Characteristics and outcomes in patients with primary intraspinal tumours

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ABSTRACT

INTRODUCTION: We report a retrospective cohort study aimed at presenting data on incidence, patient characteristics, tumour type, level of pathology, clinical status before and after surgery and complications in patients with surgically treated primary intraspinal tumours (PIST) in Western Denmark.

METHOD: Population-based data were retrieved from hospital files from 1 January 2010 to 31 December 2015.

RESULTS: In total, 78 males and 88 females with PIST were included in the study. Incidence per 100,000 persons per year in the population-based cohort was 2.18. The incidence of malignant PIST was 0.14 and the incidence of non-malignant PIST was 2.03. We found 25 extradural tumours, 100 intradural extramedullary tumours and 41 intramedullary tumours. Eleven were malignant and 155 were benign tumours. Schwannoma, meningioma and ependymoma were more common in adults, whereas haemangioblastoma, neurofibroma and epidermoid cysts were seen in 14 paediatric cases. Motor function disturbances were found in 38% of cases. Sensory disturbances were found in 54% of cases, and worsening of sensory functions was the most frequent postoperative sequela. Ataxia and neurogenic bowel/bladder dysfunction seem to constitute the highest risk in cases of intramedullary tumours. Pain was found in 75% of cases and was the most common symptom among all patients with PITS with a 58% improvement after surgery. Complications were recorded in 12% of cases.

CONCLUSIONS: The incidence of PIST seems to be higher in Western Denmark than in other European studies. PIST are rare in children.

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Primary intraspinal tumours (PIST) include tumours in the spinal canal from the level of the foramen magnum to the coccyx. These tumours represent 2-10% of all central nervous system tumours [1-6]. Tumours can derive from the spinal cord, dura, spinal nerve roots or the filum terminale. The described incidence varies between 0.3 and 1.6 per 100,000 persons per year and seems to increase over time [3, 5-10]. The incidence of different tumour subtypes depends on demographic distribution [6]. Tumours are usually divided into three groups according to their relation to the spinal cord and dura: extradural, intradural extramedullary and intramedullary.

All patients with intraspinal tumours in the Central Denmark Region (Western Denmark) are treated at the Department of Neurosurgery at Aarhus University Hospital. We present a retrospective cohort study presenting Danish data on patient characteristics, incidence, clinical outcome and mortality in patients with PIST.

METHODS

All patients who underwent surgery for PIST at the Department of Neurosurgery in Aarhus University Hospital from 1 January 2010 to 31 December 2015 were identified from hospital files using the following International Classification of Diseases (ICD) codes for surgical procedures: KABB00 (excision of lesion of spinal cord or spinal meninges), KABB10 (resection or biopsy of lesion of spinal cord or spinal meninges), KABB99 (other intervention in spinal cord or spinal meninges). As PISTs, we defined intraspinal tumours deriving from the spinal cord, dura, spinal nerve roots or filum terminale. We excluded patients with secondary tumours and patients with inconclusive histopathological findings. Cases with mesenchymal tumours (sarcomas), metastatic tumours and primary bone tumours were treated in the orthopaedic department and were excluded. Patient data were collected by file review and consulted with an epidemiologist to rule out data collection pitfalls. The following data were noted: sex, age, tumour type, level of pathology and neurological clinical status before and after surgery. Information about tumour placement (in relation to dura) was extracted from the surgical description. Data concerning surgical procedure included postoperative complications and resection rate (based on postoperative magnetic resonance imaging (MRI)). Mortality data were collected from hospital files. Outcomes according to clinical symptoms and findings after operation were based on the file's reported outcomes before and after surgery. An acute complication was defined as a complication that occurred within the first month after surgery.

Trial registration: not relevant.

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RESULTS

A total of 279 patients were identified from ICD codes. In total, 166 patients were verified to have a PIST. Seventy-eight were men and 88 women. The patients underwent a total of 171 surgical procedures.

The Central Denmark Region has a population of 1.27 million. The incidence (2010-2015) of PIST is therefore 2.1 per 100,000 persons per year. The incidence of malignant PIST is 0.1 per 100,000 persons per year, and the incidence of non-malignant PIST is 1.9 per 100,000 persons per year. Overall, nine patients were referred from other geographical regions.

We found 25 extradural (15%), 100 intradural extramedullary (60%) and 41 intramedullary tumours (25%). Eleven were malignant and 155 were benign tumours. PIST occurred most often at the lumbar level. Schwannomas, meningiomas and ependymomas were most common in adults, whereas we recorded hemangioblastoma, neurofibroma and epidermoid cysts in 14 paediatric cases (≤ 18 years old; nine boys and five girls). Two cases of malignant tumours were registered in children. Detailed epidemiological and histopathological data are given in **Table 1**.

At baseline, motor deficits were found in 38% of all patients. Motor deficits were more frequent in patients with extramedullary tumours (41%) than in patients with intramedullary tumours (29%). Postoperative improvement was most successful in cases with extradural tumours (55%) and poorest in cases with intramedullary tumours (17%).

Sensory deficits were found in 54% of all patients, and worsening of sensory functions was the most frequent postoperative sequela among all tumour groups.

Neurogenic bowel/bladder dysfunction was found in 20% of all cases. The highest frequency of worsening of these functions was observed in cases with intramedullary tumours.

Ataxia was found in 34% of patients with PIST. Improvement was observed in 29% of the surgical cases, where the most notable improvement was registered in cases of extramedullary tumours, and the highest risk for worsening or developing ataxia was recorded in cases of intramedullary tumours.

Pain was found in 75% of cases and was the most common symptom among all patients with PIST. Local back pain was the dominant symptom, especially in patients with meningioma and malignant extradural tumours. Patients with schwannoma, neurofibroma, intramedullary ependymoma or subependymoma complained more frequently about radiculopathy or mixed pain (back pain with radiculopathy) rather than back

TABLE 1

Clinical features and subtypes of primary intraspinal tumours[a].

	n	Age, average (range), yrs	Gender, male, n	Level of pathology[b]
Extradural tumours				
Schwannoma	12	57 (35-84)	7	L
Malignant peripheral nerve sheath tumour	4[c]	42 (8-68)	3	Th
Neurofibroma	2	46 (36-57)	-	L
Paraganglioma	1[c]	34	1	Th
Ganglioneurinoma	2	35 (19-51)	1	Th, S
Neuroblastoma	1	1	1	Th
Haemangiopericytoma	1	42	0	L
Haemangioma	1	28	0	Th
Lymphangioma	1	60	0	L
Subtotal	25		13	
Intradural extramedullary tumours				
Schwannoma[d]	49	59 (13-89)	28	L
Meningioma	38	61 (34-78)	9	Th
Neurofibroma	6	38 (8-71)	4	L
Paraganglioma	2	59 (38-80)	-	L
Lipoma/fibrolipoma	2	50 (35-65)	2	L
Epidermoid cyst	2	8 (3-12)	1	L
Teratoma	1	69	1	Th
Subtotal	100		45	
Intramedullary tumours				
Ependymoma	26[c]	47 (15-75)	12	L
Haemangioblastoma	4[c]	39 (13-65)	3	C
Cavernous/capillary haemangioma	3	42 (20-58)	0	L, C
Subependymoma	2	53 (52-53)	1	C, Th
Astrocytoma/glioblastoma: WHO 3/WHO 4	2[c]	38 (30-58)	2	C, L
Pilocytic astrocytoma: WHO 1	1	4	1	Th
Ganglioglioma	1	71	1	Th
Oligodendroglioma	1	58	0	L
Lipoma	1	1	0	C
Subtotal	41		20	
Total	166		78	

a) Excluded secondary intraspinal tumours, metastasis, myelomatosis and lymphomas.
b) Defined as the most proximal level.
c) Reoperation on the same patient; patient underwent 2 or 3 operations because of pathology progression.
d) 9 cases had intradural and extradural components.

TABLE 2

Clinical symptoms before and after surgery. The values are n.

	Intradural extramedullary, (N_1 = 100)			
		after surgery		
	baseline	improved	unchanged	worsened[a]
Motor deficit	40	16	59	25
Sensory deficit	56	12	67	21
Neurogenic bladder or bowel dysfunction	20	11	80	9
Ataxia	37	12	79	9
Pain	71	43	44	13

a) Includes patients with and without preoperative deficits.

pain only. Overall, 58% of the patients with pain improved postoperatively (**Table 2**). We found no significant difference in surgical outcomes between extradural, intradural extramedullary or intramedullary tumours.

Total resection was achieved in 128 surgical cases. Tumour growth after surgery was seen in 63% of the cases with malignant PIST and in 6% of the cases with benign PIST. The highest tumour growth rate was noticed in cases with intradural extramedullary tumours such as ependymoma (six cases) and malignant astrocytoma (two cases). Among 155 cases with benign tumours, postoperative MRI revealed a residual tumour in 31 cases. In the group with residual tumours, tumour growth occurred in 23% of cases, while tumour growth occurred in only 4% of cases in the group with total resection. There was a statistical difference between these two groups for the tumour growth rate ($p < 0.001$; Wilcoxon-Mann-Whitney test). In 11 malignant cases, nine patients had a residual tumour, where tumour growth was observed in 67% of cases, while only one case of tumour growth was found in the group with total resection. A statistical difference was observed in the tumour growth rate between the malignant and benign tumours ($p < 0,001$; Wilcoxon-Mann-Whitney test). We observed malignant transformations in two cases: malignant peripheral sheath tumour (MPST) to sarcoma, and astrocytoma to glioblastoma, respectively.

In total, 11 patients died; six due to PIST malignant tumour progression. Among these, six patients were found to have paragangliomas (two cases), MPST (one case), neuroblastoma (one case), glioblastoma (one case) and anaplastic oligodendroglioma (one case). In two cases (astrocytoma), patients developed clinical symptoms compatible with intracranial tumour extension. The remaining five deaths were non-tumour related (45%), where comorbidity or other malignancy (not related to PIST) was the cause of death. The follow-up ranged from three months to years and further controls are currently ongoing.

Complications were registered in 12% of all cases (**Table 3**), where cerebrospinal fluid leak (5%) and haemorrhage (3%) were the most common; 85% of complications were acute. Revision surgery was required in 30% of all cases with complications. We found no cases of 30-day mortality.

DISCUSSION

This was a population-based cohort study and it reflects the incidence rate of PIST in the Western Denmark population.

The incidence of PIST was 2.1 per 100,000 persons per year in our study. The analysed data included only the surgically managed cases in our institution. The true PIST incidence is probably even higher if we take into account conservatively managed patients. Indications for surgery may vary between institutions. The indication for surgery in our cohort was a symptomatic clinical manifestation or clinical/radiological tumour progression. The incidence may be compared with incidences reported in other studies, where incidences were based on a histologically verified cancer register [6], a state cancer register [5], neurosurgical activity including diagnostic and therapeutic management [10], a histologically/radiologically or clinically verified diagnosis [8], or a diagnosis from multiple sources [9]. Despite these different approaches, the incidence in our study still seems to be higher than those reported from other European studies [5, 6, 8 10], where the annual incidence ranges from 0.74 to 1.6 per 100,000 persons per year. A Norwegian population-based study found an incidence of 1.48 per 100,000 persons [6]. Only one study from Minnesota from 1958 reported a higher annual incidence (2.5 per 100,000) of PIST than our study (histologically verified, surgically treated PIST) [11].

Intramedullary (N_2 = 41)				Extradural (N_3 = 25)				Total (N_{tot} = 166)			
	after surgery				after surgery				after surgery		
baseline	improved	unchanged	worsened[a]	baseline	improved	unchanged	worsened[a]	baseline among all cases	improved	unchanged	worsened[a]
12	2	29	10	11	6	14	5	63	24	102	40
20	2	24	15	14	3	13	9	90	17	104	45
10	2	30	9	3	1	22	2	33	14	132	20
14	1	26	14	5	3	20	2	56	16	125	25
31	17	20	4	23	13	9	3	125	73	73	20

TABLE 3

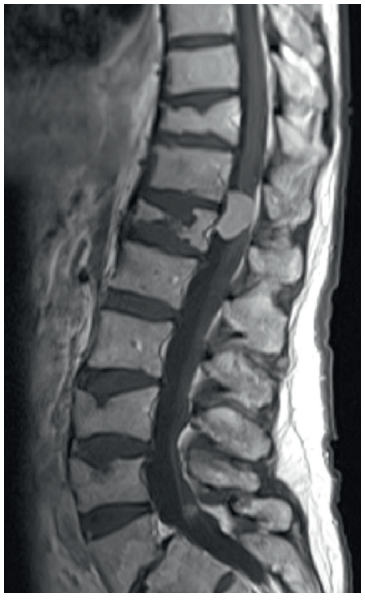
Post-operative complications in 2010- 2015.

Complication	2010	2011	2012	2013	2014	2015	Total
Liquorrhoea, n	1	1[a]	2	4[a]	1	0	9
Infection, n	2	0	0	1[a]	0	1	4
Haemorrhage, n	2	2[a]	0	0	1[a]	0	5
Olisthesis, n	2	0	0	0	0	0	2
Total, n (%)	7 (31)	3 (8)	2 (7)	5 (16)	2 (9)	1 (4)	20 (12)
No operations (no patients), n	22	40	28	31	22	28	171 (166)

a) Cases which required revision surgery.

The results were collected retrospectively from file review, which can carry a risk of desirability, expectation and interpretation bias. Therefore, the results must be interpreted with caution. 15% of PIST were extradural and 85% intradural. Hereof, two thirds were intradural extramedullary tumours and one third were intramedullary tumours. This is in line with the literature, where intradural extramedullary tumours are described in 70-80% and extradural in 20-30% of cases [12]. Schwannoma and meningioma (**Figure 1**) are the most common among the intradural extramedullary tumours, whereas ependymoma and astrocytoma are the most common among intramedullary tumours. Similar findings were previously reported in the literature [4-7, 12, 13]. We found only three cases with intramedullary astrocytoma, which is less common than reported in the literature [12]. Malignant tumours of WHO grade III or IV are rare [6, 12]. In total, in our study, 7% of all PIST were malignant. The incidence of malignant PIST was found to be similar to that reported in other published studies [6, 14].

FIGURE 1



Intraspinal meningioma in adult female.

Reviewed articles on PIST have reported pain, sensory disturbances and motor deficits as leading symptoms in patients with PIST [1, 2, 4, 7, 12]. We also found these symptoms to be common. However, in our study, pain and sensory deficits were more common than motor deficits among both intradural and extradural PIST cases. The prognosis of patients with PIST depends on the pre-operative neurological condition, the type of tumour and the resection rate [7, 12].

Our results are in accordance with these earlier findings [12, 15]. According to our results, patients with intramedullary tumours have the highest risk for ataxia and neurogenic bowel/bladder dysfunction, which may be expected from the tumour localisation. We chose to report the number of complications solely due to the low complication rate, as well as the short time span covered by this retrospective study.

CONCLUSIONS

Despite limitations due to the retrospective nature of the study, we report the patients' PIST characteristics in the Western Denmark population. We found the incidence of PIST to be higher in Western Denmark than the incidences reported for other European studies. Our results showed that most PIST are benign. Pain and sensory disturbances are the most common symptoms. Pain typically seems to improve after surgery.

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