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Surgical approaches, anaesthetic management and outcome in pediatric superior mediastinal tumors

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ABSTRACT

Background: Pediatric superior mediastinal tumors are a heterogeneous group of tumors with marked variation in pathology and extension. We reviewed our experience with different surgical approaches to tumors originating from or extending to superior mediastinum in pediatrics.

Patients and methods: The medical records of all patients who had undergone resection for superior mediastinal tumors in Children's Cancer Hospital – Egypt, between January 2008 to December 2015, were reviewed for demographic data, clinico-pathological features, radiologic findings, operative techniques and outcome.

Results: The study included 20 patients. Diagnosis included: germ cell tumors (n = 8), neuroblastoma (n = 4), soft tissue sarcoma (n = 3), thymolipoma (n = 2), infantile fibromatosis (n = 1), calcifying fibrous tumor (n = 1), and thymic carcinoma (n = 1). Tumor extension was divided into tumors extending unilaterally to one hemithorax (n = 9), tumors extending bilaterally to both hemithoraces (n = 4), and cervico thoracic junction tumors (n = 7). Extended lateral thoracotomy was used in 8 patients. Other approaches included trapdoor (n = 5), clamshell (n = 4), cervical approach (n = 2) and double level lateral thoracotomy (n = 1). There was no perioperative mortality, and postoperative morbidity was 20%. At the end of December 2016, 15 patients were alive free of disease, 5 patients developed local and/ or distant relapse.

Conclusion: Pediatric superior mediastinal tumors could be divided into 3 groups according to tumor extension. Each group has an optimum surgical approach that achieves the best exposure for adequate resection. However, further research is needed to confirm the conclusion as this was a descriptive study and the sample size was too small for valid statistical analysis.

Introduction

Primary tumors and cysts of the mediastinum in children and adults are uncommon [1–4]. In a collected series of primary mediastinal tumors and cysts, 25–49% of these lesions were malignant [1,2,4,5]. Pediatric primary mediastinal tumors are even less common, but the risk of malignancy is increased to approximately 75% [6,7]. The mediastinum is divided into compartments (superior, anterior, middle and posterior) and each compartment harbour characteristic tumors, however, they can occur in any of the mediastinal compartment due to the common occurrence of heterotopias of thymic tissue outside the anterior mediastinum [8]. Tumors arising from or extending to the superior mediastinal compartment in pediatrics are a heterogeneous group of tumors with marked variation in pathology, extension and response to chemotherapy. Due to the complexity of this compartment and variable tumor extension, different surgical approaches were

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described. Our objective was to review our experience with different surgical approaches to tumors originating from or extending to superior mediastinum in pediatrics.

Patients and methods

Patients selection

The study included all patients less than 18 years old at presentation who had undergone resection of tumors originating from or extending to the superior mediastinum between January 2008 and December 2015 at Children's Cancer Hospital, Egypt. All benign and malignant tumors that were a candidate for surgery either before or after chemotherapy were included. Cases proved to be lymphoma were excluded. During the same study period, there were 6 cases of cervicothoracic neuroblastoma encasing the major vessels in the thoracic inlet. All had >90% reduction in tumor size after chemotherapy but still encasing the major vessels at thoracic inlet. The decision was not to operate except in the case of tumor progression. All cases were followed up with no resection. All of them had a stationary disease.

Study design

This was retrospective case review study. After scientific meeting accreditation committee (SMAC) approval, we reviewed the electronic medical records for the following: demographic data, clinicopathologic features, radiographic findings, operative techniques and outcome. All patients were followed up after surgery until the end of December 2016 or time to last contact with the patient for: perioperative complications, late postoperative complications; development of local recurrence or distant metastases and mortality. Patient characteristics were described in the overall cohort using count and percentage. Event-free survival (EFS) and overall survival (OS) were estimated using Kaplan–Meier analyses. Events were defined as relapse, progressive disease (PD), secondary malignancy or death. Survival outcome was presented ±standard error. Analysis was performed using SPSS statistical package version 20.

Preoperative evaluation and chemotherapy protocols

All patients had preoperative complete blood count, liver and renal functions and coagulation profile. Tumor markers (alpha-fetoprotein (αFP) and beta human chorionic gonadotropin (β HCG)) was done if (GCT) was suspected radiologically. All patients had pre operative CT with intravenous contrast. CT angiography was done in cervicothoracic junction tumors encasing the vessels. A preoperative biopsy was done except if a benign diagnosis is concluded with certainty with imaging in a multidisciplinary team approach. After the biopsy, patients with malignant tumors received preoperative chemotherapy according to our hospital protocol as follow:

Patients with NB were intermediate risk patients and received Etoposide and Carboplatin (VP16/CARBO) alternating with cyclophosphamide, doxorubicin and vincristine (CADO), administered at 3-week intervals, with a total of 6 or 8 cycles. Patients with soft tissue sarcoma were on arm D protocol and received 4 cycles of chemotherapy before surgery and 4 cycles adjuvant with radiotherapy, in the form of 2 cycles IFX/ADR (ifosfamide/doxorubicin) and 2 cycles IFX/VP16 (ifosfamide/vepeside). One case of non-metastatic thymic carcinoma received 5 cycles of chemotherapy, 4 cycles preoperative and one cycle postoperative in the form of cisplatinum, vepeside, cyclophosphamide and vincristine. While the 5 cases of germ cell tumors received 3 cycles of preoperative chemotherapy in the form of cyclophosphamide, platinol, vepeside and bleomycin.

Surgical approaches

Posterolateral thoracotomy: The patient is placed in a full lateral decubitus position with appropriate pressure point padding. The skin incision is started at the level of the anterior axillary line over the fifth intercostal space. It is curved around the tip of the scapula and continued posteriorly along a line between the medial aspect of the scapula and the spine. It is carried upwards to the level of T4. Anteriorly, the skin incision follows the rib outline. If an additional posterior extension is required, the anterior portion of the trapezius and rhomboid muscles can be divided. If an additional anterior extension is required, the skin incision is extended to the lateral edge of the sternum and the serratus anterior and pectoralis major muscles are divided. The mammary vessels are dissected and ligated in case partial sternotomy is needed.

Trap-door: The patient is placed in the supine position, the side of the anterior thoracotomy extension is elevated 30 degrees with a longitudinal roll placed beneath the scapula, and arms are tucked at the sides. A transverse incision is begun along the superior portion of the clavicle with descending median sternotomy through the midline sternum to the desired intercostal space to the anterior-axillary line.

Clamshell: The patient is placed in the supine position and the arms are extended. A curvilinear incision is made along the inframammary crease, extending from right to left anterior axillary lines, the mammary vessels are ligated and two Finochietto retractors are used to provide the retraction. The pleural reflections are incised to gain exposure to the mediastinal structures.

Results

The study included 20 patients, 13 males and 7 females. The median age at diagnosis was 5 years (Range 2 months–16 years).

Clinical presentation and preoperative evaluation: There were 12 malignant and 8 benign tumors. The most common pathology was Germ cell tumor (GCT) followed by neuroblastoma. Shortness of breath was the commonest presentation (Table 1). Fifteen patients (75%) had initial radiologic guided biopsy. while 5 patients (25%) had surgery based on clinical and radiologic findings, thymolipoma (n = 2) and teratoma (n = 3). Eight patients had under-

Table 1
patients and tumor characteristics.

Variable		Value	
Age at presentation		Median	5 y
		Range	(2 M, 16 Years)
Sex		Male	13
		Female	7
Presenting symptoms		Shortness of breath	6
		Cough	5
		Horner's syndrome	2
		Pneumonia	2
		Accidently discovered	5
Pathology	Benign/borderline	Mature teratuma	1
		Mature cytic teratoma	2
		Immature teratoma G 1	1
		Calcifying fibrous tumor	1
		Infantile fibromatosis	1
		Thymolipoma	2
	Malignant	Soft tissue sarcoma	3
		Malignant GCT	4
		NB	4
		Thymic carcinoma	1

gone resection without preoperative chemotherapy: thymolipoma (n = 2), teratoma (n = 4), and one patient with each of the following infantile fibromatosis and calcifying fibrous tumor. Twelve patient had surgery after neoadjuvant chemotherapy: NB (n = 4), MGCT (n = 4), soft tissue sarcoma STS (n = 3) and one patient with thymic carcinoma. The median of the largest tumor diameter at the time of resection was 7 cm (range 4–18 cm). Gross total resection was done in 19 of 20 (95%) patients. All patients with benign tumors had complete gross total resection. In malignant cases gross total resection could be achieved in 11of 12 (91.6%) patients. Microscopic negative resection (R0) was achieved in 8 of 11 (72.7%) patients and macroscopic residual was left in one patient with NB achieving 90% gross resection.

Surgical approaches and postoperative morbidity: Tumor extension was divided into:tumor extending unilaterally to one hemithorax (n = 9), tumor extending bilaterally to both hemithoraces (n = 4) and cervico thoracic junction tumors (n = 7). Different surgical approaches were used based on the tumor extension (Table 2). Extended lateral thoracotomy was the most common approach (n = 8) (Fig.1a, b). Preoperative tumor extension was unilateral to one hemithorax, the pathology was heterogeneous including (GCT, Spindle cell sarcoma, synovial sarcoma, thymic carcinoma). The extent of thoracotomy varied according to tumor extension. In 3 patients the incision was extended to include transverse sternotomy to allow dissection of the tumor from the central vessels. In 2 cases, the lateral thoracotomy was extended anteriorly till the sternum. Complete gross resection was achieved in the all 8 patients. Other approaches included trap-door (n = 5) (Fig. 2a, b). Complete gross resection was done in 4 cases and in one patient with NB the tumor was encasing the vessels at the thoracic inlet so maximum debulking was done with less than 10% residual. In one patient with malignant triton tumor, there was tumor thrombus in the right innominate vein extending to superior vena cava above the level of the azygus vein. Resection of the right innominate vein and malignant thrombectomy was done after control of the superior vena cava, left innominate vein, right internal jugular and the right subclavian vein. Clamshell approach was used in 4 patients (Fig. 3a, b) and cervical approach in 2 patients (Fig. 4a, b). Double level thoracotomy was used in only 1 patient (Fig. 5a, b) with MGCT. In this case, we needed to sacrificed the phrenic nerve due to encasement by the tumor. There was no perioperative mortality. Post-operative complications were developed in 4 patients (20%). Horner syndrome was noted in one patient and three patients had Prolonged lung collapse and pneumonia, one of them needed postoperative ventilation for 3 days.

Long term outcomes

At the end of December 2016, fifteen cases were alive free of disease, 5cases developed local and/or distant relapse. Four patients died and the case of relapsed NB was lost to followed up (Table 3). Five-year event-free survival (EFS) and overall survival (OS) of all cases were 55.6 ± 15.2 and 63.5 ± 14.8 respectively (Figs. 6 and 7).

Discussion

Tumors arising from or extending to the superior mediastinum in the pediatric age group are usually large and involve other compartments. The approach to these tumors slightly differs from adults because the thorax of the child is different structurally from that of the adults in several ways. The thoracic walls are thinner and the ribs are more elastic in infants and young children than in the adults. At birth the chest is circular, but as the infant grows the transverse diameter becomes larger than the anterior-posterior dimension, giving the chest an elliptical appearance [9]. This elastic bony cage allows more retraction of the chest wall during thoracotomy. Posterolateral thoracotomy in young children gives a good access to the mediastinum and thoracic apex. It allows dissection of benign tumors from the mediastinal structure on one side and can easily approach any extension to the hemithoracic or posterior mediastinum but it doesn't give good access if there is encasing of neurovascular structures at the thoracic apex or the superior mediastinum. The disadvantage of this approach includes the division of major muscles of the chest, resulting in increased potential for blood loss and moderate time requirement for opening and closing the incision, prolonged ipsilateral shoulder and arm dysfunctions, compromised pulmonary function and chronic postthoracotomy pain syndromes [10]. Lateral thoracotomy and median sternotomy are the most commonly used approaches to large mediastinal masses. However, in large tumors that extend entirely to the hemithorax reaching the hemidiaphragm, such location preclude median sternotomy, the preferred approach is posterolateral thoracotomy [11]. In the present study we used extended lateral thoracotomy in 8 patients with tumors extending mainly to one hemithorax, the pathology was heterogeneous (Table 2). Gross

Table 2
Tumor extension and surgical approach.

Tumor extension	Surgical Approach	Resection margin	Number	Pathology n	
Tumor extending unilaterally to one hemithorax	Extended lateral thoracotomy	R0	5	Malignant GCT	1
		R0		Thymic carcinoma	1
		R0		Mature cystic teratoma	2
		R0		Immature teratoma	1
	Extended lateral thoracotomy with transverse sternotomy	R0	3	Malignant GCT	1
		R1		Spindle cell Sarcoma	1
		R1		Synovial Sarcoma	1
	Double level thoracotomy	R1	1	Malignant GCT	1
Tumor extending bilaterally to both hemithoraces	Clamshell	R0	4	Thymolipoma	2
		R0		Infantile fibromatosis	1
		R0		Mature teratoma 1	1
Cervicothoracic junction tumors	Trapdoor	R2 (1 case)	5	NB	2
				Malignant triton tumor	1
				Mixed GCT (seminoma, teratoma)	1
				Calcifying fibrous tumor	1
	Cervical	R0	2	NB	2

R0 Negative microscopic. R1 positive microscopic. R2 Gross residual.

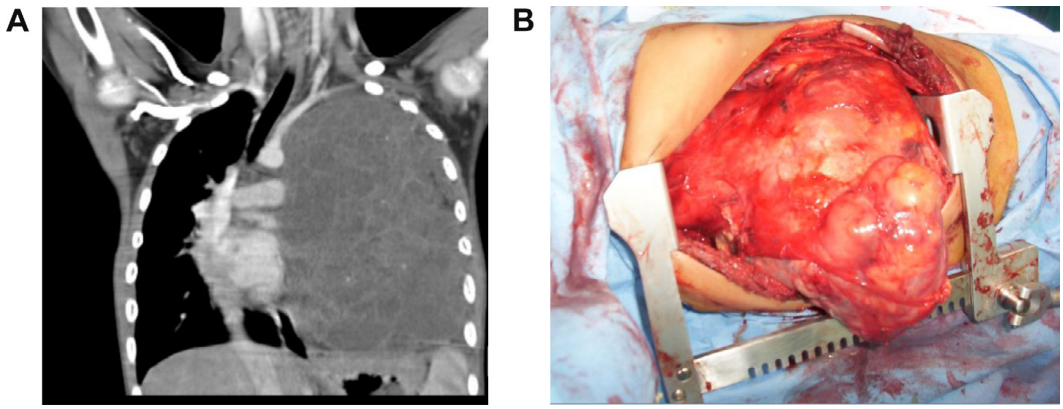

Fig. 1. (A) CT. Coronal view of mediastinal GCT. (B) Intra operative view of extended lateral thoracotomy approach.

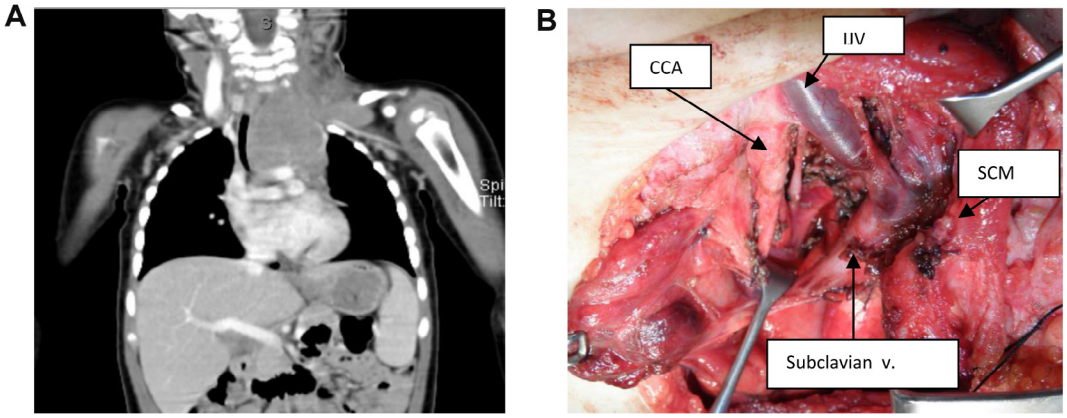

Fig. 2. (a) CT, coronal view of mediastinal NB. (b) Intraoperative view of trapdoor approach IJV: Internal jugular vein CCA: Common carotid artery SCM: Sternocleidomastoid muscle.

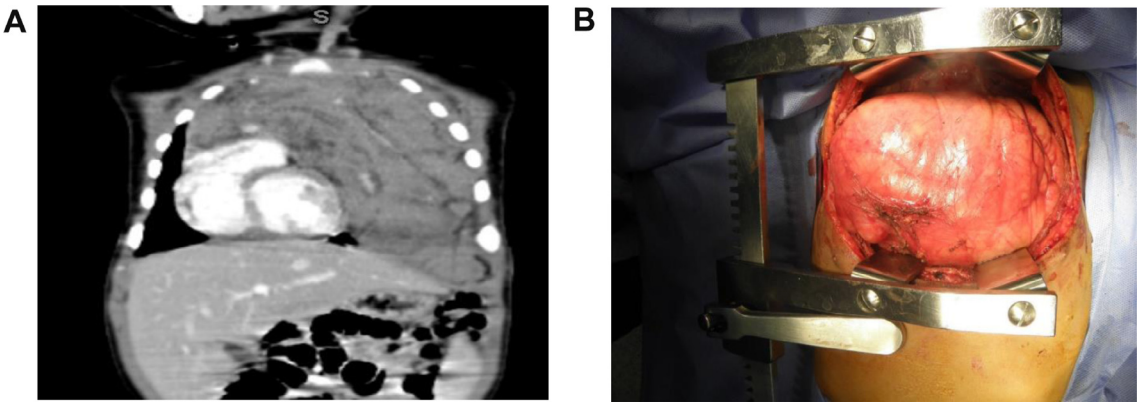

Fig. 3. (A) CT coronal view of mediastinal thymolipoma. (B) Intraoperative view of clamshell approach.

resection could be achieved in all 8 patients. All cases had smooth post-operative recovery except two cases which had prolonged lung collapse and pneumonia which responded to conservative treatment. Double level thoracotomy was used only in one case, with MGCT. The decision was to use extended lateral thoracotomy but after opening in the 4th space the tumor was adherent to the chest wall and diaphragm and the lower extension of the tumor was not accessible so another thoracotomy at the 8th space was done. Scarification of the phrenic nerve was done. The patient had postoperative pneumonia and prolonged collapse and was ventilated for 3 days. By reviewing the radiology and pathology of the cases in which we had to extend the incision or added another incision, the tumors were malignant with invasive growth pattern and extended from the mediastinum to fill the whole hemithorax reaching the hemidiaphragm. In these cases we needed a good access to both superior mediastinum and whole thoracic cavity fore save dissection of the tumor from the mediastinal structures. In the future, we would use hemiclamchell in these cases as it provid a good access to both compartments. For large tumors involving both the anterior mediastinum and one chest cavity, the hemi-clamshell incision has several advantages over traditional approaches: exposure of the mediastinum, chest cavity

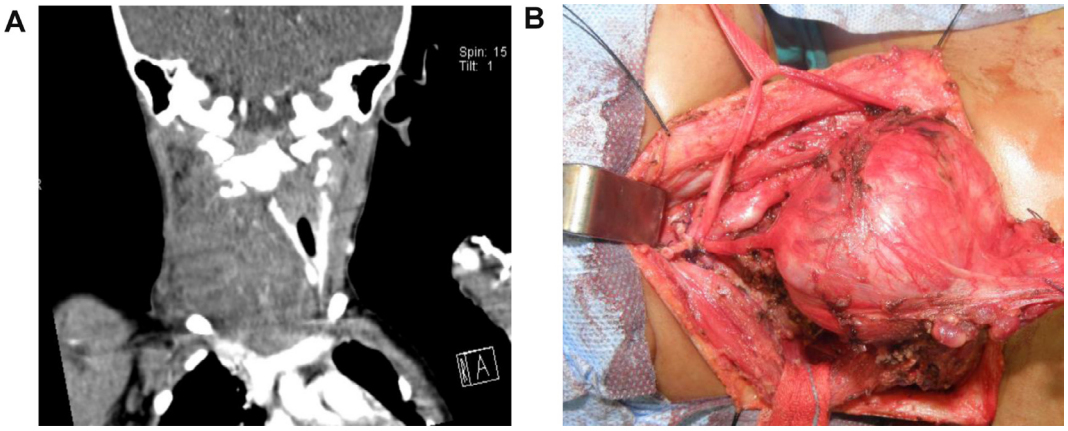

Fig. 4. (A) CT coronal view of cervicothoracic NB. (B) Intraoperative view of cervical approach.

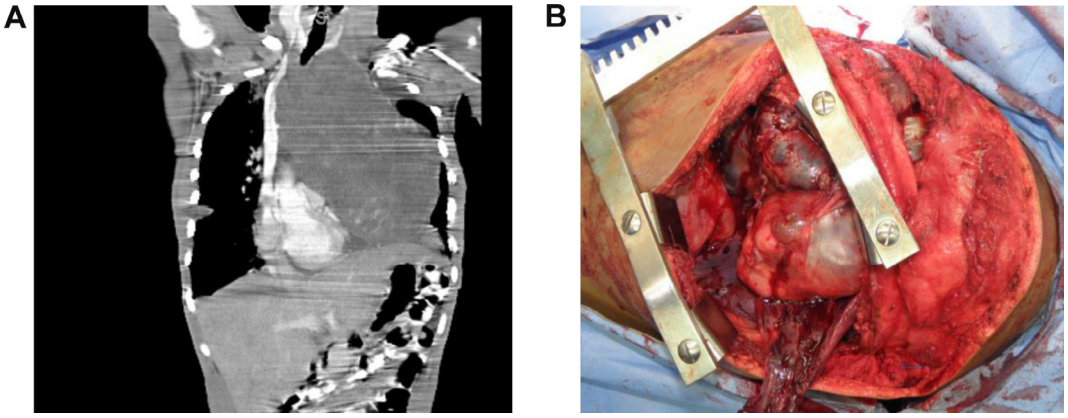

Fig. 5. (A) CT Coronal view of mediastinal GCT. (B) Intraoperative view of Double level thoracotomy approach.

Table 3
Response of malignant tumor to chemotherapy and outcome.

diagnosis	Tumor Diameters before chemotherapy	Tumor Diameters after chemotherapy	Duration between surgery and last follow up	State at last FU and timing site of relapse
Mixed GCT seminoma teratoma	16 × 7 × 6	4 × 3 × 2	72 M	Alive/free
Malignant GCT	10 × 8 × 6	6 × 4 × 4	48 M	Alive/free
Malignant GCT	18 × 14 × 10	18 × 14 × 10	7 M	Pulmonary nodules and effusion after 3 M/died after 4 M of relapse
Germinoma	11 × 11 × 9	4 × 3 × 3	24 M	Alive/free
Thymic Carcinoma	7 × 8 × 5	4 × 2 × 2	20 M	Bone/liver/nodal recurrence after 5 M/died after 15 M of relapse
Spindle cell Sarcoma	17 × 8 × 6	17 × 8 × 6	17 M	Pulmonary nodule after 13 M/died after 4 M of relapse
Malignant Triton	10 × 7 × 4	7 × 5 × 3	20 M	Alive/free
Synovial sarcoma	17 × 16 × 12	16 × 17 × 12	29 M	Pleural relapse in costophrenic angle after 21 M/ died after 8 M of relapse
NB	7 × 6 × 4	4 × 3 × 2	94 M	Alive/free
NB	8 × 6 × 7	6 × 3 × 4	8 M	Mediastinal and cervical Nodal Recurrence after 8 M/lost FU
NB	7 × 6 × 4	4 × 3 × 3	73 M	Alive/free
NB	7 × 5 × 4	7 × 5 × 3	53 M	Alive/free

and anterior cervicothoracic junction is excellent, major pulmonary resection is facilitated, and surgical resection is usually a single-step procedure [12,13]. Reports of approaches to tumors of the cervicothoracic junction in the pediatric patients have been limited to small series of fewer than four patients [14]. Different surgical approaches have been used to access cervicothoracic junction tumors. In trans manubrial osteon muscular-sparing technique, popularized by Grunenwald, access is obtained by dividing the manubrium and the first costal cartilage [15,16]. This approach has limited exposure to the anatomy visible above subclavian vein and it is recommended for localized neuroblastoma arising from the stellate ganglia [17]. Partikh et al. [18] reported the resection of cervicothoracic neuroblastoma in three patients using dartevelles technique requiring resection of the medial clavicular head.

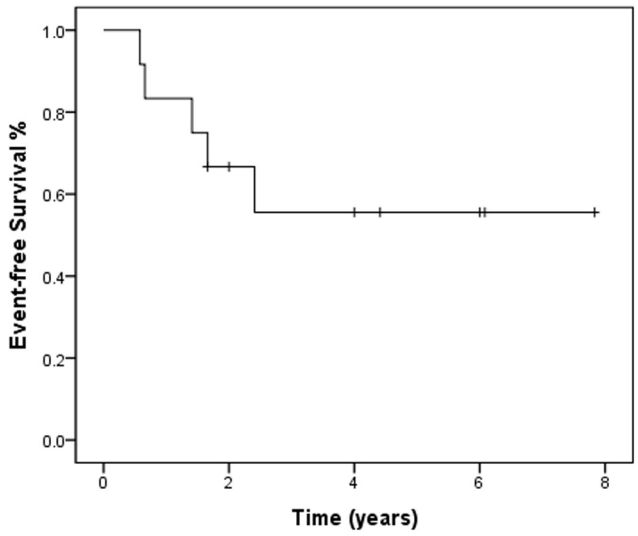

Fig. 6. EFS of the 12 patients with malignant superior mediastinal tumors.

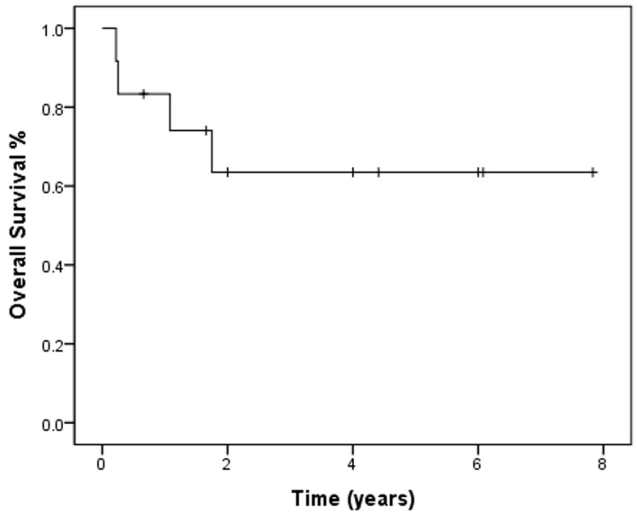

Fig. 7. OS of the 12 patients with malignant superior mediastinal tumors.

In the adult, this has been associated with shoulder girdle instability, delayed postoperative recovery and bony malunion in up to 42% of patients [19–21]. The trap-door incision is used to approach large tumors of the superior mediastinum and cervicothoracic inlet. This incision allows access to neurovascular structure at the neck and thoracic inlet proximal to the level of pulmonary hilum [14,22]. In the present study, we approached these tumors through Trapdoor incision which was used in 5 cases. The tumor extension was either limited to the superior mediastinum or extending to the neck but in all cases, the tumors were intimately related to the major neurovascular structure at the thoracic inlet. This approach allowed save control of major vessels at the thoracic inlet with resection of the innominate vein in one case. All cases had a smooth postoperative recovery with no complications. For large tumors arising in the mediastinum and extending into both hemithoraces, the clamshell incision provides excellent exposure extending to the level of lung apices and thoracic outlet with minimal respiratory complications and low rate of sternal nonunion or wound infection [23,24]. In the present study, the clamshell incision was used in 4 patients for tumors extending from the mediastinum to both hemithoraces. Complete resection was done in all cases. The cervical only approach was used in two patients in which the tumor was arising from the neck and extending to superior mediastinum above brachiocephalic vein with no encasement of the major vessels at the thoracic inlet in the preoperative imaging. The tumors were completely excised through this approach. In the present study, we reported the successful complete resection of tumors arising from or extending to superior mediastinum through different surgical approaches. The choice of the approach was a matter of the tumor extension, pathology and the age of the patient. Exposure of mediastinal tumors that extend mainly to fill one hemithorax varies with the pathology and age of the patients. Benign tumors in children with no encasement of neurovascular structures at the thoracic inlet can be safely approached through the lateral thoracotomy. As the rib cage is elastic in children, traction through lateral thoracotomy gives an access to the superior mediastinum. And when the tumor is benign it does not invade the surrounding so dissection of the tumor from the mediastinal structure can be safely done through this approach. However, in Malignant mediastinal Tumors with invasive growth pattern and in adult patients with less elastic rib cage a direct exposure of the involved compartment is needed to provide save dissection of major vessels at thoracic inlet and save resection of the tumors with minimal morbidity. So, the trap-door or hemiclashell incision should be considered according to the tumors extension. Clamshell incision is an appropriate approach for midline tumors that arise mainly from anterosuperior mediastinum with the main extension on both sides of midline with no much posterior extension to the hemithorax and no extension to the cervicothoracic junction.

Conclusion

Pediatric superior mediastinal tumors could be divided into 3 groups according to tumor extension. Each group has an optimum surgical approach that achieves the best exposure for adequate resection. However, further research is needed to confirm the conclusion as this was a descriptive study and the sample size was too small for valid statistical analysis.

The authors have no conflict of interest related to the content of this manuscript.

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