Original Article

Resection and reconstruction of mediastinal great vessels in invasive thymoma

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Abstract

OBJECTIVE: To evaluate the safety, feasibility, and outcome following radical excision of thymoma with resection and reconstruction of invaded mediastinal vessels. **STUDY DESIGN:** A retrospective study. **PATIENTS AND METHODS:** Six patients with thymoma invading the superior vena cava (SVC) and/or the brachiocephalic veins (BCVs) were reviewed in this study. All the patients underwent radical excision of the tumor along with invaded mediastinal vessels followed by vessel reconstruction or repair. The clinical presentation, operative details, postoperative course, and follow-up were reviewed and analyzed. **RESULTS:** Three patients presented with features suggestive of SVC syndrome. Contrast-enhanced computed tomography of the chest was the primary imaging modality, which detected a tumor with invasion of major mediastinal veins. WHO type B2 was the commonest histologic type, which was seen in 4 cases. Intraoperatively, SVC invasion, SVC and BCV invasion, and BCV invasions alone were seen in 1, 2, and 3 cases, respectively. The vessels were reconstructed with a prosthetic graft in 3 patients, and autologous pericardial tube graft was used in 1 patient. Two patients had primary repair of the wall of the involved vessel. Postoperative course was complicated by ventilator support requirement in 2, graft thrombosis in 2, acute renal failure in 1 and pneumonia in 1 patient. All patients are alive at the end of follow-up period ranging between 18 and 24 months. **CONCLUSION:** Thymoma excision with the reconstruction of SVC or BCV is safe and feasible in experienced hands.

Key words: Invasive thymoma, superior vena cava, vessel reconstruction

Introduction

Thymomas are slow-growing tumors of thymic epithelial cell origin. Thymomas constitute 19% of all mediastinal tumors and are the most common tumors of the anterior mediastinum.[1] They are asymptomatic until late and half of them are discovered incidentally. Myasthenia gravis is associated in about 10–50% of thymomas and may be the cause for earlier presentation. Due to their anatomical proximity, thymoma compresses the mediastinal vessels as they grow and can involve the superior vena cava (SVC) and other great vessels by direct invasion.[1] Complete rather than partial excision of thymoma improves survival. Involvement of the great vessels requires complete excision with reconstruction of the vessels. Reconstruction of these vessels is technically challenging. Herein, we present our experience of managing invasive thymomas with the involvement of the great vessels of the mediastinum.

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Materials and Methods

Between 1989 and 2009, 150 cases of thymic tumors were operated in a single surgical unit at our institute. Histopathologic examination reported thymic neuroendocrine carcinomas in 5 patients and thymomas in 145 patients. The Masaoka staging of 145 patients who were offered surgery at our hospital was: stage I: 34, stage II: 39, stage III: 56, and stage IVa: 16 patients. Six cases of invasive thymoma required reconstruction of SVC and/or brachiocephalic

vein (BCV) along with radical excision of the tumor. These 6 cases are being reviewed in this retrospective study. The data were collected from patient case file, operation notes, follow-up register, histopathologic reports, and telephonic contact with the patient. Medical data were reviewed for demographic data, clinical presentation, investigations, operative procedure and findings, histologic diagnosis, and postoperative course.

Results

All the patients were men aged between 29 and 55 years. Myasthenia gravis and pure red cell aplasia were associated in 1 case each. SVC syndrome was observed in 3 patients. Other clinical details of the patients are given in Table 1.

Contrast-enhanced computed tomography (CECT) scan of the chest showed BCV invasion in 4, SVC in 3, pulmonary vessels involvement in 2, and lung parenchyma involvement in 1 patient. A preoperative computed tomography–guided fine-needle aspirate (FNA) from the tumor reported thymoma in 4 patients. The pre- and postoperative histopathology was concordant in all patients. WHO type B2 was the commonest histology and seen in 4 patients. WHO type AB and B1 were seen in 1 patient each.

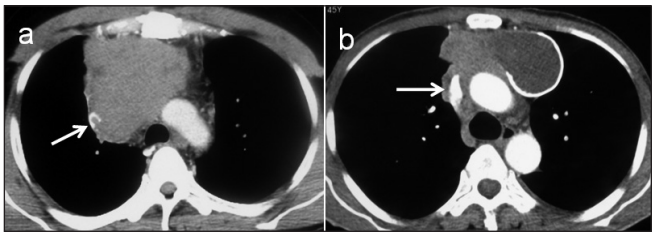

Figure 1: Contrast-enhanced computed tomography of the chest axial section showing invasion and encasement of superior vena cava in case 3 (a) and case 1 (b)

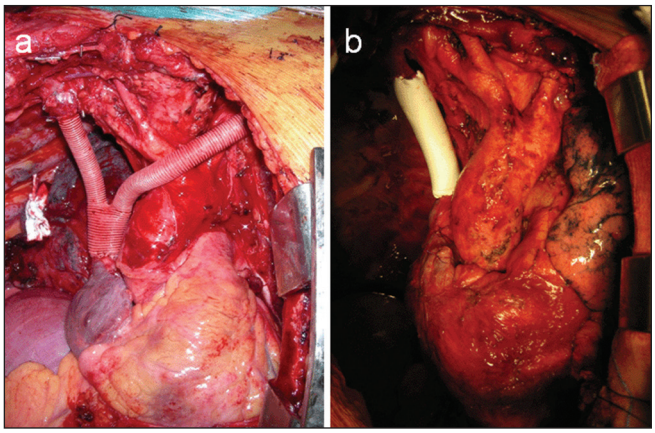

Figure 2: Intraoperative photographs showing expanded polytetrafluoroethylene graft reconstruction in case 3 (a) and case 1 (b)

Radical excision of thymoma along with other involved adjacent structures was undertaken. The mean operating time was 315 min with an average blood loss of 400 mL. Cardiopulmonary bypass facility was kept as a standby to be used if needed but none of the cases required it. Figures 1 and 2 depict the CT and intraoperative images showing the extent of involvement and vascular reconstruction in 2 of our patients. The vessels were reconstructed with expanded polytetrafluoroethylene (ePTFE) graft in cases 1–3, repaired in cases 4 and 5, and with autologous pericardial tube graft in case 6 as shown in Figure 3. In case 4, the tumor was infiltrating less than 1 cm of the anterior wall of the left BCV. The tumor was resected with the involved portion of venous wall and repaired primarily with 5-0 prolene. In case 5, the tumor was completely encasing the whole length of the left BCV till its termination in the SVC. The tumor was resected en bloc with the involved left BCV and a portion of the SVC wall near the termination of the left BCV. The SVC rent was repaired with 5-0 prolene. ePTFE grafts of 16–18 mm in diameter were used for the reconstruction of the SVC and BCV. The anastomoses were performed with 5-0 prolene. Other surgical procedures performed for complete tumor clearance

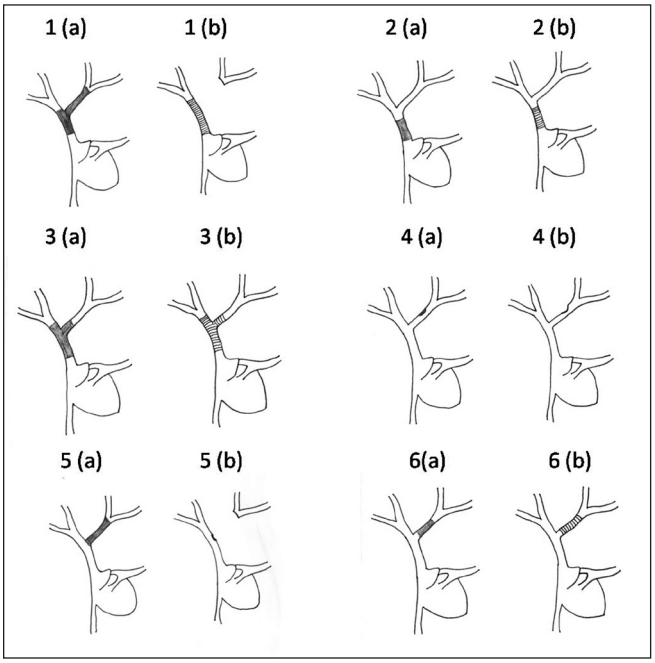

Figure 3: Schematic diagram showing vessel invasion and its reconstruction. Case 1 shows invasion of SVC, right and left BCV (a) and expanded polytetrafluoroethylene (ePTFE) graft reconstruction (b). Case 2: shows invasion of superior vena cava (SVC) (a) and ePTFE graft replacement of SVC (b). Case 3 shows invasion of SVC, right and left brachiocephalic vein (BCV) (a) and reconstruction with Y-shaped ePTFE graft (b). Case 4 shows involvement of anterior wall of left BCV (a) and repair of left BCV (b). Case 5 shows invasion of left BCV and a portion of SVC wall (a) and repair of the SVC wall (b). Case 6 shows invasion of left BCV (a) and pericardial tube graft reconstruction (b)

Table 1: Patient characteristics, operative findings, surgical procedures and follow-up

Case number	Age (y)/ sex	Symptoms/ duration	Associated conditions	WHO type/ Masaoka's stage	Tumor size (cm)	Vessels involving	Graft material	Vessel reconstruction	Other adjacent structures involved	Adjacent structure resected	Postoperative course	Follow-up (months)
1	45/M	Breathlessness, facial edema, engorged neck veins/ 12 months	None	Type B2, stage III	10 × 7.5 × 4.5	SVC, right and left BCV, right PA and PV	ePTFE (16 mm)	Graft between Right BCV and right atrium	Hilum of right lung, right atrial appendage, pericardium	Pneumonectomy, pericardium, atrial appendage	Pneumonia, oral candidiasis	19
2	55/M	Breathlessness /12 months	Pure red cell aplasia, hypothyroidism	Type B2, stage IVa	17 × 7.5 × 4.5	SVC, right PV	ePTFE (18 mm)	Graft between junction of BCVs and right atrium	Multiple deposits on right lung	Pneumonectomy	Graft thrombosis, prolonged ventilation	18
3	48/M	Neck and facial edema / 7 months	None	Type AB, stage III	15 × 10 × 7	SVC, right and left BCV	Y-shaped ePTFE (16 mm)	Graft between the both BCV and SVC	Right phrenic nerve	None	Uneventful	20
4	29/M	Slurring of speech/ 3 months	Myasthenia Gravis	Type B1, stageIII	7 × 3 × 3	Left BCV	None	Rent in Left BCV closed with 5-0 Prolene	None	None	Pneumonia	18
5	49/M	Incidental detection	None	Type B2, stage III	9 × 8 × 7	Left BCV	None	Resection of left BCV with primary repair of SVC	Pericardium, upper lobe of left lung, left phrenic nerve	Wedge resection of left upper lobe lung, pericardium, left phrenic nerve	Uneventful	24
6	52/M	Breathlessness, neck and facial edema/24 months	None	Type B2, stage III	8.6 × 8 × 6	Left BCV	Autologous pericardial tube graft	Left BCV reconstructed	Left phrenic nerve	None	Graft thrombosis, prolonged ventilation, acute renal failure	24

M, male; BCV, brachiocephalic vein; SVC, superior vena cava; PA, pulmonary artery; PV, pulmonary vein; ePTFE, expanded poly tetrafluoroethylene.

included pneumonectomy in 2 patients (main pulmonary artery was infiltrated by tumor) and wedge resection of the left upper lobe of lung in 1 patient.

Case 2 developed partial thrombosis of the prosthetic graft and case 6 with pericardial tube graft also developed thrombosis of the graft in the immediate postoperative period. Both required prolonged mechanical ventilator support (70 days in case 2 and 54 days in case 6). Other postoperative complications included pneumonia in 2 and acute renal failure and oral candidiasis in 1 patient each.

All the patients received adjuvant radiotherapy and chemotherapy. Total radiation dose of 45 Gy was given in 25 fractions over a 5-week period to the tumor bed. They also received 6 cycles of combination chemotherapy (cyclophosphamide, epirubicin, and carboplatin). There were no mortalities at the end of follow-up period ranging between 18 and 24 months.

Discussion

Thymoma, the most common tumor of the anterior mediastinum, is malignant in about 20–30% of cases.[2] Malignancy in thymomas are determined by invasion into local structures and gross appearance.[3,4] Local invasion occurs in the pleura (30%), pericardium (25%), lung (8%), recurrent laryngeal nerve (4%), and rarely the great vessels, whereas extrathoracic metastases occur only in 5% of cases.[1]

Traditionally, thoracic malignancies with the involvement of great vessels of mediastinum were considered inoperable due to poor long-term results of such extensive and risky surgery coupled with low graft patency rate. However, the long-term graft patency has improved remarkably with the availability of new prosthetic materials. It has also been observed that unlike lung or esophageal cancer, complete excision of thymoma is associated with better prognosis. The 10-year survival rate for stage III thymomas (Masaoka staging) increases from 31% to 35% with incomplete excision to 75% to 94% with complete excision.[5,6] Fujisawa *et al*[7] found a significant difference in survival in patients with SVC involvement between those with complete resection and reconstruction and those with incomplete resection. With such encouraging outcomes with complete excision, resection and reconstruction of the great vessels in cases of invasive thymomas is justified and being practiced increasingly.

The need for preoperative biopsy in the anterior mediastinal tumors is still being debated as it increases the possibility of tumor seedlings.[8,9] Our practice is to perform preoperative biopsy only in cases with unusual presentations or in cases with invasion into vital organs because such extensive resections carry a higher risk. Preoperative biopsy was sought in all of these cases except in case 5, in whom the invasion to the left BCV was made only intraoperatively. CT-guided FNA of the tumor was used as it is minimally invasive and provides diagnosis with reasonable accuracy. The pre- and postoperative histopathologic diagnosis was concordant with WHO type B2 being the commonest type.

The presence of intervening fat planes in CT has been used to predict vascular invasion in cases with malignant thymoma. Fat plane integrity has been categorized as complete preservation, partial preservation or obliteration, and complete obliteration.[10] Two dimensional echocardiography has been found to be useful in predicting intra cardiac extension of the mass.[11] CT was the primary imaging modality in all our cases. But, the intraoperative assessment was highly reliable than CT in determining the invasiveness in our experience as in case 5, wherein the left BCV involvement was only identified intraoperatively. The patients with preoperative CT evidence of tumor completely encasing the aorta or its branches were not subjected to surgery. However, there were many patients in whom the CT scan revealed no plane between tumor and aorta or even flattening of the surface of the aorta, suggesting invasion. Fortunately, at surgery, all except one could be resected with careful and meticulous dissection. In one patient, the procedure had to be abandoned due to infiltration of myocardium and the arch of aorta.

Three of our cases presented with features of SVC syndrome and were relieved of the symptoms in the postoperative period. The SVC involvement may be circumferential or only confined to one wall. Three different techniques have been suggested to manage this. These include localized resection and direct suture repair, repair with a pericardial graft, or ePTFE patch and circumferential resection with replacement by a prosthetic graft or autologous vein. Politi and his colleagues[12] suggested tangential resection and patch repair when the involvement is less than 20% of circumference and replacement for more than 30% circumferential involvement. They have reported a patency rate of 80% at the end of 1 year in 11 of the patients on CT angiography. Chen *et al*[13] advise prosthetic graft replacement for SVC involvement of more than 2 cm in length and more than half of the circumference. Cardiopulmonary bypass may be required in case of intracardiac extension. In case 1, the tumor was invading the right atrial appendage but there was no intracardiac extension.

Various biologic and synthetic materials, such as autologous vein, bovine pericardium, Dacron and ePTFE have been tried in the reconstruction of the vessels. Limited availability of the autologous veins and time-consuming preparations discourage the widespread use of this conduit. Bovine jugular vein is associated with high thrombotic risk.[14] Chen *et al*[13] used Dacron graft for vessel reconstruction in their series of 15 patients with anterior mediastinal tumors, out of which 9 patients were malignant thymomas. At a median follow-up of 35 months, disease-free survival ranged from 10 to 43 months. Schimizu *et al*[15] reconstructed SVC with Teflon and ePTFE in 8 cases of malignant thymic tumors. Graft occlusion occurred in only 1 SVC graft and 2 BCV grafts at 1 month of follow-up. Amirghofran and his colleagues[16] have used Dacron graft to reconstruct SVC in a case of intracardiac invasive thymoma. The graft has remained patent at 5 years of follow-up. However, ePTFE graft is currently being favored in view of its long-term patency. Smooth PTFE is used for long tracts, whereas ringed ones for shorter tracts. The survival rate at 3 years was 27% for 13 patients with mediastinal–pulmonary malignancies who had resection of their tumor and SVC with reconstruction using PTFE.[17,18] Garcia-Rinaldi demonstrated patency of ePTFE for 4 years.[19]

Mortality due to prosthetic graft complications range from 4.5% to 12%.[20,21] The most dangerous complication with the use of prosthetic materials is the thrombosis and pulmonary embolism. Endoprosthetic thromboses have been reported to be as high as 86% at 3 years in one of the series.[18] Thrombosis is often related to anastomotic techniques, type and diameter of prosthesis, and incorrect surgical choice. PTFE prostheses with a diameter of 18–20 mm are suggested for SVC reconstruction to avoid gradient variations and high pressure in the BCV. PTFE prostheses with smaller diameter (10–14 mm) was advised for bridging between the innominate vein and right atrium.[12] Perioperative anticoagulant therapy, soaking the artificial vessels in heparin–salt water and use of eversion sutures lessen the risk of thromboses. Self-expanding stent has been used successfully for early graft thrombosis.[22] We routinely gave intravenous heparin to all patients with vascular reconstruction to prevent graft thrombosis. Graft thrombosis in the early postoperative period was seen in 2 cases (cases 2 and 6) despite being on continuous intravenous heparin anticoagulation. The intravenous infusion of heparin was started at a dose of 1000 units/h and subsequently titrated to achieve activated partial thromboplastin time (aPTT) value of 2 times the patient's preheparin aPTT. They were continued on oral anticoagulant warfarin, 5 mg per day, and the dose was titrated according to international normalized ratio value. However, a follow-up CT angiography showed complete graft occlusion in case 6. The left upper limb, facial, and neck edema subsided gradually due to the development of collateral vessels.

Another complication in the early postoperative period was the risk of neurologic complications due to SVC clamping. In procedures requiring total SVC clamping, SVC should be clamped above the azygos vein to allow lateral circulation, avoiding brain damage. If clamped below the azygos vein and lasts for more than 60 min, SVC bypass may be necessary.[23] Clamping for more than 105 min may lead to symptoms of cerebral stasis and may require mechanical ventilation.[12] None of our patients had any neurologic deficits either in the postoperative period or in the follow-up period. Prolonged ventilator support was given to 2 of our cases (2 and 6). None of them had myasthenia gravis. In case 2, the patient was on mechanical ventilator support for 70 days. The patient was a known case of chronic obstructive pulmonary disease that required a right pneumonectomy also for complete tumor clearance. He was also detected to have hypothyroidism in the postoperative period. He was discharged from the hospital on bilevel positive airway pressure (BIPAP) support. The intermittent BIPAP support was slowly weaned off over a period of 2 months. In case 6, the left phrenic nerve was completely encased by the tumor and had to be resected with the tumor.

Perusal of the available literature clearly indicates that patients who had complete tumor resection with SVC and reconstruction with an ePTFE graft not only have immediate relief of SVC obstructive symptoms but also prolongation in survival. In experienced hands, the operative risk is low. Even today, patients with large, invasive thymomas particularly with the involvement of great vessels are either subjected to nonsurgical palliative treatments or only "debulking surgery". The tumor is shaved off the vital infiltrated structures and the residual disease is expected to be treated by radiotherapy and/or chemotherapy. However, it is now well known that thymomas are neither highly radiosensitive nor highly chemosensitive and "complete surgical resection," followed by adjuvant postoperative treatment, offers the best opportunity of long-term survival (and possible cure in some) of these patients. Unfortunately, many centers still do not pursue such an approach toward these patients.

In conclusion, we feel that extensive resections of the tumor tissue with involved adjacent organs and vessels are feasible, safe, and improve survival in invasive thymomas.

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