

Paravertebral malignant tumors of childhood: analysis of 28 pediatric patients

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Abstract

Purpose To evaluate the clinical features and treatment results of the primary paravertebral malignant tumors (PMTs) in our department.

Methods Medical records of 28 children with primary PMTs treated between 1988–2007 were analyzed retrospectively.

Results Primary PMTs constituted 4.8% of the cancer cases in our department. Tumor diagnoses were mostly neuroblastoma (46.4%) and soft tissue sarcomas (35.7%). These cases presented with pain (64.3%), motor dysfunction (42.8%), sphincter dysfunction (35.7%), palpable mass (32.1%), and sensory deficits (7.1%). All tumors were extradural. Physical examination revealed motor deficits (53.6%), deep tendon reflex alterations (53.6%), sphincter dysfunction (35.7%), pathologic reflexes (25%), abnormal cutaneous reflexes (25%), and sensory deficits (17.8%).

Sixteen had cord compression (CC; 13 clinical, three radiological CC). Eleven of them presented with advanced disease. Seven were managed by surgical departments by primary surgery (three unresponsive). Others were managed by pediatric oncology: five with corticosteroids ± chemotherapy (one unresponsive), one with radiotherapy (RT), and two with surgery for the clinical CC. Surgery was tumor excision in nine, laminectomy in nine, laminotomy in one, and delayed surgery after chemotherapy in two cases. In chemotherapy and surgery groups, there were neurologic sequela associated with the advanced disease at diagnosis in 38% and 37%, respectively. At 3-year median follow-up, nine patients died, 17 are alive (four with neurologic sequela), and two are lost of follow-up.

Conclusion Majority of cases presented with advanced disease. Late referral is the major cause of morbidity and mortality. The CC caused by PMTs should be initially managed with corticosteroids ± chemotherapy to avoid the adverse late effects of RT and surgery.

Keywords Paravertebral malignant tumors · Spinal cord compression · Childhood

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Introduction

Paravertebral malignant or benign tumors seen in children and adolescents may show extension to spinal canal through intervertebral foramina. These patients commonly present with radicular or back pain and neurological deficits related to spinal cord compression (CC). In any child presenting with these symptoms, paravertebral malignant tumors (PMTs) such as neuroblastoma, ganglioneuroblastoma, soft tissue sarcomas (STS), Ewing sarcoma, primitive neuroectodermal tumor, rhabdomyosarcoma, Langerhans

cell histiocytosis (LCH), and more uncommonly vertebral osteosarcoma should be considered. Spinal cord compression is one of the oncologic emergencies, so the diagnosis and appropriate treatment should be made urgently. Here, we reported our clinical experience with paravertebral malignant tumors in children.

Materials and methods

We reviewed the medical records of 575 children and adolescents with malignant tumors (lymphomas and solid tumors) who had been diagnosed and treated in our Pediatric Oncology Department between Jan 1, 1988 and Dec 31, 2007. All patients were under 19 years old. Patients with primary PMTs were enrolled and medical records were retrospectively evaluated regarding to age, gender, and complaints at admission, clinical findings, primary tumor site and extension, diagnostic and therapeutic interventions, histopathological diagnosis, treatment results, and sequelae. Patients with leukemia were not included in this study, because of leukemias were treated in Pediatric Hematology Department in our center. Patients with primary brain or spinal tumors, patients with spinal seeding or relapsed disease, and patients having paravertebral benign tumors were excluded.

Statistical analysis The Statistical Package for the Social Sciences 11.0 program was used for data analysis. Patient characteristics were summarized using descriptive statistics.

Results

The hospital records of 575 children with lymphomas and solid tumors seen in our department between Jan 1, 1988 and Dec 31, 2007 were evaluated. Of these, 28 (4.8%) children had primary PMTs. The median age of diagnosis was 5.6 years (2 months–17 years), male to female ratio was 1:1. Table 1 shows some clinical features of these patients at admission and the distribution of primary PMT sites.

Radiological evaluation was performed by magnetic resonance imaging (MRI) in 24 (86%), by computerized tomography (CT) in 24 (86%), and by direct radiography in 22 (76%). Combined radiography, MRI, and CT evaluation was performed in 21 (75%) children. All primary PMTs were extradural lesions in our patients. Sixteen patients had radiological findings of CC, and 13 (81%) of them also had clinical findings of CC (Table 2). Pathologic findings by neurological examination were as follows: motor deficits in 15 (53.6%), alterations of deep tendon reflexes (DTRs) in 15 (53.6%), bladder sphincter and/or intestinal dysfunction in ten (35.7%), pathologic plantar reflexes in seven (25%),

Table 1 Clinical characteristics of children with primary paravertebral malignant tumors

	Patients with PMT (n (%))
Patient number	28
Median age of diagnosis (ranges)	5.6 years (2 months–17 years)
Gender	
Male/female ratio	1
Median duration of complaints (ranges)	7 weeks (1–28)
Complaints at admission	
Pain (radicular and/or back pain)	18 (64.3)
Motor deficit	12 (42.8)
Sphincter dysfunction	10 (35.7)
Palpable mass	9 (32.1)
Sensory deficits	2 (7.1)
Paleness	1 (3.6)
Primary tumor site	
Above the T10 vertebral level	11 (39.3)
Cervical	3
Cervicothoracal	1
Thoracal	7
T10–L2 vertebral level	14 (50)
Thoracolumbar	5
Lumbar	5
Lumbosacral	4
Cauda equina	3 (10.7)
Sacral	3

T10 thoracal 10, L2 lumbar 2, PMT paravertebral malignant tumor

superficial skin reflexes deficits in seven (25%), and sensory deficits in five (17.8%; Table 3).

Sixteen of these patients were primarily admitted to our Pediatric Oncology Department. Seven of these cases had clinical signs of CC and five of them were put on corticosteroid therapy immediately after diagnosis. Twelve

Table 2 Existence of the clinical and radiological findings of spinal cord compression, according to the level of paravertebral tumor

	Clinical findings of CC		Radiological findings of CC	
	+	–	+	–
	n (%)	n (%)	n (%)	n (%)
Level of PMT				
Above the T10 vertebral level (n=11)	5 (38.5)	6 (40)	6 (37.5)	5 (41.7)
T10–L2 (n=14)	7 (53.8)	7 (46.7)	9 (56.3)	5 (41.7)
Cauda equina (n=3)	1 (7.7)	2 (13.3)	1 (6.3)	2 (16.7)
Total	13 (46.4)	15 (53.6)	16 (57.1)	12 (42.9)

(+) Determines if the relevant features are present, (–) Determines if the relevant features are absent

PMT paravertebral malignant tumor, CC cord compression, T10 thoracal 10, L2 lumbar 2

Table 3 Physical examination findings according to the level of primary tumor

Level of PMT	Physical examination findings					
	Motor deficits (+)	Sensory deficits (+)	Pathologic DTR (+)	Pathologic plantar reflexes (+)	Bladder sphincter and/or intestinal dysfunction (+)	Deficits in superficial skin reflexes (cremaster/anal/abdominal reflexes) (+)
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)
Above the T10 vertebral level (n:11)	5 (17.8)	1 (3.6)	5 (17.8)	1 (3.6)	2 (7.1)	1 (3.6)
T10 - L 2 (n:14)	8 (28.5)	3 (10.7)	8 (28.5)	4 (14.3)	5 (17.8)	4 (14.3)
Cauda equina (n:3)	2 (7.1)	1 (3.6)	2 (7.1)	2 (7.1)	3 (10.7)	2 (7.1)
Total	15 ^a (53.6)	5 ^b (17.8)	15 (53.6)	7 (25)	10 (35.7)	7 (25)

(+) Determines if the relevant features are present, (–) Determines if the relevant features are absent

PMT paravertebral malignant tumor, T10 thoracic 10, L2 lumbar 2, DTR deep tendon reflex

^a Motor deficits were detected by physical examination in three patients although they had no complaint

^b Sensory deficits were detected by physical examination in three patients although these had no any complaints about it

patients were initially admitted to surgical departments, and six of them had clinical findings of CC at admission; however, no data was available in medical records regarding the initial corticosteroid administration for these cases (Table 4). Bone marrow examination (BME) was performed in 26 patients, and tumoral involvement was documented in five (19%). The tumor diagnosis was made by histopathologic

Table 4 Diagnostic methods, diagnosis, and initial corticosteroid administration

	Radiological + clinical CC Present (n=13)	Radiological CC Present (n=3)	Radiological ± clinical CC Absent (n=12)	Total <i>n</i> (%)
Diagnostic procedure				
Primary surgery	9	1	5	15 (53.6)
Total resection	3	–	3	
Partial resection	6	1	2	
Open biopsy	3	2	–	5 (17.8)
Trucut biopsy	1	–	6	7 (25)
Out of primary lesion biopsy	–	–	1	1 (3.6)
Histopathologic diagnosis				
SNS tumors	5	1	7	13 (46.4)
STS	6	–	4	10 (35.7)
LCH	2	1	1	4 (14.3)
Hodgkin's lymphoma	–	1	–	1 (3.6)
Initial CS administration				
(+)	6	2	2	10 (35.7)
(–)	7	1	10	18 (64.3)
Total	13	3	12	28 (100)

(+) Determines if the relevant features are present, (–) Determines if the relevant features are absent

CS corticosteroid, SNS sympathetic nervous system, STS soft tissue sarcomas, LCH Langerhans cell histiocytosis

examination of the tumor after primary surgery in 53.6% patients (Table 4). The diagnoses of patients and the median age at diagnosis are shown in Table 5.

Sixteen (57%) had cord compression (13 clinical, three radiological CC). Eleven of them presented with advanced disease. Primary treatment for patients with radiological ± clinical CC (n=16) was decompression surgery in ten (complete resection in three, partial resection in seven), chemotherapy in five, and radiotherapy in one (Table 6). Seven were managed by surgical departments by primary surgery (three unresponsive). Others were managed by pediatric oncology; five with corticosteroids ± chemotherapy (one unresponsive), one with radiotherapy, and two with surgery for the clinical CC. One of these two patients who underwent decompressive surgery was initially diagnosed with ganglioneuroma by Trucut biopsy. Following surgical excision, a diagnosis of ganglioneuroblastoma was made and chemotherapy was given to the patient.

Table 5 Histopathologic diagnosis and median age of diagnosis

Histopathologic diagnosis	<i>n</i> (%)	Median age of diagnosis (ranges)
Sympathetic nervous system tumors	13 (46.4%)	2 years (2–6 years)
Neuroblastoma	8	
Ganglioneuroblastoma	5	
Soft tissue sarcomas	10 (35.7%)	13 years (1–17 years)
Ewing sarcoma	4	
Primitive neuroectodermal tumor	2	
Rhabdomyosarcoma	2	
Small round cell tumor	2	
Langerhans cell histiocytosis	4 (14.3%)	9 years (1–13 years)
Hodgkin's lymphoma	1 (3.6%)	7 years
Total	28	

Table 6 Therapeutic interventions and outcome

Patients with spinal cord compression (<i>n</i> =16)						
Diagnosis	Primary treatment (<i>n</i>)	Response to the primary treatment (<i>n</i>)	Continuation treatment (<i>n</i>)	Follow up time (months)	Outcome	Neurologic sequela
SNST (<i>n</i> =6)	CT (3)	PR (3)	(1) CT, delayed surgery, RT	75	AWD (relapsed)	(-)
			(1) CT+RT	108	NED	(+)
			(1) CT+delayed surgery	13	NED	(-)
	Primary surgery with MacR (3)	PR (1) PD (2)	(1) CT, CR	33	NED	(-)
			(2) CT	10	DOD	(-)
			2	DOD	(+)	
STS (<i>n</i> =6)	CT (2)	PR (1) PD (1)	(1) CT, RT	11	AWD ^a	(+)
			(1) CT: NR, PD	3	DOD	(+)
	Primary surgery with MacR (2)	PD (1) PR (1)	(1) CT, RT: PD	52	DOD	(+)
			(1) CT	36	LFU with disease	(+)
	Primary surgery without R (2)	CR (1) PR (1)	(1) CT, RT	140	NED	(-)
		-	1	LFU with disease	(+)	
LCH (<i>n</i> =3)	RT (1)	CR (1)	(1) CT	89	NED	(-)
	Primary surgery with MacR (1)	PR (1)	(1) RT	216	NED	(-)
	Primary surgery without R (1)	CR (1)	(1) CT	213	NED	(-)
Hodgkin's lymphoma (<i>n</i> =1)	Primary surgery with MacR (1)	PR (1)	(1) CT, disease relapsed at out of primary site and she received CT again; CR	46	NED	(-)
Patients without spinal cord compression (<i>n</i> =12)						
SNST (<i>n</i> =7)	CT (3)	CR (2) PR (1)	CT	111	NED	(-)
			CT	22	NED	(-)
			CT	1	DOD	(-)
	Primary surgery without R (3)	CR (3)	CT	216	NED	(+)
			CT	135	NED	(-)
			-	20	NED	(-)
	Primary surgery with MacR (1)	PR (1)	Refused further therapy	22	DOD	(-)
STS (<i>n</i> =4)	Primary surgery with MacR (3)	PR (1) PD (2)	CT, RT	19	DOD	(-)
			CT, RT	15	DOD	(-)
			CT, RT	26	DOD	(+)
	Primary surgery without R (1)	PR (1)	CT, RT	204	NED	(+)
LCH (<i>n</i> =1)	Primary surgery without R (1)	CR (1)	RT	162	NED	(-)

(+) Determines if the relevant features are present, (-) Determines if the relevant features are absent

CT chemotherapy, RT radiotherapy, SNST sympathetic nervous system tumor, STS soft tissue sarcoma, LCH Langerhans cell histiocytosis, MacR macroscopic residue, R residue, PR partial remission, NR nonresponse, PD progressive disease, CR complete remission, AWD alive with disease, NED no evidence disease, DOD died of disease, LFU lost of follow-up

^aTreatment is going on

Primary treatment for patients without CC (*n*=12) were primary surgery in nine (complete resection in five, partial resection in four) and chemotherapy in three (Table 6). Tracheal compression and respiratory distress was the indication for urgent chemotherapy in one infant with cervical ganglioneuroblastoma. Surgery was tumor excision in nine, laminectomy in nine, laminoplasty in one, and delayed surgery after chemotherapy in two cases.

For patients with CC initially, 11 (69%) cases had advanced disease at admission and seven cases (44%) had neurologic sequela despite the treatment. Initial treatment was surgery in four and chemotherapy in three of these seven patients, and three of them also received radiotherapy. Other nine patients in this group were treated without sequela. For patients without CC initially (*n*=12), three cases (25%) had neurologic sequela, one related with

progression of disease + surgery, one related with surgery, and one related with surgery + radiotherapy.

In chemotherapy and surgery groups, neurological sequelae associated with advanced disease at diagnosis were present in 38% and 37%, respectively. At 3 years of median follow-up, nine patients died, 17 are alive (four with neurological sequela), and two are lost of follow-up.

Discussion

Paravertebral masses may occur as a consequence of benign or malignant tumors. Benign tumors include plexiform neurofibroma, hemangioma, angioliopoma, and osteoblastoma. Also an infectious process, especially paravertebral *Mycobacterium tuberculosis* abscess (Pott's disease) should be kept in mind in developing countries. The majority of childhood primary paravertebral tumors are chemosensitive malignant tumors that might cause CC. Cord compression may be the presenting symptom or develop at any time during the course of malignant tumors in children.

Majority of our patients presented with advanced disease and had radicular and/or back pain (64%), motor deficits (42.8%), and bladder and/or bowel dysfunction (35.7%) at admission. The rate of noted sensory deficits was low (7%), which could be related to the difficulties in expressing and/or assessing the sensory deficits experienced by these children. In children, complaints of back pain and/or radicular pain should be taken seriously and spinal CC should be ruled out since these complaints can be the first sign of a paravertebral mass. Local or radicular pain is the most frequent (80%) and early sign of CC [1]. Neurological deficits may appear during progression of the process and may cause irreversible sequela. In patients presented with radicular/back pain and/or neurologic dysfunction, detailed neurologic examination is essential and if indicated, imaging studies should be performed immediately.

Half of our patients had either motor deficits and/or DTR alterations, one third with sphincter dysfunction, one fourth with abnormal cutaneous reflexes, and nearly one fifth with sensory deficits. Clinical cord compression was detected in 13 patients. Radiologic evaluation was performed for all patients. Computerized tomography and MRI studies were the preferred imaging modality for bone and soft tissue involvement, respectively. In 17 patients, both of these imaging modalities were performed. Sixteen (57%) had radiological cord compression and 11 of these patients presented with advanced disease.

All primary PMTs were extradural lesions and sites were T10–L2 vertebral level in 50%, above T10 level in 39.3%, and cauda equina in 10.7%. The level of spinal cord involvement can be determined by clinical examination;

however, the presence of a paravertebral mass cannot be excluded by the absence of neurological dysfunction as it had been the case in three of our patients who had only radiological findings of CC.

In nearly half of our cases with primary PMTs, the tumor diagnosis was sympathetic nervous system (SNS) tumors (46.4%). The others had STS (35.7%), LCH (14.3%), and Hodgkin's lymphoma (3.6%). The diagnosis of 16 patients with CC was SNS tumors in six, STS in six, LCH in three, and Hodgkin's lymphoma in one. Our results were consistent with the previous reports [1, 2]. Klein et al. [2] reported 113 children with spinal CC and solid malignant tumors including neuroblastoma ($n=32$), Ewing's sarcoma ($n=30$), osteogenic sarcoma ($n=16$), rhabdomyosarcoma ($n=14$), Hodgkin's disease ($n=8$), STS ($n=4$), and germ cell tumor ($n=2$), hepatoma ($n=1$). Pollono et al. [3] reported 70 children with spinal CC and solid malignant tumors including central nervous system tumors ($n=18$), STS ($n=17$), neuroblastoma ($n=10$), LCH ($n=5$), and Hodgkin's lymphoma ($n=2$). Bouffet et al. [4] reported 17 children with spinal CC and solid malignant tumors including neuroblastoma ($n=10$), Ewing's sarcoma ($n=4$), lymphoma ($n=2$), and osteosarcoma ($n=1$). Aysun et al. [5] reported 12 children with spinal CC and solid malignant tumors including neuroblastoma ($n=7$), non-Hodgkin lymphoma ($n=3$), rhabdomyosarcoma ($n=1$), and Ewing's sarcoma ($n=1$).

The age of our patients varied with the histological type of the tumor. The age was <2 years in seven of 13 patients with sympathetic nervous system tumors, >10 years in seven of ten patients with soft tissue sarcoma, and >6 years in three of four patients with Langerhans cell histiocytosis. These results were consistent with the common occurrence of these specific childhood tumor types.

Spinal cord compression is one of the oncological emergencies that can be seen at the time of presentation or during oncological treatment because of progressing refractory disease or during relapse. Immediate recognition and appropriate urgent intervention may prevent morbidity. Late referral or delayed diagnosis is the major cause of morbidity and mortality. The tumor may cause CC by infiltrating through intervertebral foramina or by involving vertebral body. Clinical neurological improvement can be achieved by dexamethasone and/or chemotherapy. Bone marrow examination is necessary and should be performed in children with primary PMTs with a diagnostic aim before corticosteroid therapy since bone marrow findings may change with corticosteroids. The diagnosis of leukemia, lymphoma, and bone marrow metastatic neuroblastoma can be revealed by BM (bone marrow) examination and this prevents unnecessary surgical intervention [6]. Tumor involvement of BM was detected in five patients

and the diagnosis of neuroblastoma was made by bone marrow involvement, radiologic findings, and elevated vanillylmandelic acid level in 24-h urine in one patient. Sixteen patients were initially admitted to our Pediatric Oncology Department, and eight of them received corticosteroid therapy after BM aspiration.

In our cases that were initially managed by surgeons, primary surgery was performed in 100% (12/12) of patients. On the other hand, 44% (seven of 16) of the patients who were initially managed in Oncology Department with equal eventual sequela underwent primary surgery. In chemotherapy and surgery groups, the incidence of neurological sequela associated with advanced disease at diagnosis was high (38% and 37%, respectively). Radiotherapy was given to one patient with LCH at the vertebral body who had a risk for pathologic fracture. There is a difference in the initial management of children with PMTs with or without CC by surgery and oncology departments. However, it is hard to compare the absolute outcomes of chemotherapy, surgery, and radiotherapy. Cord compression caused by PMTs should initially be managed with corticosteroids with an aim to rescue the cord compression. If no response can be obtained with corticosteroids, anticancer chemotherapy is another option to avoid the adverse late effects of radiotherapy and surgery since childhood PMTs are mostly chemosensitive tumors. Leukemia, lymphoma, and stage 4 neuroblastoma can be diagnosed with BM aspiration, and specific chemotherapy can be started immediately [1, 7–11]. Katzenstein et al. [7] reported lower rates of orthopedic sequela in chemotherapy group rather than laminectomy group although similar rates of neurologic recovery for both groups in patients with neuroblastoma. De Bernardi et al. [8] reported that patients with neuroblastoma treated with chemotherapy usually did not require additional therapy. Chemotherapy should be considered as the first choice of treatment for spinal cord compression particularly caused by leukemias and malignant lymphomas [6, 9–11]. In cases that underwent biopsy for a PMT causing clinical cord compression, corticosteroids, or appropriate chemotherapy should be continued while waiting for the histopathological diagnosis. If BM aspiration reveals no diagnosis and if a trucut or open biopsy seems to cause potential morbidity, the most probable tumor diagnosis can be predicted according to the patient's age, clinical and radiological findings, and chemotherapy can be given.

Late referral or advanced disease-related serious neuropathological findings may require surgical interventions. In children, decompressive laminectomy (posterior approach) is considered as an effective surgical approach for PMTs that causes CC [1, 2, 12]. But since laminectomy can cause spinal instability and growth problems in children, the rationale of surgical management and alternative treatment

modalities should be discussed by multidisciplinary teams. In experience of our center, laminectomy was performed in nine patients, but in recent years, laminoplasty was preferred in three cases (primary surgery (one), delayed surgery (two)). The surgical procedure related spinal deformity risk was reported in lower rates by laminoplasty rather than laminotomy [13–15].

Neurologic sequelae might be related with advanced disease and treatment modalities. The neurological status at admission was the main factor determining morbidity. For patients with CC initially, 11 (69%) cases had advanced disease at admission and seven cases (44%) had sequela despite the treatment. Initial treatment was surgery in four and chemotherapy in three of these seven patients. Three of them also received radiotherapy. Surgery- and/or radiotherapy-related neurologic sequela developed in three patients who had no CC at admission, due to treatments (primary surgery ($n=3$) and radiotherapy ($n=2$)). One of them also had progression of disease. If there are no clinical CC findings and there is no risk of vertebral body collapse, chemotherapy should be considered as an initial treatment for chemosensitive primary PMTs of childhood.

Conclusion

The majority of childhood primary paravertebral tumors are chemosensitive malignant tumors that can cause CC. Neurologic, radiologic evaluation, and oncologic diagnosis should be made immediately. Late referral is the major cause of morbidity and mortality. The PMTs with/without CC should be initially managed with corticosteroids \pm chemotherapy to avoid the adverse late effects of RT and surgery. Pediatric patients with paravertebral tumors should be managed by multidisciplinary approach by expert teams consisting of pediatric oncologists, neurosurgeons, radiation oncologists, radiologists, pathologists, and physiotherapists. Treatment should be tailored for each patient and the aim of treatment should include improving quality of life besides cure for children with primary PMTs.

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