	IIIB		exc N2	CT/RT+S+CT	CDDP	VP-16	45	76	56	55	44	NR
Marra [36]	2007	31	IIB	IIIA	IIIB		inc N2, 3	CT/RT+S	CDDP	VP-16 or PTX	45	94	69	74	46	54
Pourel [37]	2008	72	IIB	IIIA	IIIB		inc N2	CT/RT+S	CDDP	VP-16	45	98	NR	62	51 (3 year)	36.5
Kunitoh [38]	2008	57	IIB	IIIA	IIIB		inc N2	CT/RT+S	CDDP	MMC	45	68	21	61 (3 year)	56	NR
Kappers [39]	2008	9	IIB	IIIA	IIIB		inc N2	CT/RT+S	CDDP	VDS CBDCA or GEM	20–39	100	47	75	39	38

radiotherapy (tumour and mediastinum) followed by 14.2-Gy small-field boost-radiotherapy. This study included 37 patients, and a completeness of resection was achieved in 97%. However, complete response was seen in 40% only and 5 years' actuarial survival of all patients was 50%, which still is remarkable, given the advanced stage of the patients. Interestingly, the occurrence or absence of recurrence in the brain did not have any influence on survival.

Interesting results also derive from the group of the Massachusetts General Hospital [31], which compared induction CT/RT with radiotherapy only. Thirty-five patients, again with N0/1 disease only were treated and CT/RT was significantly superior to RT only in all parameters (complete or near-complete response rate, 35% vs 87%; completeness of resection, 80% vs 93%; 4 years' actuarial survival, 49% vs 84%; local recurrence, 30% vs 0%).

Based on these data, the modern treatment standard for sulcus superior tumours has become the combination of induction CT/RT followed by radical surgical resection. However, it is also obvious that there exists remarkable variability in the individual protocols for such a treatment. Choice of chemotherapeutic agents, the number of CT cycles, timely sequence of application, mode and intensity of RT, all these parameters are hardly standardised yet and vary according to the preferences of different groups.

To optimise the conditions for trimodality treatment, patients should also be referred to experienced centres with large numbers of lung surgery.

3.5. Special surgical aspects of treatment of superior sulcus tumours

3.5.1. Surgical approaches

The distinct anatomical location of superior sulcus tumours has demanded the development of special surgical approaches for adequate exposure of the tumour and the involved adherent structures. The first successful approach, which later on was named by the authors, was developed by Paulson and colleagues [66] and was the so-called 'high posterior thoracotomy'. This incision, extending around the tip of the scapula, and further midway between the posterior edge of the scapula and the spinous processes, up to the level of C7, allowed for excellent exposure of the posterior chest wall, including the transverse processes, the vertebrae and the roots of the thoracic nerves and the plexus. However, resection of the subclavian vessels is difficult with this approach, and therefore a special hook-formed extension, which runs anteriorly towards the sternoclavicular joint, was developed later by others [67,68].

3.5.1.1. Transcervical–thoracic approach. Dartevelle and his group developed an anterior transcervical approach for resection of anterior types of Pancoast tumours. This incision runs along the anterior border of the sternocleidomastoid muscle and continues laterally above the clavicle [26]. The medial portion of the clavicula is excised and, in this way, an excellent exposure of the entire thoracic inlet is provided, which allows for a safe dissection and complete surgical clearance of involved segments of the subclavian vessels, phrenic nerve and brachial plexus. Dartevelle and his group have emphasised that most cases of sulcus superior tumour

may be treated with this approach without the need for the large posterolateral thoracotomy as described by Paulson [62]. However, although this approach accounts for lower morbidity than the posterior approach, the transection of the clavicula still causes postoperative alterations in the shoulder mobility and cervical posture [3]. This problem led to the development of the transmanubrial L-shaped incision.

3.5.1.2. Transmanubrial L-shaped incision. This further development of the above-described technique was later made by Grunenwald and colleagues [69], who modified the Dartevelle approach from transclavicular to transmanubrial, thus preserving the integrity of the clavicula and its muscular insertions by raising both in the form of an osteomuscular flap. The approach allows for equal good access as the Dartevelle incision, but has the main advantage of significantly lower morbidity.

3.5.1.3. Anterior trans-sternal approach. This incision consists of an upper median sternotomy, together with an extension into the anterior fourth intercostal space, and a transverse incision above the clavicle at the base of the neck. It provides excellent exposure of tumours involving the anterior upper chest wall, particularly when the subclavian artery or the superior vena cava is involved as well [70].

3.5.2. Limits to resectability

3.5.2.1. Lymph node involvement. Lymph node status is an important prognostic factor for NSCLS in general and for sulcus superior tumours in particular [63,71]. However, acceptance of sulcus superior tumour patients with mediastinal lymph node involvement for surgery has been variously handled in the literature. Many protocols completely exclude patients with N2 disease from further surgical treatment (Ruschet et al. [35], Mass General paper). Others do accept patients with minimal or well-defined mediastinal lymph node involvement for induction therapy, followed by surgical resection in the situation of response. For example, Kwong et al. [34] did not exclude sulcus superior tumour patients with positive mediastinal lymph nodes from trimodality treatment and found no difference in survival for positive or negative pre-treatment mediastinal lymph nodes. In most papers, however, results of patients with persistent N2 disease turned out to be clearly inferior to those of patients with N0/1 only. On the other hand, no clinical trial has yet compared CR with CR induction followed by surgery in sulcus superior tumour patients with N2 involvement.

Another important issue is the valuation of ipsilateral supraclavicular lymph node disease. According to the current UICC classification, these nodes are classified as N3 disease. However, for the situation of sulcus superior tumour, supraclavicular lymph node involvement might inhere a different and better prognostic character compared to the situation of other lung tumours, since these nodes are in close vicinity of the tumour and therefore could have the characteristics of the biological behaviour of local nodes [4,63].

3.5.2.2. Vascular involvement. Vascular involvement has historically been considered to be a relative contraindication for surgical resection of sulcus superior tumour, however, with the earlier described advances in surgical techniques and in combination with multimodality induction therapy, tumours that were previously deemed unresectable can now safely and effectively be resected [9,26]. For this reason, vascular involvement itself is not considered any more to be a prognostic factor for outcome, as long as a radical resection and free margins are obtained during surgical resection.

3.5.2.3. Neural involvement. There is wide acceptance [44,62] that extensive local involvement of the brachial plexus constitutes a contraindication to surgical resection because of the poor survival and high rate of incomplete resection [62]. However, resection of the lower parts of the plexus, especially of the C8 T1 roots has been performed in surgical treatment of sulcus superior tumour [64]. The neurological consequences of this are well described; with T1 root resection resulting in diffuse weakness of the intrinsic muscles of the hand, whereas resection of the C8 nerve root of the lower trunk of the brachial plexus results in permanent paralysis of the hand muscles [2]. The final decision to resect or spare the neural roots however has always to be taken intra-operatively. Of course, the aim of any such operation should always be to achieve full radicality.

3.5.2.4. Vertebral body involvement. Similar to the invasion of vessels and neural structures, invasion of the spine was considered to be a contraindication for an oncologically meaningful resection for a long time due to the inherent poor prognosis [7,26]. This however was caused in part by the lack of both adequate surgical techniques for the resection of the spine, as well as multimodality treatment concepts.

The necessary surgical techniques to deal with this problem have meanwhile been developed by several groups from the Memorial Sloan-Kettering Cancer Center [72], MD Anderson Cancer Center [73] and from France [74]. These surgical procedures should be performed by an experienced team, including a neurosurgeon or orthopaedic surgeon, since these techniques include laminectomy, single- and multilevel partial and hemi-vertebrectomy as well as resection of whole vertebral bodies. Grunenwald and colleagues [74] emphasised the importance of local tumour control when he reported 2-year survival rates of 52% for radically resected cases vs only 13% for cases which were not radically resected. These data give evidence that radical excision of sulcus superior tumour involving the spine can be safely performed and results in improvement of overall prognosis.

4. Recurrence and prognostic factors

Various papers have tried to identify prognostic factors for tumour recurrence. In general, the three most important factors are completeness of resection, T and N status of the tumour [28]. Anderson and associates [49] have stressed the importance of positive resection margins, N2 disease and vertebral body involvement. Ginsberg et al. [4] found

Horner's syndrome, N2/N3 disease, T4 disease and incomplete resection, in general, to be adverse prognostic factors. Okubo and associates [10] found that incomplete resection, particularly tumour invasion to the brachial plexus, influenced the prognosis. Sartori and colleagues [8] identified N2 involvement, as well as vertebral body and great vessel invasion, as ominous factors, whereas pain relief after irradiation was of good prognostic value. In another paper, lobectomy was associated with a better overall survival than limited pulmonary resection [4].

The improvements achieved in survival of patients with superior sulcus tumours treated with trimodality therapy are paralleled by a decrease in local recurrence as well. When local recurrence rates were as high as 72% [39] after sequential radio- and/or chemotherapy only, the incidence was found to be reduced to approximately 30—40% after concurrent chemoradiotherapy [39] and even below 30% [34,35,37,38] after trimodality therapy. In another paper, Kappers et al. [39] did not see any recurrence after trimodality treatment.

In patients with locally advanced NSCLC who undergo induction treatment followed by surgery, the pattern of failure however shifts towards distant recurrence, particularly the brain. For Pancoast tumours the expected incidence of brain as a first site of recurrence has been described as high as 24% [50]. Interestingly, the occurrence of brain metastasis did not impact on survival at least in one important paper [34]. Further studies are needed to evaluate potential impact on disease progression of prophylactic cranial irradiation [36].

5. Conclusion

Treatment of sulcus superior tumour has evolved significantly over time. Deriving from therapeutically nihilism, the consequent development of a large variety of surgical techniques, together with the evolution of multimodality treatment concepts resulted in a clear prognostic improvement. Today, induction CR followed by surgical resection has become the established standard of care for patients with sulcus superior tumour in the absence of other contraindications.

References

[1] Pancoast H. Importance of careful roentgen-ray investigations of apical chest tumors. J Am Med Assoc 1924;83:1407—11.

[2] Rusch VW. Management of Pancoast tumors. Lancet Oncol 2006;7:997—1005.

[3] Pitz CC, de la Riviere AB, van Swieten HA, Duurkens VA, Lammers JW, van den Bosch JM. Surgical treatment of Pancoast tumors. Eur J Cardio-thorac Surg 2004;26:202—8.

[4] Ginsberg RJ, Martini N, Zaman M, Armstrong JG, Bains MS, Burt ME, McCormack PM, Rusch VW, Harrison LB. Influence of surgical resection and brachytherapy in the management of superior sulcus tumor. Ann Thorac Surg 1994;57:1440—5.

[5] Millar J, Ball D, Worotniuk V, Smith J, Crennan E, Bishop M. Radiation treatment of superior sulcus lung carcinoma. Australasian Radiol 1996;40:55—60.

[6] Neal CR, Amdur RJ, Mendelhall WM, Knauf DG, Block AJ, Million RR. Pancoast tumor: radiation therapy alone versus preoperative radiation therapy and surgery. Int J Radiat Oncol Biol Phys 1991;21:651—60.

[7] Dartevelle P, Macchiarini P. Resection of superior sulcus tumors. In: Kaiser LR, Kron IL, Spray TL, editors. Mastery of cardiothoracic surgery. Philadelphia: Lippincott-Raven; 1998. p. 257—65.

[8] Sartori F, Rea F, Calabro F, Mazzuco C, Bortoloti, Tomio L. Carcinoma of the superior pulmonary sulcus. J Thorac Cardiovasc Surg 1992;104:679—83.

[9] Wright CD, Moncure AC, Shepard JO, Wilkins Jr EW, Mathisen DJ, Grillo HC. Superior sulcus lung tumors. Results of combined treatment (irradiation and radical resection). J Thorac Cardiovasc Surg 1987;94:69—74.

[10] Okubo K, Wada H, Fukuse T, Yokomise H, Inui K, Ike O, Mizuno H, Aoki M, Hitomi S. Treatment of Pancoast tumors: combined irradiation and radical resection. J Thorac Cardiovasc Surg 1995;43:284—6.

[11] Fuller DB, Chambers JS. Superior sulcus tumors: combined modality. Ann Thorac Surg 1994;57:1133—9.

[12] Martinod E, D'Audiffret A, Thomas P, Wurtz AJ, Dahan M, Riquet M, Dujon A, Jancovici R, Giudicelli R, Fuentes P, Azorin JF. Management of superior sulcus tumors: experience with 139 cases treated by surgical resection. Ann Thorac Surg 2002;73:1534—40.

[13] Netter FH. The Ciba collection of medical illustrations. Summitt, NJ: Ciba Pharmaceutical; 1948.

[14] Komaki R. Preoperative radiation therapy for superior sulcus lesions. Chest Surg Clin N Am 1991;1:13—35.

[15] Narayan S, Thomas Jr CR. Multimodality therapy for Pancoast tumor. Nat Clin Pract Oncol 2006;3(9):484—91.

[16] Weinreb JC, Naidich DP. Thoracic magnetic resonance imaging. Clin Chest Med 1991;12(1):33—54.

[17] Laissy JP, Soyer P, Sekkal SR, Tebboune D, Servois V, Sibert A, Menu Y. Assessment of vascular involvement with magnetic resonance angiography (MRA) in Pancoast syndrome. Magn Reson Imaging 1995;13(4):523—30.

[18] Gould MK, Kuschner WG, Rydzak CE, Maclean CC, Demas AN, Shigemitsu H, Chan JK, Owens DK. Test performance of positron emission tomography and computed tomography for mediastinal staging in patients with non-small cell lung cancer: a meta-analysis. Ann Intern Med 2003;139(11):879—92.

[19] MacManus MP, Hicks RJ, Matthews JP, Hoqq A, McKenzie AF, Wirth A, Ware RE, Ball DL. High rate of detection of unsuspected distant metastases by PET in apparent stage non-small cell lung cancer: implications for radical radiation therapy. Int J Radiat Oncol Biol Phys 2001;50(2):287—93.

[20] Vallieres E, Karmy-Jones R, Milligan MS, Wood DE. Pancoast tumors. Curr Probl Surg 2001;38(5):293—376.

[21] Annema JT, Versteegh MI, Veselic M, Voigt P, Rabe KF. Endoscopic ultrasound-guided fine-needle aspiration in the diagnosis and staging of lung cancer and its impact on surgical staging. J Clin Oncol 2005;23(33):8357—61.

[22] Annema JT, Vesselic M, Versteegh MI, Willems LN, Rabe KF. Mediastinal restaging: EUS-FNA offers a new perspective. Lung Cancer 2003;42(3):311—8.

[23] Chardack WM, Maccallum JD. Pancoast tumor; five-year survival without recurrence or metastases following radical resection and postoperative irradiation. J Thorac Surg 1956;31(5):535—42.

[24] Shaw RR. Pancoasts tumor. Ann Thorac Surg 1984;37(4):343—5.

[25] Dartevelle P, Chapelier AR, Macchiarini P, Lenot B, Cerrina J, Ladurie FL, Parquin F. Anterior transcervical-thoracic approach for radical resection of lung tumors invading the thoracic outlet. J Thorac Cardiovasc Surg 1993;105:1025—34.

[26] Dartevelle PG. Herbert Sloan Lecture. Extended operations for the treatment of lung cancer. Ann Thorac Surg 1997;63(1):12—9.

[27] Fadel E, Missenard G, Chapelier A, Mussot S, Leroy-Ladurie F, Cerrina J, Dartevelle P. En bloc resection of non-small cell lung cancer invading the thoracic inlet and intervertebral foramina. J Thorac Cardiovasc Surg 2002;123(4):676—85.

[28] Rusch VW, Parekh KR, Leon L, Venkatraman E, Bains MS, Downey RJ, Boland P, Bilsky M, Ginsberg RJ. Factors determining outcome after surgical resection of T3 and T4 lung cancers of the superior sulcus. J Thorac Cardiovasc Surg 2000;119:1147—53.

[29] Martinez-Monge R, Herreros J, Aristu JJ, Aramendia JM, Azinovic I. Combined treatment in superior sulcus tumors. Am J Clin Oncol 1994;17:317—22.

[30] Attar S, Krasna MJ, Sonett JR, Hankins JR, Slawson RG, Suter CM, McLaughlin JS. Superior sulcus (Pancoast) tumor: experience with 105 patients. Ann Thorac Surg 1998;66:193—8.

[31] Wright CD, Menard MT, Wain JC, Donahue DM, Grillo HC, Lynch TJ, Choi NC, Mathisen DJ. Induction chemoradiation compared with induction

radiation for lung cancer involving the superior sulcus. Ann Thorac Surg 2002;73:1541—4.
[32] Barnes JB, Johnson SB, Dahiya RS, Temes RT, Herman TS, Thomas Jr CR. Concomitant weekly cisplatin and thoracic radiotherapy for Pancoast tumors of the lung: pilot experience of the San Antonio cancer Institute. Am J Clin Oncol 2002;25:90—2.
[33] Miyoshi S, Iuchi K, Nakamura K, Nakagawa K, Maeda H, Ohno K, Nakahara K, Nakano N, Okumura M, Ohta M. Induction concurrent chemoradiation therapy for invading apical non-small cell lung cancer. Jpn J Thorac Cardiovasc Surg 2004;52(3):120—6.
[34] Kwong KF, Edelman MJ, Suntharalingam M, Cooper LB, Gamiliel Z, Burrows W, Hausner P, Doyle LA, Krasna MJ. High-dose radiotherapy in trimodality treatment of Pancoast tumors results in high pathologic complete response rates and excellent long-term survivial. J Thorac Cardiovasc Surg 2005;129(6):1250—7.
[35] Rusch VW, Giroux DJ, Kraut MJ, Hazuka M, Winton T, Johnson DH, Shulman L, Shrepherd F, Deschamps C, Livingston RB, Gandara D. Induction chemoradiation and surgical resection for superior sulcus non-small cell lung carcinomas: long term results of southwest oncology Group Trial 9416 (Intergroup Trial 0160). J Clin Oncol 2007;25(3):313—8.
[36] Marra A, Eberhardt W, Poettgen C, Theegarten D, Korfee S, Gauler T, Stuschke M, Stamatis G. Induction chemotherapy, concurrent chemoradiation and surgery for Pancoast tumor. Eur Respir J 2007;29:117—27.
[37] Pourel N, Santelmo N, Naafa N, Serre A, Hilgers W, Mineur L, Molinari N, Reboul F. Concurrent cisplatin/etoposide plus 3D-conformal radiotherapy followed by surgery for stage B(superior sulcus T3N0)/non-small cell lung cancer yields a high rate of pathological complete response. Eur J Cardiothorac Surg 2008;33(5):829—36.
[38] Kunitoh H, Kato H, Tsuboi M, Shibata T, Asamura H, Ichinose Y, Katakami N, Nagai K, Mitsutomi T, Matsumura A, Nakagawa K, Tada H, Saijyo N, Japan Clinical Oncology Group. J Clin Oncol 2008;26(4):644—9.
[39] Kappers I, Belderbos JS, Burgers JA, van Zandwijk N, Groen HJ, Klomp HM. Non-small cell lung carcinoma of the superior sulcus: favourable outcomes of combined modality treatment in carefully selected patients. Lung cancer 2008;59(3):385—90.
[40] Haas LL, Harvey RA, Langer SS. Radiation management of otherwise hopeless thoracic neoplasms. J Am Med Assoc 1954;154(4):323—6.
[41] Morris RW, Abadir R. Pancoast tumor: the value of high dose radiation therapy. Radiology 1979;132(3):717—9.
[42] Van Houtte P, MacLennan I, Poulter C, Rubin P. External radiation in the management of superior sulcus tumor. Cancer 1984;54:223—7.
[43] Ashe WM, McDonald JR, Clagett OT. Nonspecific pneumonitis of the left upper lobe (simulating the middle lobe syndrome and producing an early superior pulmonary sulcus syndrome). T Thorac Surg 1951;21(1):1—6.
[44] Attar S, Miller JE, Satterfield J, Ho CK, Slawson RJ, Hankins J, McLaughlin JS. Pancoasts tumor: irradiation or surgery? Ann Thorac Surg 1979;28(6):578—86.
[45] Bretz G, Lott S, El-Mahdi A, Hazra T. The response of superior sulcus tumors to radiation therapy. Radiology 1970;96(1):145—50.
[46] Kirsh MM, Dickerman R, Fayos J, Lampe I, Pellegrini RV, Gago O, Sloan H. The value of chest wall resection in the treatment of superior sulcus tumors of the lung. Ann Thorac Surg 1973;15:339—46.
[47] Stanford W, Barnes RP, Tucker AR. Influence of staging in superior sulcus (Pancoast) tumors of the lung. Ann Thorac Surg 1980;29:406—9.
[48] Komaki R, Roh J, Cox JD, Lopes da Conceicao A. Superior sulcus tumors: results of irradiation of 36 patients. Cancer 1981;48:1563—8.
[49] Anderson TM, Moy PM, Holmes EC. Factors affecting survival in superior sulcus tumors. J Clin Oncol 1986;4:1598—603.
[50] Komaki R, Derus SB, Perez-Tamayo C, Byhardt RW, Hartz A, Cox JD. Brain metastasis in patients with superior sulcus tumors. Cancer 1987;59: 1649—53.
[51] Ricci C, Rendina EA, Venuta F, Francioni F, De Giacomo T, Pescarmona EO, Ciriaco P. Superior pulmonary sulcus tumors: radical resection and palliative treatment. Int Surg 1989;74:175—9.
[52] Herbert SH, Curran Jr WJ, Staffort PM, Rosenthal SA, McKenna WG, Hughes EN. Comparison of outcome between clinically staged, unresected superior sulcus tumors and other stage non-small cell lung carcinomas treated with radiation therapy alone. Cancer 1992;69:363—9.
[53] Schraube P, Latz D. The value of radiotherapy in the treatment of Pancoast tumor of the lung. Strahlenther Onkol 1993;169:265—9.
[54] Strojan P, Debevec M, Kovac V. Superior sulcus tumor (SST): management at the Institute of Oncology in Ljubljana, Slovenia, 1981—1994. Lung Cancer 1997;17:249—59.
[55] Hagan MP, Choi NC, Mathisen DJ, Wain JC, Wright CD, Grillo HC. Superior sulcus lung tumors: impact of local control on survival. J Thorac Cardiovasc Surg 1999;117:1086—94.
[56] Komaki R, Roth JA, Walsh GL, Putnam JB, Vaporciyan A, Lee JS, Fossella FV, Chasen M, Delclos ME, Cox JD. Outcome predictors for 143 patients with superior sulcus tumors treated by multimodality approach at the University of Texas MD Anderson Cancer Center. Int J Radiat Oncol Biol Phys 2000;48:347—54.
[57] Paulson DL. Carcinoma in the superior pulmonary sulcus. Ann Thorac Surg 1979;28(1):3—4.
[58] Hilaris BS, Martini N, Luomanen RKJ, Batata MA, Beattie Jr EJ. Superior sulcus lung cancer: a 35 year experience. Int J Radiat Oncol Biol Phys 1979;5:54.
[59] Miller JI, Mansour KA, Hatcher Jr CR. Carcinoma of the superior pulmonary sulcus. Ann Thorac Surg 1979;28(1):44—7.
[60] Shahian DM, Neptune WB, Ellis Jr FH. Pancoast tumors: improved survival with preoperative and postoperative radiotherapy. Ann Thorac Surg 1987;43(1):32—8.
[61] Paulson DL. Superior sulcus tumors; results of combined therapy. NY State J Med 1971;71(17):2050—7.
[62] Paulson DI. Carcinomas in the superior pulmonary sulcus. J Thorac Cardiovasc Surg 1975;70:1095—104.
[63] Hilaris BS, Martini N, WongGY, Nori D. Treatment of superior sulcus tumor (Pancoast tumor). SurgClin North Am 1987;67(5):965—77.
[64] Maggi G, Casadio C, Pischedda F, Giobbe R, Cianci R, Ruffini E, Molinatti M, Mancuso M. Combined radiosurgical treatment of Pancoast tumor. Ann Thorac Surg 1994;57:198—202.
[65] Muscolino G, Valente M, Andreani S. Pancoast tumors: clinical assessment and long term results of combined radiosurgical treatment. Thorax 1997;52:284—6.
[66] Shaw RR, Paulson DL, Kee JL. Treatment of superior sulcus tumor by irradiation followed by resection. Ann Surg 1961;154(1):29—40.
[67] Niwa H, Masaoka A, Yamakawa Y, Fukai I, Kiriyama M. Surgical therapy for apical invasive lung cancer: different approaches according to tumor location. Lung Cancer 1993;10(1-2):63—71.
[68] Tatsumura T, Sato H, Mori A, Miyazaki M, Koyama S, Tsujimoto M, Furuno T. A new surgical approach to apical segment lung diseases, including carcinomas and inflammatory diseases. J Thorac Cardiothorac Surg 1994;107(1):32—6.
[69] Grunenwald D, Spaggiari L. Transmanubrial osteomuscular sparing approach for apical chest tumors. Ann Thorac Surg 1997;63(2):563—6.
[70] Masaoka A, Ito Y, Yasumitsu T. Anterior approach for tumor of the superior sulcus. J Thorac Cardiovasc Surg 1979;78(3):413—5.
[71] Chiles C, Davis K, Williams 3rd DW. Navigating the thoracic inlet. Radiographics 1999;19(5):1161—76.
[72] Bilsky MH, Vitas TW, Boland PJ, Bains MS, Rajaraman V, Rusch VW. Surgical treatment of superior sulcus tumors with spinal and brachial plexus involvement. J Neurosurg 2002;97(3):301—9.
[73] York JE, Walsh GL, Lang FF, Putnam JB, McCutcheon IE, Swisher SG, Komaki R, Gokaslan ZL. Combined chest wall resection with vertebrectomy and spinal reconstruction for the treatment of Pancoast tumors. J Neurosurg 1999;91(1):74—80.
[74] Mazel C, Grunenwald D, Laudrin P, Marmorat JL. Radical excision in the management of thoracic and cervicothoracic tumors involving the spine: results in a series of 36 cases. Spine 2003;28(8):782—92.