Extended Resections for Thymic Malignancies

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Abstract: Almost all series reporting on the results of resection in thymic tumors indicate that the performance of a complete resection is probably the most important prognostic factor. This issue is not a factor in Masaoka stage I and II tumors that are almost always easily completely resected and have an excellent prognosis. Masaoka stage III tumors that invade the pericardium, lungs, or great vessels have relatively higher incomplete resection rates, significantly higher recurrence rates, and thus a worse prognosis. There are several small reports on the efficacy of resection of the great veins when involved by a thymic malignancy with low morbidity and meaningful long-term survival. Superior vena cava reconstruction is commonly performed by a polytetrafluroethylene, venous, or pericardial graft. These cases can usually be identified preoperatively and, thus, considered for induction therapy. Because these types of cases are almost always of marginal respectability in terms of obtaining a true en bloc resection, there is an increasing enthusiasm for offering induction therapy in an effort to enhance resectability. Preliminary results suggest increased R0 resection rates and improved survival with induction therapy for locally advanced tumors. The optimal induction treatment is unknown. The ultimate extended surgery for advanced thymic tumors is an extrapleural pneumonectomy performed for extensive pleural disease (Masaoka stage IVA). These rarely performed operations are done for IVA disease found at initial presentation and for recurrent disease as a salvage procedure. Again these advanced patients are probably best managed by induction chemotherapy followed by resection.

Key Words: Thymic malignancy, Superior vena cava resection, Pleuropneumonectomy.

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Almost all series reporting on the results of resection in thymic tumors indicate that the performance of a complete resection is probably the most important prognostic factor.[1] This issue is not a factor in Masaoka stage I and II tumors that are almost always easily completely resected and have an excellent prognosis. Masaoka stage III tumors that invade the pericardium, lungs, or great vessels have relatively higher incomplete resection rates, significantly higher recurrence rates, and thus a worse prognosis.[1–3] Resection of the pericardium or lung usually represents little technical challenge and will not be commented on further. Resection of the great veins represents more of a technical challenge, seems to be associated with a relatively poor prognosis, and is increasingly performed.[4–6] Simple innominate vein invasion is usually managed by simple resection without reconstruction with little short-term morbidity. Several reports suggest that innominate vein invasion is a poor prognostic factor.[4–6] As such if invasion is identified before resection, strong consideration should be given for induction therapy to increase the chance of a R0 resection (Figure 1).

SUPERIOR VENA CAVA INVASION

Superior vena cava (SVC) invasion by lung or mediastinal tumors has been addressed either by lateral tangential excision (for limited areas of invasion) or by SVC resection and reconstruction (for extensive invasion or endovascular tumor). Accumulating experience with the more common scenario of lung cancer invasion has led to increasing use of SVC resection in thymic tumors.[7–12] There are no significant series detailing the results of SVC resection in just thymic tumors, so results must be extrapolated to an extent from the large reported series, which typically entail a mixture of malignancies. Most authors have concluded that for T4 lung cancer with SVC invasion, the results are worthwhile with relatively limited perioperative morbidity and mortality (in the absence of N2 disease and with a R0 resection).[9,10] Similarly, most authors have concluded that SVC resection is worthwhile in thymic tumors as long as there is a reasonable chance of completing a R0 resection.[7–12] Given the typical biology of thymic tumors of local invasion with rare extrathoracic metastases and the importance of a complete resection, SVC resection makes biologic sense, especially when compared with lung cancer. Most if not all the patients should undergo induction chemotherapy (or chemoradiotherapy) in an effort to downstage the tumor as much as possible. The usual sequence is induction chemotherapy, then resection, and then adjuvant radiation. Several series of unresectable or advanced Masaoka stage III tumors have been reported, suggesting a benefit to induction therapy with increased R0 resection rates and improved survival.[13,14] The contrast enhanced computed tomography scan should be scrutinized carefully by the thoracic surgeon to look for extensive abutment, invasion, or intraluminal tumor within the innominate vein and SVC (Figure 2). Usually an accurate prediction can be made preoperatively of the likely need for SVC resection.

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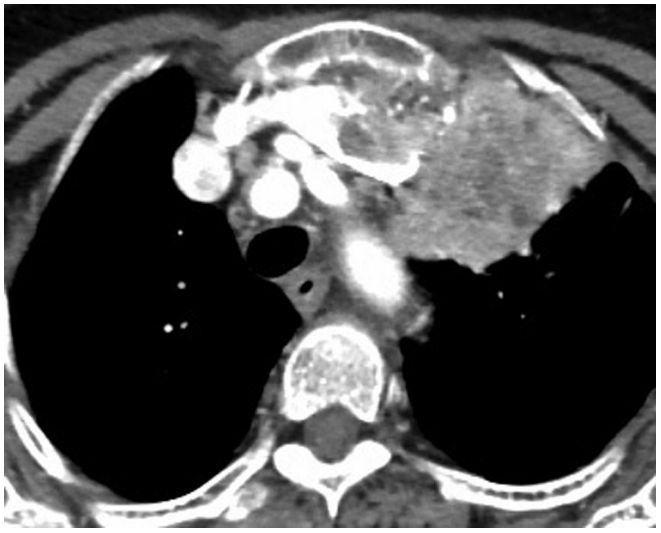

FIGURE 1. A computed tomography scan of a patient with left innominate vein invasion with intraluminal tumor from a thymic carcinoma.

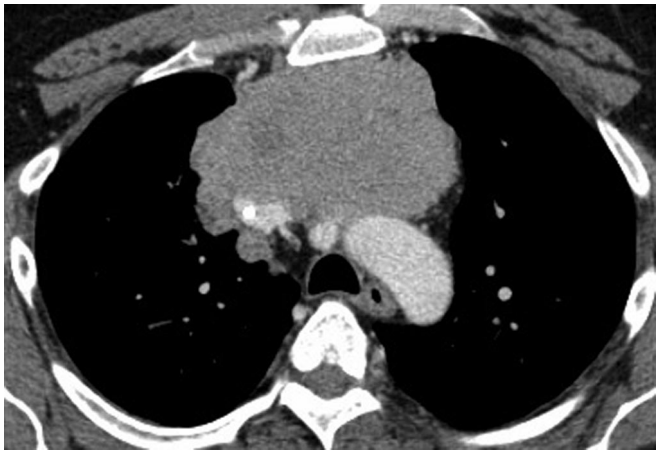

FIGURE 2. A computed tomography scan of a patient with superior vena cava (SVC) compression and infiltration from a B3 thymic tumor. Note the deformity of the anterior wall of the SVC. Resection and reconstruction were necessary.

TECHNIQUE OF SVC RESECTION

The anesthesiologist should be alerted to the possibility of SVC resection. Intravenous access should be secured in both the arm and below the diaphragm. When the SVC is clamped, the head of the bed should be raised to enhance venous drainage of the brain. The blood pressure should be controlled and increased if needed after clamping to maintain cerebral perfusion pressure.[15] Patients who have the SVC syndrome with complete occlusion preoperatively obviously tolerate SVC clamping without any issues. Typically, the resection of the tumor is carried out until the tumor is left only attached to the SVC before SVC clamping, resection, and reconstruction. This minimizes clamp time and facilitates expeditious reconstruction with the specimen out of the way. Usually the phrenic nerve is involved if the SVC is invaded, and so, it must be resected as well. Consideration should be given to a concomitant diaphragm plication to minimize postoperative dyspnea. Lateral resection can be done for limited (<25%) circumference involvement. Repair can be performed with autologous vein, autologous or bovine pericardium, arterial homografts, or polytetrafluroethylene (PTFE) vascular patch.

For the more common extensive involvement, complete SVC resection and reconstruction are performed. Usually the right innominate vein is anastomosed to the neo-SVC. Alternative reconstructions include those of SVC to SVC, left innominate to SVC, and right internal jugular to SVC. If a choice needs to be made between using either the right or the left innominate vein, most surgeons chose the right as it is usually larger, lies in a more direct plane, and graft length estimation is easier because the retractor does not need to be closed for right length estimation. Most surgeons have abandoned Y type of reconstructions of both innominate veins because of poor long-term patency rates, presumably due to reduced flow compared with unilateral grafts.[8] Repair can be performed with a spiral vein graft, a bovine pericardium tube graft (typically made by stapling a sheet into a tube over a cylindrical mandrill), an arterial homograft, or a ringed PTFE graft.[7–17] Most surgeons use ringed PTFE grafts because of their easy availability and good long-term results. If needed, resections may extend to encompass the right atrium.[17] Anticoagulation after SVC resection and reconstruction is variable and controversial with no clear consensus. Most surgeons either recommend permanent aspirin or at least short-term warfarin anticoagulation to reduce the risk of SVC thrombosis.[10]

RESULTS OF SVC RESECTION

Perioperative morbidity and mortality are quite low from SVC resection (Table 1). Specific complications related to SVC resection include hemodynamic instability because of intraoperative clamping, early SVC graft thrombosis, and cerebral edema from prolonged SVC clamping. There is also a risk for late SVC graft thrombosis from 5 to 10%. Survival was not reported in any series for thymic tumors alone. Two series reported on mediastinal tumor survival with 5-year estimates of approximately 50% (Table 1).[9,10]

TABLE 1. Results of SVC Resection in Thymic Tumors

References	No. of Cases (Thymic/Total)	Operative Mortality (%)	Graft Patency	Survival
Shintani et al.[7]	11/18	0	7/10	NS
Chen et al.[8]	11/15	0	15/15	14/15 alive with 35 mo follow-up
Spaggiari et al.[9]	9/70	4 (7.7)	64/70	45%, 5 yr
Lanuti et al.[10]	3/19	1 (5)	17/19	56%, 5 yr
Leo et al.[11]	8/72	2 (2.8)	70/72	NS
Okereke et al., in press	10/38	2 (5)	36/38	27/38 alive

SVC, Superior vena cava; NS, not stated.

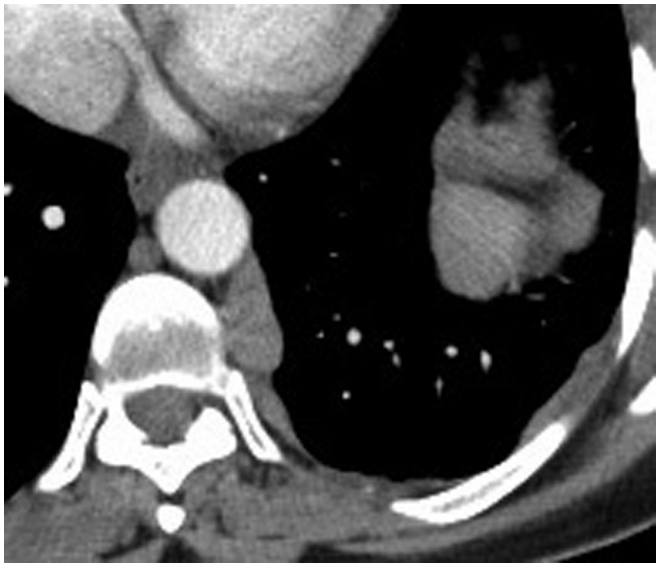

FIGURE 3. A computed tomography scan of an isolated parietal pleural metastases from a recurrent B2 thymoma after resection in the left paravertebral gutter. A local pleurectomy was performed after chemotherapy.

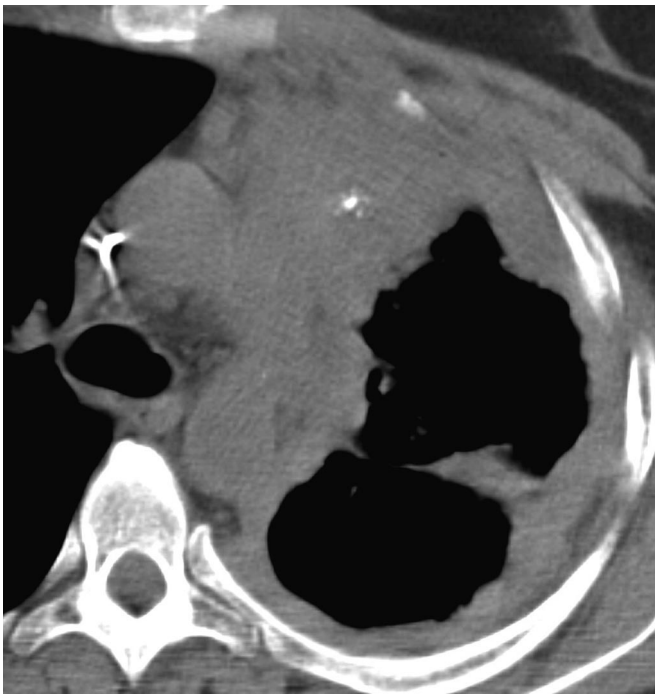

FIGURE 4. A computed tomography scan of a large B3 thymoma with extensive lung and pleural involvement, which required pleuropneumonectomy for resection.

PLEUROPNEUMONECTOMY FOR EXTENSIVE IVA DISEASE

Thymic tumors have a predilection for pleural metastases both at initial presentation of locally advanced tumors and with recurrent tumors. Minimal pleural disease is typically treated by regional or complete parietal pleurectomy in conjunction with chemotherapy (Figures 3, 4).[18] Extensive, often confluent pleural disease is usually also associated with widespread lung invasion and requires pleuropneumonectomy for near complete resection. Although at first glance this seems like heroic surgery, the biology of this tumor with long survival even with a recurrence favors an aggressive approach. Numerous case reports have demonstrated the feasibility of this concept. More recently, several small series have been reported that demonstrate reasonable results (Table 2).[19–21] Although a true en bloc complete resection cannot be performed, the amount of disease that is left is typically not visible and truly microscopic. Most cases require resection of the ipsilateral pericardium and diaphragm as well, similar to that of mesothelioma resection. Typically induction chemotherapy is given before resection to maximize any possible downstaging. Radiation should be given rarely as an induction agent, because the lung and pleura will be removed and the involved field is quite large, leading to increased toxicity. Radiation is typically given as an adjuvant for any areas the surgeon had a concern for intraoperatively. Similar to mesothelioma treatment, it is easier and safer to give radiation to the hemithorax once the lung is removed.

TABLE 2. Results of Pleuropneumonectomy for Thymic Tumors

References	No. of Patients (Thymoma/ Cancer)	Induction Therapy	Mortality	Adjuvant Therapy	Survival
Wright[19]	5, all B3	2/5	0	5/5	75%, 5 yr
Huang et al.[20]	4, all thymomas	4/4	0	4/4	78%, 5 yr
Ishikawa et al.[21]	4, all thymomas	4/4	0	3/4	75%, 5 yr

TECHNIQUE OF PLEUROPNEUMONECTOMY FOR EXTENSIVE IVA DISEASE

The preoperative cardiopulmonary evaluation should be through in these patients because a pneumonectomy is a significant physiologic insult. Complete pulmonary function tests, a quantitative ventilation perfusion scan if lung function is abnormal, an echocardiogram, and a stress test if there is any suspicion of coronary disease are the standard tests. A positron emission tomography or computed tomography scan is helpful to eliminate the possibility of extrathoracic disease before this major resection. Most surgeons use a posterolateral thoracotomy for the operative approach. Others have described a mediansternotomy approach or a clamshell/hemiclamshell approach. In large part, this revolves around the extent of the mediastinal component of the tumor, with larger tumors benefitting from anterior access rather than lateral access.

The typical patient is resected by a large posterolateral thoracotomy with division of both the latissimus and the serratus anterior muscles.[22] Usually the sixth rib is resected to enhance access. Often a lower thoracotomy is done under the

divided latissimus to enhance access to the diaphragm if needed. The subpleural plane is entered bluntly with the surgeon's fingers, and a complete resection of the parietal pleura is done off the anterior, lateral, and posterior chest walls. The mediastinal pleura is dissected next with care to avoid injury to important mediastinal structures such as the vagus, aorta and arch vessels, esophagus, and azygos. The pericardium is entered at its periphery and resected as well. The artery and two veins to the lung are stapled and divided followed by the bronchus. The diaphragm is usually resected. If so and if there is minimal diaphragm involvement, it is useful to maintain the peritoneum relatively intact. The diaphragm is reconstructed with PTFE with anchoring to the chest wall with nonabsorbable sutures. The pericardium is reconstructed with PTFE with fenestrations or with absorbable mesh.

RESULTS OF PLEUROPNEUMONECTOMY FOR EXTENSIVE IVA DISEASE

The results of pleuropneumonectomy are rather good despite the aggressive nature of the operation.[19–21] The perioperative morbidity and mortality that have been reported are rather low and probably reflect in part careful patient selection and also an absence of smoking on the patient population (Table 2). The reported 5-year survival in the three larger series is approximately 75% and is quite remarkable (Table 2).[19–21] Caution is in order although as many recurrences occur after 5 years, and there is usually a long time between recurrence and death. Nonetheless, these results seem to justify this aggressive approach to this rare subset of thymic tumor patients.

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