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RESEARCH ARTICLE

Spinal Cord Compression as Clinical Presentation of Malignant Hematopoietic Diseases in Pediatric Patients

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ABSTRACT:
Spinal cord compression (SCC) is an unusual manifestation of leukemias and lymphomas in children and defines an oncological emergency frequently unsuspected, being a cause of severe sequelae. Our aim was to analyze the characteristics of patients who presented signs or symptoms of spinal cord compression in early phases of malignant hematopoietic diseases. From November-1988 to July-2022, 3878 patients with leukemia and lymphoma were diagnosed. Of them, 36 children (0.92%) presented spinal cord compression signs/symptoms in early phases of their diagnosis: Acute Lymphoblastic Leukemia (n=18), Acute Myeloblastic Leukemia and Myeloid Sarcoma (n=7), Non-Hodgkin Lymphomas (n=9) and Hodgkin Lymphoma (n=2). Clinical characteristics, images and hematological findings, treatment strategies, results and sequelae were analyzed. Sex distribution was 3.5/1 (M/F) and the media age at diagnosis was 10 (range: 4.9-16.9) years. The most common symptoms were back pain (34/36), functional impotence (27/36) and sphincter compromise (10/36). The media time from symptom onset to diagnosis was 47,5 (range: 0-300) days. Magnetic resonance imaging was performed on 33 (92%) patients and showed epidural mass (n=16) or vertebral collapse (n=17) in all of them. Two patients received initial radiotherapy and 11 decompressive surgeries for the management of the urgency spinal cord compression. Bone marrow aspiration was the diagnostic procedure in 69% of cases. All patients received chemotherapy and 94% achieved complete remission. Severe sequelae were observed in 10 patients (paraplegia with neurogenic bladder and kyphoscoliosis). Leukemia and lymphoma should be considered as a differential diagnosis when spinal cord compression is suspected, and magnetic resonance imaging is the mandatory study to confirm this diagnosis as a matter of urgency. Bone marrow involvement was evident due to hematological alterations in 95% of cases allowing to guide the diagnosis and initiate treatment early to reduce sequelae.

Introduction:

Spinal cord compression (SCC) is an unusual but serious complication in patients with leukemia and lymphoma, that implies a challenge for pediatricians and pediatric hematologist and oncologists. It constitutes a real clinical and oncological emergency that can be diagnosed at the beginning or during the evolution of a malignant disease, so the diagnosis and appropriate treatment should be made urgently. Despite their impact on patient morbidity and mortality, very limited data are available on incidence and doable etiologies of malignant spinal cord compression in the pediatric population. According to records reported in previous studies, its incidence in the pediatric population is around 3 to 6% and occurs more frequently secondary to extramedullary tumors in particular neuroblastoma and Ewing's sarcoma or tumors of the central nervous system[1-5]. Others differential diagnosis that could be considered in patients with symptoms to spinal cord compression are rhabdomyosarcoma, Langerhans cell histiocytosis, and more uncommonly vertebral osteosarcoma[3]. Although spinal cord compression is infrequent as an early manifestation of acute leukemias and lymphomas in pediatrics, they should be considered in the differential diagnosis, especially when the patient has systemic or hematological manifestations. Early diagnosis and proactive treatment are crucial to improve patient prognosis and survival and to reduce the morbidity and the neurological sequelae that could become irreversible[1,3,5-8].

Spinal cord compression can be classified into three groups, based on tumor location: extradural, intradural/extramedullary, and intradural/intramedullary[1,5]. It can be caused by different mechanisms that including direct spread of tumor, extension of tumor through vertebral foramina into epidural space and bone disease within vertebrae with secondary cord compression. The diagnosis in children can be particularly difficult at an early phase, especially in infants, thus increasing morbidity[5].

Back pain is the earliest and most frequent symptom, occurring in 70-96% of children with cord compression; it used to be initially localized and typically its intensity increases in the evolution of several weeks. The signs and symptoms appear as the process progresses, passing through motor weakness, altered sensitivity to paralysis and sphincter incontinence, because of complete neurological damage[7,9-12]. When recognized early, the symptoms of spinal cord compression can be prevented, minimized, or possibly reversed. However, failure to recognize the condition and its serious nature, together with limited awareness of the importance of early referral for treatment, can result in irreversible paralysis[6].

In children with back pain, formal neurologic examination is mandatory. The accurate history and physical examination should lead to suspect the level where spinal cord compression may be developing. The imaging method of choice in the assessment of SCC is magnetic resonance imaging (MRI) because it is non-invasive, has a sensitivity of 93% and a specificity of 97%. Because of the frequency of several levels of compression, imaging of the entire spine is recommended and essential to plan treatment[5,7,13].

The aim of this study was to analyze characteristics of patients who presented symptoms of SCC in early phases of leukemias and lymphomas, review clinical features, evaluate treatment response and sequelae.

Methods:

This is an analytical, retrospective study of patient younger than 18 years of age diagnosed with leukemia or lymphoma who presented signs or symptoms suggestive of spinal cord compression at the time of diagnosis or during the course of the disease. The study was performed at a tertiary care pediatric center in Argentina. We reviewed the database of patient with hemopoietic disease (n=3878) admitted in the Hematology and Oncology department from November 1988 to July 2022 and identified that 36 patients (0.92%) presented symptoms or signs of SCC in the early phases of diagnosis.

A new record was made in which we include these 36 patients, and we analyzed age, gender, characteristics of underlying disease, symptoms at diagnosis, hematological compromise and spinal integrity. The frequency of onset of pain, functional impotence and sphincter involvement were recorded, alongside other signs or symptoms including fever, asthenia, loss weight, visceromegaly, lymphadenopathies and involvement of other organs. Furthermore, we register the administered treatment, the response to therapy and long-term sequelae. Full neurological history with details of the occurrence of motor and sensory deficits and sphincteric deficits were recorded. The patients were classified by underlying pathology: acute lymphoblastic leukemia (ALL); acute myeloblastic leukemia (AML); myeloid sarcoma (MS); non-Hodgkin lymphoma (NHL) including Burkitt lymphoma, diffuse B-cell lymphoma, and lymphoblastic lymphoma; and Hodgkin lymphoma (HL).

We analyzed the elapsed time from the beginning of the symptoms to diagnosis of the

hematological malignancy and its correlation with images and hematological findings.

Emergency computed tomography and/or magnetic resonance imaging of the spinal cord was performed as part of initial workup to confirm SCC and to assess the level of spinal cord involvement and its anatomic site. The findings obtained by imaging were recorded specifying the existence of spinal canal invasion and spinal cord compression. All patients analyzed showed pathological findings: epidural mass with and without medullary canal invasion and/or spinal cord compression, or vertebral collapse fracture.

The presence of bone marrow disease was determined by bilateral bone marrow aspirate and biopsy. If bone marrow was not compromised or if the patient required emergency surgery, the diagnosis was defined by decompressive surgery with the biopsy or resection of the tumor.

The number of patients who underwent a neurosurgical procedure (biopsy, laminectomy, exeresis) and oncology treatment received, either chemotherapy or radiotherapy, were also analyzed. Additionally, we evaluated response to therapy, adverse event and long-term sequelae. Patients were followed until death or for a minimum 6 months after diagnosis, the mean follow-up was 49 (range: 1-305) months.

Quantitative data are expressed as means or median for continuous, nonparametric variables and frequency for categorical variables. More advanced statistical analysis was not carried out, because the numbers in each diagnostic and etiological group were so low.

Results:

From November-1988 to July-2022 a total of 3878 patients, younger than 18 years were diagnosed with leukemias and lymphomas in the Hematology and Oncology department. Of them, 2221 were Acute Lymphoblastic Leukemias, 781 Acute Myeloblastic Leukemias, 585 Non-Hodgkin´s Lymphomas and 921 Hodgkin´s Lymphomas. We identified 36 patients (0,92%) who presented symptoms or signs of spinal cord compression. The diagnoses of these patients were ALL=18; AML=7; NHL=9 and HL=2. Clinical characteristics, subtypes diagnosis and symptoms/signs of the patients are analyzed and described in Table I. Of the 36 patients, the distribution by sex was 28 boys and 8 girls (3.5/1) and the media age at diagnosis was 10 (4.9-16.9) years.

Table I. Patients characteristics

Case	Age (years)	Gender	Diagnosis	Evolution time (days)	Funtional impo-tence	Back pain	Sphincter compromise
1	16.9	M	B-ALL	15	Yes	Yes	No
2	10.3	F	B-ALL	-	-	Yes	-
3	8.7	M	B-ALL	30	No	Yes	No
4	10.8	M	B-ALL	30	Yes	Yes	No
5	12.2	F	B-ALL	60	Yes	Yes	No
6	7.1	M	B-ALL	-	Yes	Yes	No
7	12.7	M	B-ALL	30	Yes	Yes	No
8	10.2	M	B-ALL	60	Yes	Yes	No
9	10.1	M	B-ALL	10	Yes	Yes	No
10	7.7	M	B-ALL	30	Yes	Yes	No
11	6.11	M	B-ALL	1	No	Yes	No
12	11.7	M	B-ALL	15	No	Yes	No
13	9.3	M	B-ALL	15	Yes	Yes	Yes
14	7.3	M	B-ALL	120	Yes	Yes	No

15	9.1	F	B-ALL	30	Yes	Yes	No
16	9	F	B-ALL	30	No	Yes	No
17	14.11	M	B-ALL	45	Yes	Yes	No
18	5.4	M	B-ALL	45	Yes	Yes	No
19	4.9	M	AML	-	Yes	Yes	-
20	14.1	M	AML	20	No	Yes	No
21	6.1	M	AML	0	Yes	No	Yes
22	15.2	M	MS	-	No	Yes	No
23	4.11	M	AML	3	Yes	Yes	Yes
24	11.2	F	AML	15	Yes	Yes	Yes
25	10.6	M	AML	10	Yes	Yes	Yes
26	16.6	M	NHL (Burkitt)	60	Yes	Yes	Yes
27	4.11	M	NHL (Burkitt)	40	Yes	No	No
28	7.1	F	NHL (Burkitt)	5	Yes	Yes	No
29	6.8	M	NHL (Burkitt)	10	Yes	Yes	Yes
30	13.5	M	LNH (LBL)	120	Yes	Yes	No
31	12.2	M	NHL (Burkitt)	21	Yes	Yes	No
32	6.5	F	NHL (Burkitt)	90	Yes	Yes	Yes
33	11.6	F	NHL (DLCL)	300	Yes	Yes	Yes
34	6.11	M	LNH (LBL)	50	Yes	Yes	Yes
35	6.11	M	HL	120	No	Yes	No
36	15.6	M	HL	90	No	Yes	No

B-ALL, Acute Lymphoblastic Leukemia B; AML, Acute myeloblastic leukemia; NHL, No Hodgkin Lymphoma; LBL, Lymphoblastic lymphoma; DLCL Diffuse large B-Cell lymphoma; LH, Hodgkin Lymphoma.

The most frequent initial symptoms suggestive of SCC were back pain (34/36) and functional impotence (27/36), representing 94.4% and 75% respectively. Sphincter involvement occurred in 10 patients (28%), all of them with epidural mass.

Fifty-three percent of the patients presented other symptoms of systemic disease such as fever, weight loss and asthenia. Other clinical signs were cervical lymphadenopathy, exophthalmos, facial paralysis and subcutaneous nodules, liver and spleen enlargement. One patient (case 7) who was diagnosed with an ALL and vertebral collapse presented acute tumor lysis syndrome and hypercalcemia.

The time elapsed since the appearance of SCC symptoms and the diagnosis of leukemia or lymphoma had a wide range, with a mean time of 47,5 (range: 0-300) days. In 4 cases this data was not available.

Blood counts abnormalities were observed in 26 of 36 (72%) patients, all with a diagnosis of acute leukemia. Bone marrow aspiration was performed in patients that presented hematological alterations and in 95% of cases these findings allowed to define the diagnosis. Hematological involvement is described in Table II. Most of the

patients diagnosed with AML (5/7) and 3 with ALL disclosed involvement in 3 hematopoietic series. Anemia was detected in 94% of patients with ALL, 55% presented leukopenia or leukocytosis and 44% thrombocytopenia. Bone marrow was involved in one of nine patients diagnosed with NHL and in the two cases of HL.

Table II. Hematologycal findings and bone marrow involvement

Patient/ Diagnosis	Anemia	Leukocytosis/ Leukopenia	Thrombocyto-penia	Bone marrow compromise	Diagnosis by BM aspirate
1/ALL	Yes	Yes	No	Yes	Yes
2/ALL	Yes	No	No	Yes	Yes
3/ALL	Yes	Yes	No	Yes	Yes
4/ALL	No	Yes	Yes	Yes	Yes
5/ALL	Yes	No	No	Yes	Yes
6/ALL	Yes	Yes	Yes	Yes	Yes
7/ALL	Yes	No	Yes	Yes	Yes
8/ALL	Yes	No	Yes	Yes	No
9/ALL	Yes	Yes	No	Yes	Yes
10/ALL	Yes	Yes	Yes	Yes	Yes
11/ALL	Yes	No	Yes	Yes	Yes
12/ALL	Yes	Yes	No	Yes	Yes
13/ALL	Yes	Yes	No	Yes	Yes
14/ALL	Yes	No	No	Yes	Yes
15/ALL	Yes	Yes	No	Yes	Yes
16/ALL	Yes	No	No	Yes	Yes
17/ALL	Yes	Yes	Yes	Yes	Yes
18/ALL	Yes	No	Yes	Yes	Yes
19/AML	Yes	Yes	Yes	Yes	Yes
20/AML	Yes	Yes	Yes	Yes	Yes
21/AML	Yes	Yes	Yes	Yes	Yes
22/AML	No	Yes	No	No	No
23/AML	Yes	Yes	Yes	Yes	Yes
24/AML	Yes	Yes	Yes	Yes	Yes
25/AML	Yes	No	Yes	Yes	Yes
26/NHL	No	No	No	No	No

27/NHL	No	No	No	Yes	Yes
28/NHL	No	No	No	No	No
29/NHL	No	No	No	No	No
30/NHL	No	No	No	No	No
31/NHL	No	No	No	No	No
32/NHL	No	No	No	No	No
33/NHL	No	No	No	No	No
34/NHL	No	No	No	No	No
35/HL	No	No	No	Yes (biopsy)	No
36/HL	Yes	Yes	No	Yes	Yes

Other sites compromised by the disease were lymph node areas in HL patients and in one patient with NHL. Two patients presented subcutaneous nodules on admission. The central nervous system was involved in 3 patients with ALL, in 3 LNH and in two AML.

Magnetic resonance imaging was performed in 33 of 36 cases admitted with suspected SCC. In one patient it was not possible to access the images and in two cases a CT was performed due to the impossibility of performing MRI. Imagining findings are described in Table III. MRI revealed the presence of an epidural mass or vertebral collapse in all cases: 16 ALL, 6 LMA, 9 NHL, and 2 HL. CT and bone scintigraph showed pathological findings in 11 and 5 cases respectively. Spine radiography showed vertebral collapse or osteoporotic lesions, but no pathological lesions were found with this method in most patients.

The location of the vertebral and/or epidural 6involvement was dorsal or dorso-lumbar in 26 patients (72%), lumbo-sacral in 8 (22%), dorso-lumbo-sacral and cervico-dorso-lumbar in the patients with HL. Medullary canal invasion was evident in all NHL cases, in 6 AML and one HL. The pathological findings observed in patients with ALL diagnosis were vertebral collapse fracture, dorsal epidural mass and one patient presented lesions with heterogeneous hypo and hyperintense signal related to infiltrative changes in bone marrow. Spinal cord compression was evident in 8 patients with NHL, in 5 patients with AML and only in 1 patient with ALL, all of them with epidural mass. In 69% (n=25) of the patients, the diagnosis was made by bone marrow aspirate and in the rest, by biopsy of epidural mass or of lymph nodes in the HL cases.

In Table III is described that 14 patients required a surgical initial procedure (ALL= 2; AML= 4; NHL= 8). In 3 cases, a biopsy of the lesion was performed, and 11 patients required decompressive laminectomy: 5 with macroscopically complete resection, 3 partial and 3 biopsies without resection.

All patients received chemotherapy according to the protocols in progress at our institution. Complete remission (CR) was achieved in 94,4% (34/36) of the patients, 2 patients died on induction and 3 patients relapsed after achieving a CR (Table III). Five patients received radiotherapy, in 2 cases for the management of initial symptoms and in 3 deferred according to the treatment protocol (2 AML and 1 HL). The observed adverse events were: 2 deaths during induction, 2 deaths in CR (due to sepsis) and 3 relapses followed by death due to disease progression.

Sequelae were observed in 28% of our patients. One (case 23) of these 10 patients developed severe neurological disability even had not received radiotherapy or laminectomy and achieved CR only with chemotherapy treatment. A patient (case 20) diagnosed with AML who received local radiotherapy as an initial emergency therapeutic, without undergoing decompressive surgery, presented severe irreversible neurological sequelae, which could be associated with transverse myelitis secondary to radiotherapy.

As is showed in Table III, the recorded sequelae were paraplegia and neurogenic bladder in 4 patients with myeloid neoplasms and in 1 patient with LNH; non-severe spinal deviations (kyphosis-kyphoscoliosis) in 3 patients with NHL undergoing wide laminectomies and in one patient with HL undergoing radiotherapy and a sensory-

motor sequelae in the foot was observed in 1 patient with NHL.

Table III. Characteristics of imaging finding, treatment, follow-up time and sequelae

Patient/ Diagnosis	Imaging findings	Localization	Surgery	Radiothe-rapy	Follow up time (months)	Survival/ Sequelae
1/ALL	Epidural mass	Dorsal	Yes/ Laminec-tomy/ Exeresis	Yes	57	Alive/-
2/ALL	Vertebral collapse fracture	Dorso-Lumbar	No	No	12	Relapse and dead/No
3/ALL	Vertebral collapse fracture	Dorsal	No	No	103	Alive/ No
4/ALL	Vertebral collapse fracture	Dorso-Lumbar	No	No	1	Dead on induction
5/ALL	Vertebral collapse fracture	Dorsal	No	No	60	Alive/No
6/ALL	Vertebral collapse fracture	Dorso-Lumbar	No	No	64	Alive/No
7/ALL	Vertebral collapse fracture	Dorso-Lumbar	No	No	1	Dead on remission/No
8/ALL	Vertebral collapse fracture	Lumbar	Yes/Biopsy	No	77	Alive/ No
9/ALL	Vertebral collapse fracture	Dorso-Lumbar	No	No	60	Alive/ No
10/ ALL	Vertebral collapse fracture	Dorso-Lumbar	No	No	69	Alive/No
11/ ALL	Epidural mass	Dorsal	No	No	41	Alive/No
12/ ALL	Vertebral collapse fracture	Lumbar	No	No	4	Alive/No
13/ ALL	Vertebral collapse fracture	Dorsal	No	No	7	Alive/No

14/ ALL	Vertebral collapse fracture	Dorso-Lumbar	No	No	15	Alive/No
15/ ALL	Vertebral collapse fracture	Dorso-Lumbar	No	No	32	Alive/No
16/ ALL	Vertebral collapse fracture	Dorso-Lumbar	No	No	25	Alive/No
17/ ALL	Lesions with heterogeneous signal	Dorso-Lumbo-Sacral	No	No	12	Alive/No
18/ ALL	Vertebral collapse fracture	Lumbo-Sacral	No	No	10	Dead on remission/No
19/ AML	Epidural mass	Cervico-Dorsal	Yes/ Laminec-tomy/ Biopsy	Yes	65	Alive/ Paraplegic and neurogenic bladder
20/ AML	Epidural mass	Dorsal	No	Yes	305	Alive/ Paraplegic and neurogenic bladder
21/ AML	-	Dorsal	Yes/ Laminec-tomy/ Exeresis	Yes	98	Alive/No
22/ MS	Epidural mass	Lumbo-Sacral	Yes/Biopsy	No	36	Alive/ No
23/ AML	Epidural mass	Dorsal	No	No	66	Alive/ Paraplegic and neurogenic bladder
24/ AML	Epidural mass	Lumbo-Sacral	No	No	27	Alive/No
25/ AML	Epidural mass	Dorsal	Yes/ Laminec-tomy/ Exeresis	No	13	Relapse and Dead/ Bladder dysfunction and paraplegia
26/ NHL	Epidural mass	Lumbo-Sacral	Yes/ Laminec-tomy/ Exeresis	No	44	Alive/ Monoparesis
27/ NHL	Epidural mass	Dorsal	No	No	147	Alive/No
28/ NHL	Epidural mass	Dorsal	Yes/ Laminec-tomy/ Exeresis	No	17	Alive/ Kyphoscoliosis

29/ NHL	Epidural mass	Dorsal	Yes/ Laminec-tomy/ Exeresis	No	13	Alive/ kyphosis
30/ NHL	Epidural mass	Lumbo-Sacral	Yes/Biopsy	No	1	Dead on induction
31/ NHL	Epidural mass	Dorso-Lumbar	Yes/ Laminec-tomy	No	8	Alive/No
32/ NHL	Epidural mass	Lumbo-Sacral	Yes/ Laminec-tomy	No	6	Relapse and dead/Bladder dysfunction and paraplegia
33/ NHL	Vertebral collapse fracture	Dorso-Lumbar	Yes/ Laminec-tomy/ Exeresis	No	48	Alive/No
34/ NHL	Epidural mass	Lumbar	Yes/ Laminec-tomy/ Exeresis	No	58	Alive/ Kyphos-coliosis
35/ HL	Epidural mass	Cervico-Dorso-Lumbar	No	Yes	132	Alive/ Scoliosis
36/ HL	Vertebral collapse fracture	Dorso-Lumbo-sacral	No	No	43	Alive/No

Discussion:

The spinal cord compression is a rare but extremely serious condition in medical practice, requires an urgent approach and could be the result of an unknown malignant disease[3,5,14]. This clinical presentation occurs in 3–5% of children with cancer, and solid tumors represent the most frequent cause of SCC in this group[3,4,6,15]. Reports of children diagnosed with leukemias or lymphomas and SCC, support the importance of considering malignant hematological diseases[8,16,17,18] in the diagnostic approach to patients with symptoms suggestive of SCC and unknown etiology[6,19]. Due to the delay in diagnosis and starting an effective treatment, SCC can lead to the possible long-term irreversible neurological sequelae, as we were able to demonstrate in 10 patient of our series. Persistent pain lasting more than two months in children is often associated with a specific diagnosable lesion in up to 75% of patients[5,14]. In this age group, complaints of back pain and/or radicular pain should be taken seriously, and spinal cord compression should be ruled out since these complaints can be the first sign of a paravertebral mass. Nevertheless, clinical symptoms may include not only pain, but fever, weight loss, weakness, neurological deficits, bowel and bladder dysfunction and other unusual symptoms. In our study we observed that 20 patients had systemic symptoms, 27 had functional impotence, and in 10 cases bowel or bladder dysfunction was found.

Neurological deficits may appear during progression of the process and may cause irreversible sequelae, as it had been the case of 2 patients (number 21 and 25) of our cohort, both diagnosed with AML and evolved to spinal cord compression during hospitalization. Since spinal tumors are rare in children, a high level of suspicion is necessary, detailed neurologic examination is essential and if indicated imaging studies should be performed immediately for early diagnosis and treatment that may prevent morbidity.

This atypical form of presentation in the case of leukemias and lymphomas was reflected in our series. Only 9 (1,5%) children with NHL, 25 (0,8%) with acute leukemias and 2 (0,7%) with HL presented with clinical signs suggestive of SCC; these findings concur with that observed in previous studies[6,8,16,20-22].

The media age of our patients was 10 years and just as the gender distribution of our cohort both was like previously reported[6,16,19].

Back pain occurred in 80% of children with spinal cord compresion[3] and was usually the first symptom referred[16]. It was often manifested weeks or months before diagnosis, due to its frequent

underestimation. Functional sensory-motor impotence and sphincter compromise usually add later to pain, as we also observed in our series. Therefore, the lack of sensory-motor compromise does not rule out the diagnosis of spinal cord compression. It is necessary to act opportunely in the presence of back pain as an isolated symptom in pediatric patients[8,20], and the presence of a mechanical compression should be promptly ruled out.

Magnetic resonance imaging spine is the gold standard for diagnosis of spinal cord involvement and should be performed before 24 h have elapsed the clinical suspicion of SCC[5,6,23]. The tumor may infiltrate through intervertebral foramina or by involving vertebral body. In our study, all performed MRI or computed tomography scans of the patients showed pathology; the most frequent location was dorsal and dorsal-lumbar, similar to previous studies reported[6,19]. The magnitude and effect of delay in radiologic confirmation of spinal cord compression reflect the need for improving physicians' awareness of the importance of emergency referral to specialized center for early diagnosis and intervention of this patients.

In our cohort, all cases diagnosed with ALL corresponded to precursor-B immunophenotype, most of them (17/18) presenting with vertebral fractures and collapse without SCC by images. One patient with ALL and epidural mass in this series was a lymphoblastic blast crisis of chronic myeloid leukemia (case 1). In the NHL group, the diagnosis corresponded to precursor B lymphoblastic lymphoma (n=2) and mature B-cell lymphomas (n=7). All AML with epidural involvement presented t(8;21)(q22;q22)/*RUNX1::RUNXT1* and FAB M2 subtype. The reported experience of our hospital in patients with AML with t(8;21)(q22;q22) and extramedullary involvement showed no differences in survival between patients with myeloid sarcoma and without this finding, suggesting that prognosis of the disease could be related to cytogenetic-molecular findings and response to treatment, more than to presence of extramedullary involvement in accordance with previous studies reported[8,16,19,25-28]. However, preceding studies have demonstrated that spinal cord compression is the major cause of morbidity in children with systemic malignancy[6,23].

Most malignant hemopoietic diseases in childhood show a high degree of chemosensitivity, in consequence, early diagnosis and timely treatment should be emphasized, to avoid the progression of neurological symptoms and the eventual sequelae[8,16,19,20,29]. Nevertheless, strict control of the patient in induction is necessary due to the possibility of a slow response and the need for decompressive neurosurgery. In our cohort all patients received chemotherapy and 95% of them achieved CR, confirming the good prognosis of these diseases in spite of the initial presentation.

As we previously mentioned, late referral or delayed diagnosis is the major cause of morbidity and mortality. The initial management in patients with suspected SCC is complex and the guidelines should emphasize the urgency to reach an etiological diagnosis. Any initial therapeutic strategy must consider the preservation or the re-establishment of neurological function, the reduction of skeletal deformities as a priority. In addition, it must try to avoid second neoplasms induced by radiotherapy or chemotherapy.

Chemotherapy should be considered as the first choice of treatment for spinal cord compression particularly caused by leukemias and malignant lymphomas[3,15,17]. In cases requiring biopsy for a tumor causing clinical cord compression, corticosteroids, or appropriate chemotherapy should be continued while waiting for the histopathological diagnosis.

Although it was not the focus of this study, it should be carefully taken into account that the doses of corticosteroids used routinely in the emergency to mitigate neurological sequelae can interfere with the diagnosis and staging of lymphoid neoplasms[6,15]. In our series, 2 patients diagnosed with epidural NHL received corticosteroids prior to diagnosis and after that, a biopsy of the mass with a histopathological analysis was performed for achieving to the diagnosis. None of them had bone marrow involvement, but it was not possible to rule out involvement prior to corticosteroid administration.

The precise role of surgery in the management of spinal lymphoma remains unclear, and mechanical instability remains the only agreed upon surgical indication[30]. The diagnosis of leukemia or lymphoma can be revealed by bone marrow examination, and this prevents unnecessary surgical intervention. Laminectomy, with or without mass resection, does not appear to be necessary in patients with correctly diagnosed leukemias or lymphomas, who can receive timely treatment and respond adequately to it[8,16,19,29,30]. The role of surgery should be limited to diagnostic biopsy in patients with localized epidural lymphoma, who do not present bone marrow involvement, considering that a bone marrow aspirate should be performed urgently in suspected malignant etiology[31]. We highlight that in 69% of our sample the diagnosis was reached by bone marrow aspirate.

Patients with NHL and myeloid sarcoma without bone marrow involvement were diagnosed through some surgical procedure. It is important to

observe that 1 patient was diagnosed with NHL by performing a bone marrow aspiration (stage-IV), without the request for any surgery, despite presenting a normal blood count at the time of developing SCC symptoms.

Irreversible neurological damage should always be a cause for concern in patients with SCC. Almost a third of our patients had severe sequelae including paraplegia with neurogenic bladder and kyphoscoliosis.

It is important to keep in mind that suspecting a hematopoietic disease as a cause of SCC should lead to an early consultation with the hematologist/oncologist for diagnostic purposes. A bone marrow sample can allow a rapid diagnosis avoiding other interventions that may involve additional morbidities.

Conclusion:

Spinal tumors in children are rare lesion, however, persistent back pain in children and adolescents is a warning sign of organic compromise. After clinical SCC suspicion initial evaluation may include MRI. Malignant hematopoietic diseases should be included in the differential diagnosis, mainly if they occur in association within blood count values alterations or other signs and/or symptoms of systemic disease. Response to treatment and neurological function recovery is favorable if diagnosis is early and the treatment timely, to reverse spinal cord compression.

Therefore, it is important to direct all efforts to diagnose and treat this type of disease opportunely. Spinal tumors in children should be rapidly undertook to improve outcomes and quality of life. Our study also reinforces the need to improve medical awareness of this pathology and the importance of early referral to a specialized center.

Conflicts of interest statement

The authors have no conflicts of interest to declare.

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