

Original Article

Delay in diagnosis of primary intradural spinal cord tumors

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Abstract

Background: It has been our impression in recent years that there is a significant delay in diagnosis (DID) of patients in Israel harboring intradural spinal cord tumors (IDSCTs). DID can lead to irreversible deficits and unnecessary suffering. Our goal was to identify the incidence and the specific reasons for DID of IDSCTs in patients operated upon at our institution.

Methods: A retrospective record review, with additional telephone survey, of 101 patients operated upon at our institute between the years 1996 and 2009 was conducted. The patients who were not diagnosed locally and those who were diagnosed during routine spinal imaging studies as part of their basic disease check-up were excluded. Accordingly, neurofibromatosis and medical tourist patients were excluded.

Results: The clinical presentation of IDSCTs in our study was similar to the descriptions given in previous reports. The average age was 41.9 ± 23.3 years. Most tumors were ependymomas, astrocytomas, and schwannomas. The most common symptoms were motor or sensory disturbance, back pain, walking disturbance, and sphincter control deficit. The median time to diagnosis was 12.0 ± 37.0 months (range 3 days to 20 years). We found DID in 82.2% of the cases. 62.4% of the cases were defined as “*unreasonable delay*.” The most common reasons for DID were “*classical symptoms with a wrong diagnosis*” and “*delayed imaging*.”

Conclusions: Based on the results of this study, the incidence of unreasonable delays in diagnosis of primary IDSCTs in Israel is very high. In order to shorten the time to diagnosis, primary and secondary care physicians need to increase their awareness of symptoms that may be associated with these lesions. We hereby offer feedback for care providers, relevant to the diagnostic workup of these patients. Such a feedback must be delivered by neurosurgeons to the community they are serving.

Key Words: Delay in diagnosis, dura, intramedullary, paraplegia, primary spinal cord tumors, spinal cord compression

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INTRODUCTION

Primary spinal cord tumors are quite rare and can lead to significant disability, and even mortality.^[8] Previously reported average *time to diagnosis* of spinal cord tumors is between 8.1 and 17 months.^[8,10,12] Over years of experience, we noted with concern and some frustration that many patients with primary intradural spinal cord tumors (IDSCTs) were referred to our system with accumulated irreversible neurological function loss that appeared and worsened during the diagnostic process of their disease. Our primary impression was that there is a significant, and sometimes unreasonable, *delay in diagnosis* (DID) of IDSCTs in Israel.

Early diagnosis of IDSCTs has been shown to be important,^[9,13,16,21,22] in the sense that recognition of these tumors at the onset of the disease can trigger appropriate treatment which can prevent acute neurological conditions caused by spinal cord compression. It can also improve long-term prognosis by allowing management of smaller tumors. Furthermore, proper treatment following early diagnosis might minimize these patients' physical and mental suffering, as well as mitigate rehabilitation expenses.

The reported incidence of IDSCTs is about 0.3 per 100,000 per year, with a majority of extramedullary lesions.^[11,23] Primary spinal cord tumors account for 4–10% of all CNS tumors. The most common primary extramedullary spinal cord tumors are meningiomas and nerve sheath tumors. Astrocytomas and ependymomas account for most intramedullary spinal cord tumors. The classical clinical presentation is progressive neurological disturbance and/or back pain.^[8,10,11,24] While most IDSCTs are potentially resectable, the functional outcome depends primarily on the preoperative neurological status.^[3,5,6,20]

We aimed to characterize the diagnostic process of primary IDSCTs in Israel and find the incidence of DID. We aimed to describe the clinical presentation, and the response of both the patients and the medical system to signs and symptoms that are caused by IDSCTs. Ultimately, we desired to offer feedback for primary and secondary care providers relevant to the diagnostic workup of these patients.

MATERIALS AND METHODS

A retrospective record review of 101 patients with primary IDSCTs was conducted. A questionnaire was filled for each patient with the File Maker Pro 7 database. In specific cases in which a DID was suspected, the patients and their families were contacted. By a telephone survey, we tried to further identify the reasons that led to the delay, while tracking the course of the disease from the

onset of symptoms until diagnosis. The local institutional review board committee authorized the study.

All patients were operated at the neurosurgical department in a medical center in Israel between the years 1996 and 2009. The patients who were not diagnosed in Israel and patients who were diagnosed as part of their basic disease check-up were excluded. Accordingly, more than 50 patients on medical tourism and neurofibromatosis affected patients were excluded. We obtained data concerning demographic variables, medical history, clinical presentation, symptoms and signs that appeared during the diagnostic process, patient's behavior, medical referral patterns and histological and radiological findings. The diagnostic time was defined as the period of time from the onset of signs and symptoms as noticed by the patient to the performance of imaging which revealed the underlying tumor. Patients were further stratified into three categories of DID according to both objective and subjective variables [Table 1]. Ultimately, DID was defined either at the occurrence of considerably short DID due to understandable reasons (reasonable delay) or when a progression of symptoms and/ or signs without a proper response by the system was documented.

We graded both the preoperative and postoperative neurological functioning status according to the modified McCormick Scale^[4,17] [Table 2]. In this manner, we estimated both the neurological status upon diagnosis and the operative outcome.

Statistical analysis

The association between demographic and clinical

Table 1: Criteria for stratifying delays in diagnosis

Type of delay	
No delay	As symptoms and/or signs were noted, patients sought medical aid, proper referral to specialists was done, and appropriate imaging studies were conducted
Reasonable delay	Understandable reasons led to a considerably short delay in diagnosis
Unacceptable delay	A progression of symptoms and/or signs without a proper response by the system

Table 2: Modified McCormick Scale

Grade	Modified McCormick Score
1	Intact neurologically, normal ambulation, minimal dysesthesia
2	Mild motor or sensory deficit, functional independence
3	Moderate deficit, limitation of function, independent w/ external aid
4	Severe motor or sensory deficit, limited function, dependent
5	Paraplegia or quadriplegia, even w/flickering movement

parameters and DID was examined using the Chi-square test for binary and categorical variables. Continuous variables were examined for shape of distribution, and several transformations were applied in case the variables were not normally distributed. Analysis of variance was then carried out to compare between the three categories of DID. Variables measured on ordered scale were similarly analyzed using the Kruskal–Wallis non-parametric analysis of variance.

A multivariate logistic regression model was applied to the data in order to explore the independent association of background and clinical variables [age, gender, Health Maintenance Organization (HMO), rural/urban life, background illness, involvement of primary care physician (PCP)/orthopedic surgeon (OS)/neurologist in the diagnostic process, passivity of patients, and types and pathologies of the tumors] with DID. Three model building techniques were employed: forced entry of all parameters into the model, forward selection, and backward elimination. All statistical analyses were performed using the SAS for Windows version 9.1.3.

RESULTS

- Research population:** Intradural tumors appeared in both genders and in a variety of ages. 55.9% ($n = 56$) of the patients were males. The average age was 41 ± 23 years, in the range of 3 months to 91 years. 26% ($n = 27$) of the patients were 21 years old or younger. Most patients lived in urban areas (89.2%, $n = 90$). The patients were medically insured by the common HMOs in Israel. 53.9% ($n = 54$) of the patients suffered from medical problems that are frequent in the general population, such as chronic cardiovascular and respiratory diseases.
- Tumors:** We collected both intramedullary and extramedullary tumors that were evenly spread along the spinal cord [25.8% ($n = 26$) cervical, 42.6% ($n = 43$) thoracic, 31.6% ($n = 32$) sacral/lumbar]. The most common histological findings were ependymomas, followed by schwannomas, meningiomas, and astrocytomas. Tumors were measured by the number of spinal levels they spanned. 55% of the tumors comprised 1–2 spinal levels. The anatomical and histological characteristics are presented in Table 3.
- Presenting symptoms:** The most common presenting symptoms were neurological disturbances (43.5%, $n = 44$), back pain (37.6%, $n = 38$), and a combination of both (18.8%, $n = 19$). 2% (3 patients) suffered from other symptoms as well. Among the neurological disturbances, we were surprised by a high incidence of motor and sensory disturbances and a significant occurrence of radiculopathy (29% of all patients, $n = 30$), walking disturbances, and sphincter control deficits.
- Symptoms on diagnosis:** Most patients (80.1%, $n = 81$) suffered neurological disturbances, worsening pain, or addition of new symptoms along the diagnostic process. Upon diagnosis, 60% ($n = 60$) suffered from back pain, 61.8% ($n = 61$) from motor disturbances, 52% ($n = 52$) from walking disturbances, 42.2% ($n = 42$) from sensory disturbances, and 38.2% ($n = 38$) suffered from sphincter control deficit. The findings are presented in Table 4.
- Physical examination:** Physical examination on diagnosis revealed motor deficits in 69.7% ($n = 70$) of the patients, pathological reflexes in 65.3% ($n = 66$) of the patients, and sensory deficits in 55.4% ($n = 56$) of the patients. Scoliosis was documented in 20% ($n = 20$) of the medical records.
- The medical system:**
 - Primary physician:** Most patients referred to their PCP when the symptoms appeared (70.4%, $n = 69$). The other patients referred to OS (15.3%, $n = 15$), hospitals (7.2%, $n = 7$), neurologists (2%, $n = 2$), or other specialists (5.1%, $n = 5$) before presenting to their PCP.
 - Diagnosing physician:** Most patients were referred to diagnostic imaging by a neurologist (31%, $n = 31$), an OS (25%, $n = 25$), hospital (24%, $n = 24$), or by other specialists (15%, $n = 15$). Only 5% ($n = 5$) were referred to the diagnostic imaging by their PCP.
- Time to diagnosis:** The median time to diagnosis was 12.0 ± 37.0 months (range 3 days to 20 years). 25.3% ($n = 24$) of the patients were diagnosed more than 2 years after their primary symptom appeared.
- DID:**
 - Incidence:** 17.8% ($n = 18$) of the patients were

Table 3: Anatomical and histological characteristics of PIDSCTs in Israel

Type	Ependymoma % (n)	Schwannoma % (n)	Meningioma % (n)	Astrocytoma % (n)	Other % (n)	Total % (n)
Extramedullary	10.9	32.6	43.5	4.3	8.7	44.1
Intramedullary	36.8	2.6	0	50	10.5	38.2
Cauda equina/ conus medullaris	58.8	29.4	0	0	11.8	17.6
Total	28.7 (29)	20.8 (21)	19.8 (20)	20.8 (21)	9.9 (10)	100 (101)

Table 4: Symptoms of patients with PIDSCTs in Israel

Symptom	% on diagnosis
Motor disturbance	61.8
Sensory disturbance	42.2
Day or night back pain	60
Night back pain	37.9
Radiculopathy	31
Walking disturbances	52
Sphincter control deficit	38.2

diagnosed without a delay, 19.8% ($n = 20$) with a reasonable delay, and 62.4% ($n = 63$) of the patients answered our definition of unacceptable delay in diagnosis.

- b. *Reasons:* There were three main reasons for DID. 77.2% ($n = 78$) were wrongly diagnosed despite classical symptoms, 76.2% ($n = 77$) experienced delays in proper imaging studies despite a clinical impression of cord compression, and 33.3% ($n = 33$) of the patients exhibited passive behavior. In most cases, a combination of few of the reasons mentioned led to DID.
9. *Univariate analysis:* We aimed to identify the risk factors for DID. The patients were stratified according to specific characteristics and were further divided according to the incidence of DID. The P values of this Chi-square analysis are presented in Table 5.
 - a. We found no correlation between demographic variables and occurrence of DID.
 - b. We found no correlation between anatomical and histological characteristics of the tumors and occurrence of DID.
 - c. We found a difference in the incidence of DID when patients were stratified according to their HMO. It seemed that patients who were medically insured by CLALIT Health Services experienced more delays compared to patients who were medically insured by MACCABI Health Services. This finding was not statistically significant, yet important to mention as a part of our feedback to the medical system in Israel. The two other HMO groups were too small to represent a population that is divided into three categories.
 - d. A correlation between the incidence of DID and the involvement of OS in the diagnostic process was found. This correlation will be discussed in the multivariate analysis section.
10. *Multivariate analysis:*
11. A correlation was found between the involvement of OS in the diagnostic process and a high incidence of unacceptable DID (RR 5.37, CL 95% 1.77–16.25, $P = 0.0029$). We further reviewed this group of patients. It was found that in several cases, the DID appeared prior to the involvement of OS in the diagnostic process. In these cases, it was the OS who eventually

Table 5: P values, univariate analysis

Variable	P value
Year of diagnosis	0.31
Gender	0.67
Health Maintenance Organization	0.23
Religion	0.21
Rural/urban	0.67
Background illness	0.79
Tumor height	0.29
Tumor histology	0.67
Tumor type	0.52
Conus medullaris or cauda equina involved	0.13
Tumor's length	0.63
Neurologist involved in the diagnostic process	0.22
OS involved in the diagnostic process	<0.0001
Hospital involved in the diagnostic process	0.23
First physician	0.15

PCP: Primary care physician, OS: Orthopedic surgeon

referred the patients to the diagnostic imaging. Accordingly, this finding might be a statistical fault.

12. *Operative outcome:*

13. We graded both the preoperative and postoperative neurological function status according to the modified McCormick Scoring Scale [Table 2]. Every second patient suffered limitation of function upon arrival to surgery (McCormick Score 3–5). It was found that most patients experienced stabilization in their neurological functioning status following the operation. Therefore, the better the patient's neurological status upon entering the OR, the better was their prognosis. The neurological function status scores are presented in Table 6.

DISCUSSION

Incidence of and reasons for delay in diagnosis of primary intradural spinal cord tumors

The incidence of DID of primary IDSCTs in Israel is shockingly high. About two-thirds of 101 patients who were included in this study experienced unacceptable DID. A combination of factors led to this alarming phenomenon. Patients and physicians acted in a passive manner, which reflected their unawareness to the meaning of obvious signs and symptoms related to cord compression. The other factors were: caretakers were not found to be cognizant of the importance of fast and efficient workup, too many patients underwent incomplete physical examinations, waste of precious time with multiple counseling, and postponement of referral to proper imaging studies. Consequently, many patients suffered significant neurological and symptomatic deterioration, and irreversible handicap due to longstanding and progressive cord compression.

Table 6: Pre- and postoperative neurological function status, graded according to the McCormick Scoring Scale

		Postoperative modified McCormick Score					Total
		1	2	3	4	5	
Preoperative	1	6	1	2	0	0	10
modified	2	2	28	7	4	1	42
McCormick	3	0	10	20	2	0	33
Score	4	0	1	4	6	4	14
	5	0	0	0	1	0	1
	Total	8	40	34	13	5	100

Delay in diagnosis: A complicated definition

There is an inherent difficulty defining DID, as a solitary timeline criterion is not sufficient. For example, a patient who suffered a significant neurological deterioration over a short period of time without proper medical response was defined as “unacceptable delay,” while a patient who suffered a longstanding isolated common back pain was not defined as such, even though retrospectively his pain originated from the primary IDSCCT. Ultimately, we used a combination of both objective and subjective variables and stratified the patients accordingly.

Primary intradural spinal cord tumor: A diagnostic challenge

Primary IDSCCTs are somewhat difficult to diagnose. There are several reasons for this difficulty, such as the rarity of the tumors, misleading common symptoms, and relatively expensive imaging techniques required with magnetic resonance imaging (MRI). The first factor leads to a low level of suspicion, unawareness to classical symptoms, and belittling the importance of early diagnosis, both by the physicians and patients. Physicians may not be considering spinal cord tumors while conducting a differential diagnosis. In many cases, primary IDSCCTs cause non-specific symptoms that are usually attributed to more common diseases. Back pain is commonly classified under an orthopedic umbrella, as benign musculoskeletal diseases cause most of these cases. The high incidence of this complaint leads to wear, and to an inappropriate management of “red flags.” Another example is a complaint of sphincter control deficit that is usually attributed to benign prostate hypertrophy in men, stress incontinence and detrusor dysfunction in women, and incomplete toilet training among children. We found that this symptom, despite its high incidence among primary IDSCCTs patients, was not followed by a complete neurological investigation. Additionally, the fact that motor and sensory disturbances were not always followed by proper anamnesis, physical examination, and imaging studies is unacceptable. Each of such cases must be followed by thorough neurological investigation.

Children should be dealt with extra caution, as the clinical presentation of pediatric primary IDSCCTs is diverse and differs from that of adults. A new limp and

apparent loss of already acquired motor skills should always raise the possibility of a spinal cord lesion. Back pain, a rare complaint in this population, should be addressed with a complete neurological investigation. Abdominal pain and unexplained hydrocephalus were also linked with spinal cord lesions^[24] and should raise the suspicion of the pediatrician.

MRI when spinal cord lesion is suspected

Most patients with primary IDSCCTs were not diagnosed by their PCPs. It seemed that PCPs avoided conducting MRI studies as they encountered patients with progressive back pain and neurological disturbances. Instead, patients were referred to multiple counseling and inappropriate imaging studies, while their symptoms and neurological deficits progressed. In only a few cases, a refusal of the medical system to conduct an MRI was documented. We assume that physicians tend to conduct more available imaging studies that are not suitable in these cases, since MRI devices are few and not readily accessible in Israel. Consequently, despite the increased availability of this efficient imaging technique around the world, in Israel, we could not detect a decrease in the incidence of DID between the years 1996 and 2009.

The medical authorities should consider the cost-effectiveness of increasing the availability of MRI, which can allow revealing primary IDSCCTs (and other structural diseases) earlier. A diagnosis of a spinal cord tumor at an advanced stage might result in longer hospitalization periods, more complex operations, and exhausting and pricey neurological rehabilitation.

Educational objectives

The reasons for DID indicate ignorance and insufficient awareness, both of physicians and patients, to classical symptoms of cord compression and lack of understanding to the required urgency of medical investigation. It is important that practitioners be aware of these symptoms and acknowledge the implications of delayed diagnosis of primary IDSCCTs. Symptoms such as night or progressive back pain, walking disturbances, sphincter control deficits, neurological disturbances, radiculopathy, and progressive scoliosis should raise the suspicion of a spinal cord lesion, and be followed by prompt medical investigation. A specialist must be involved without delay, along with an immediate referral to spinal cord MRI.^[14,15] Once an MRI study is requested, the execution and interpretation should not be postponed. The use of computed tomography and X-ray imaging is inappropriate when the suspicion of a compression by a spinal cord lesion is raised. It is the task of the neurosurgical and orthopedic communities to help in the process of better education and awareness.

Delay in diagnosis of primary intradural spinal cord tumors in a high standard medical system

The medical system in Israel has emerged as an

exceptional and developed combination between public and private healthcare.^[2] All Israeli citizens are medically insured, and PCPs as well as top rated specialists and well-equipped emergency centers are readily accessible.^[19] According to the World Health Organization (WHO), Israel has one of the highest physician-to-population ratios in the world, being approximately 20% higher than the Organisation for Economic Co-operation and Development average. Life expectancy was found to be significantly higher than the global average (78.3 years for men, 82.2 for women), while infant mortality was among the lowest in the world (5.1 per 1000 live births).^[19] Therefore, our findings do not reflect an inferior health system, but rather stand isolated.

Literature review

We present the widest scale project concerning the diagnostic process of primary IDSCTs. Few previous studies dealt with the problematic time to diagnosis of these lesions. Previous description of anatomical and histopathologic characteristics, clinical presentation, patients' and physicians' behavior, and the length of diagnostic processes were similar to our findings. In Japan,^[12] researches investigated the diagnostic process of 60 cases of IDSCTs. They found that 10 of 20 patients with thoracic lesions were referred to an MRI of an incorrect level and were wrongly diagnosed as having spinal degenerative disorders. Patients with cervical lesions tended to wait a long time before attending a physician. Dutch investigators^[10] collected a series of 108 patients with both intradural and extradural tumors. They found that 35% of patients were diagnosed more than 2 years after the onset of symptoms. It was concluded that a high level of suspicion and acknowledging the classical symptoms of cord compression are the most important factors in shortening the time to diagnosis of IDSCTs. A neurosurgical department from Germany^[1] reported a series of 10 patients who were unsuccessfully treated for degenerative spine disease and were referred to their department for surgical treatment. Eight of these patients were preoperatively diagnosed with spinal cord tumors, while two were diagnosed intraoperatively. All patients had coexisting radiological signs of a degenerative spine disease. The writers underlie the fact that since degenerative spine diseases are very common in the general population, there is a high probability that the existence of clinical and radiological signs of these pathologies would delay the conductance of MRI and prevent the diagnosis of spinal cord tumors. They found an incidence of 0.5% patients in which spinal cord tumors were responsible for symptoms thought to be of degenerative origin. MRI was the most helpful tool in diagnosing these lesions. In few previous studies, along with the present one, no improvement in the time to diagnosis of primary IDSCTs was found along the last few decades.^[5,7,18] Overall, there is a worldwide consensus that

the diagnosis of spinal cord tumors is prone to be delayed. It seems that the alarming findings of our study are not limited to Israel, but rather represent an international trend that needs to be promptly addressed with improved awareness, knowledge of alarming symptoms, and an easier availability of MRI.

CONCLUSIONS

The characteristics and the diagnostic process of primary IDSCTs were described according to the experience of the Department of Neurosurgery in our institute. A very high incidence of DIDs of primary IDSCTs was detected. It is important to increase awareness of these rare lesions and educate about the significance of early diagnosis.

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