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Spinal cord compression resulting from Burkitt's lymphoma in children

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Abstract We report seven cases of spinal cord compression resulting from Burkitt lymphoma in boys aged 15 years and below. This became manifest clinically as acute or rapidly progressive spinal cord compression. All the patients showed total paraplegia with a sensory loss at thoracic level and sphincter disturbances. Four patients were operated on, the operation permitting exeresis of an epidural tumor. In three cases surgery was followed by chemotherapy. One patient was treated exclusively with chemotherapy. Owing to the effectiveness of chemotherapy, surgery should be considered only in cases of rapid deterioration or for diagnostic purposes.

Key words Lymphoma · Burkitt lymphoma · Spinal cord compression · Childhood lymphoma

Introduction

Burkitt lymphoma (BL) is a widespread monoclonal B immunoblastoma, which grows particularly fast and is endemic in Black Africa and New Guinea, where it accounts for 50% of childhood cancers [16, 17]. Chemotherapy is so effective that it now leads to cure in many patients. The influence of Epstein-Barr virus (EBV) and its cytogenic and molecular abnormalities make BL a research model for cancerogenetic studies. It is increasingly observed that BL is the lymphoma most often associated with auto-immune deficiency syndrome (AIDS) [4].

Only a few articles in the medical literature deal specifically with spinal cord compression in BL [9, 12, 22]. In this paper we report on seven cases of spinal cord compression in BL in children.

Patients and methods

Between 1973 and 1990, we recorded 286 cases of treatable spinal cord compression, 22 of which were caused by malignant hemopathy, 8 by BL, 7 by Kahler disease, 3 by lymphoblastoma; 3 by myeloblastic leukemia and 1 by Hodgkin's disease. Of the 8 patients who presented with spinal cord compression caused by BL, 7 were males under 15 years of age: their average age was 10.6 years. They were admitted to the department of neurology and neurosurgery of our hospital. The diagnosis was made or confirmed by histological examination of the tumors removed at operation, and of material obtained by needle biopsy of a bladder tumor in 1 patient. The morphological assessment of the tumor was based on the criteria for international classification of diffuse high-malignancy lymphoma [2].

The patients presented clinically with acute or rapidly progressing spinal cord compression lasting about 1 week. All patients were paraplegic, with sensory loss at the thoracic level and functional disturbance of the sphincters. Severe back pain was noticed in two cases. One patient had splenomegaly and another presented with tumors in the bladder and in the kidney. All patients had a high erythrocyte sedimentation rate (ESR) of above 90 mm in the first hour. The albumino-cytological dissociation was constant. No abnormal cells were found in the cerebrospinal fluid (CSF).

Standard X-rays of the spine were normal, but myelography showed an extradural obstruction (Fig. 2). The operation permitted exeresis of the epidural tumor in four patients. In three cases surgery was followed by chemotherapy, and one patient was treated exclusively with chemotherapy.

Case histories (Table 1)

Patient 1

An 8-year-old boy was admitted in 1973 with a 10-day history of paraplegia. He had severe anemia requiring immediate transfusion.

Table 1 Details of patients

Patient no.	Age (years)	Sex	Clinical presentation	Myelography, block at	Surgery	Chemotherapy	Outcome
1	8	M	Paraplegia, altered general state, splenomegaly, ascites, adenopathies	–	No	No	Autopsy
2	10	M	Paraplegia, hepatomegaly, splenomegaly	T1	Yes	No	No neurological improvement (after 2 months)
3	10	M	Paraplegia, altered general state	T9	Yes	Yes	No neurological improvement (after 2 months)
4	8	M	Paraplegia, submaxillary swelling	T6	No	No	No follow up
5	15	M	Paraplegia	T4	Yes	Yes	No neurological improvement (after 3 months)
6	6	M	Paraplegia	T9	Yes	Yes	Complete recovery, alive 12 years later
7	12	M	Paraplegia	T10	No	Yes	Complete recovery, alive 2 years later

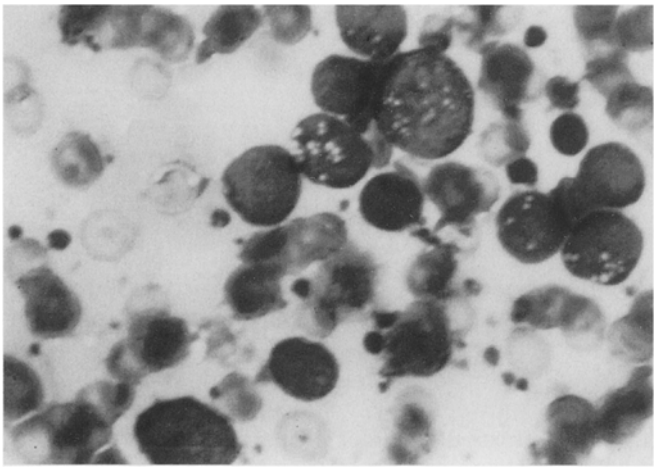

Fig. 1 Patient 3: spread of basophilic, monomorphic cells with cytoplasm full of vacuoles, suggesting Burkitt's lymphoma (Giemsa, ×1200)

Spinal cord compression at level T10–11 was suspected. He had ascites, venous collateralization , splenomegaly, multiple lymphadenopathies, and a left lumbar mass that had been growing continuously over a 2-year period. Several subcutaneous nodules were palpated within the abdominal wall.

The laboratory investigations showed severe anemia with ESR at 88 mm at 1st h/104 mm at 2nd h. The CSF had a protein content of 10 g/l. The X-ray examinations showed a mass in the left flank on the plain abdominal film. No abnormality was seen on the X-ray of the spine, The intravenous pyelogram (IVP) was normal. Hematological studies showed no abnormalities in the bone marrow biopsy. No myelography was performed in view of the advanced stage of cord compression.

The clinical course was that of rapid progression with marked deterioration over 2 days, cachexia, hyperthermia, increasing ascites and leg edema and finally death.

Autopsy confirmed BL, with tumor masses in the epidural and paravertebral areas and adenopathies.

Patient 2

A 10-year-old boy was admitted in 1975 with motor deficit of the inferior limbs, which was caused by paraplegia at the level of T3. This condition had been observed over a period of 3 days prior to admission. The physical examination showed hepato-splenomegaly. An ESR of 98/107 was recorded. The CSF cell count was normal, as was the protein assay. The X-ray of the spine showed no abnormality. The suboccipital myelography demonstrated an extradural obstruction at the level of T1. Histological and hematological examination of the bone marrow and splenic and liver biopsies showed no abnormalities.

Surgically, exeresis of the epidural mass was performed, which on histopathological examination proved to be BL. However, this patient could not be followed up because his parents took him away.

Patient 3

A 10-year-old boy was admitted in 1976 with motor deficit of the inferior limbs, which had started 1 week earlier in association with fever, diffuse pains, urinary retention and ileus, general malaise and drastic weight loss. The neurological examination revealed flaccid paraplegia at the level of T12. The ESR was 90 mm in the first hour and CSF protein, 4.0 g/l. The cell count was normal. The standard X-rays of the spine showed a normal anatomy, whereas myelography demonstrated an extradural obstruction at the level of T9.

A laminectomy was performed, allowing exeresis of a tumor. The histological examination disclosed that this was a BL. Postoperative chemotherapy with four cycles of methotrexate and cyclophosphamide did not improve the clinical situation.

Patient 4

An 8-year-old boy without any known previous illness presented in 1979 with weakness when walking followed by flaccid paraplegia of sudden onset and urinary incontinence. Neurological examination revealed flaccid paraplegia at T6 in association with sensory loss. A physical examination showed a bulky and painful left submaxillary swelling as the only physical abnormality. The ESR was 112/118, the CSF protein assay, 2.5 g/l with a normal CSF cell count. The plain film of the spine was normal, whereas myelography documented obliteration of the spinal canal at T6–7. Histological examination of the biopsy specimen taken from the submandibular swelling demonstrated cells characteristic of BL.

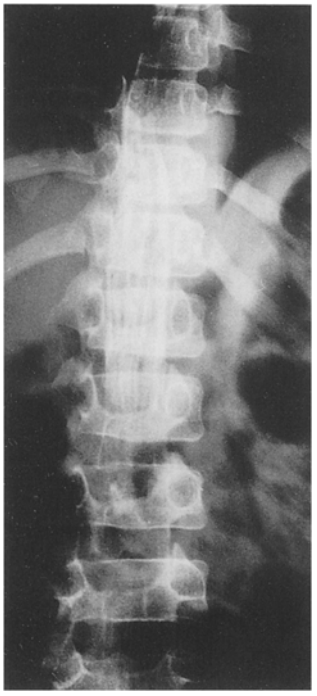

Fig. 2 Patient 3: myelography. Extradural obstruction at T10

Table 2 Comparison of main features of Burkitt lymphoma in different regions. Males predominate with a ratio of 2:1

	Black Africa	North Africa	Europe and USA
Incidence	High	Low	Very low
Age of patients (years)	5–9	5–7	6–15
Location of tumor	Jaws	Abdomen	Abdomen
EBV	100%	90%	15%

The patient could not be followed up because his parents took him away.

Patient 5

In 1980 this 15-year-old boy with an unremarkable prior history developed a motor deficit of the left lower limb overnight, which progressed to complete paralysis of both lower extremities 3 days later. Despite the good physical condition of the patient, he presented with spastic paraplegia at T6 in association with loss of bladder control. The laboratory profile showed an ESR of 114/137, CSF protein of 3 g/l and normal CSF cell count. Radiologically the vertebral column was normal, whereas a suboccipital myelography showed a complete obstruction of the extradural space at T4.

Laminectomy allowed resection of the obliterating tumor mass, which on histological examination proved to be a BL. Postoperatively, four cycles of cyclophosphamide and methotrexate were given. However, this regimen did not influence the clinical course of the illness; the patient was unable to achieve recovery, and the spastic paraplegia was converted to flaccid paraplegia.

Patient 6

In 1981, a 6-year-old boy was admitted after having flaccid paraplegia, priapism and urinary retention for 1 month. The ESR was 105/130. The standard X-rays of the spinal column were normal. However, the myelography showed extradural obstruction at T9. Analysis of the CSF showed an albumino-cytological dissociation. The results of all other clinical examinations performed were normal.

Therapy took the form of a laminectomy and exeresis of a bulky reddish epidural tumor extending from T8 to T11. Histological examination confirmed that this was a BL (Fig. 1). The patient underwent four cycles of chemotherapy with cyclophosphamide and methotrexate. He recovered full neurological function within a few weeks and is now attending school regularly.

Patient 7

A 12-year-old boy in general poor condition was hospitalized with flaccid paraplegia, which developed within a week after he had started to suffer severe back pains. He had several inguinal adenopathies, splenomegaly, a tumor in the left kidney and another in the bladder.

A myelography demonstrated a complete epidural obstruction at the level of T10 (Fig. 2), and the tumours in the kidney and the bladder were identified by ultrasonography. A needle biopsy of the bladder tumor led to the histological diagnosis of BL. The patient underwent chemotherapy with cyclophosphamide, vincristine, doxorubicin and prednisone, followed by a spectacular recovery within 1 month without surgery.

Results

There was no operative mortality. Immediate postoperative assessment of the patients showed no clinical improvement on the basis of surgery alone. Complete recovery occurred in one patient after combined surgery and chemotherapy. In one patient a spectacular recovery occurred following chemotherapy alone.

Most of our patients could not be adequately followed up, as they were taken away from the hospital or withdrawn from the outpatient treatment by their parents or guardians, who judged the disease incurable. Consequently, except in one patient we could not determine the prognosis of the illness in the medium or long term. The small number of our patients also limits our ability to say anything about the prognosis.

Discussion

In 1958, Denis Burkitt described a tumor of the jaw, suggesting a lymphoma, in a 7-year-old child in Uganda [2]. BL is classified in the group of high-malignancy lymphomas. The specific genetic abnormality that characterizes the Burkitt cell is a translocation involving chromosome 8 and chromosome 14 and, more rarely, chromosome 22 or 2 with the activation of the *c-myc* gene. Epidemiological studies show that males are afflicted more often than females, irrespective of race, with a male-to-female ratio of 2:1 (Table 2) [7, 17].

Three geographic forms of the disease have been identified [13, 16, 21]. In sub-Saharan Africa, which is an endemic region, BL accounts for 80% of childhood tumors, occurring predominantly in the maxilla [21]. The link with Epstein-Barr virus (EBV) is constant, and it is suspected that malaria has a supporting role. This malignant disease falls within the scope of non-Hodgkin lymphoma (NHL), with a high incidence in children aged between 3 and 10 years. An African study of 430 cases showed involvement of the facial area in 40%, abdominal tumors in 40% and a combination of both in 20% of the cases [10].

In North Africa, the incidence is low [16, 21]: BL accounts for 15% of childhood tumors and about one half of all NHL. The tumor is mostly found in the abdominal region, but also, less often, in the facial area. Ninety per cent of such lymphomas are associated with EBV.

In Europe and North America, the frequency is estimated at 3% of childhood tumors, which represents between 35% and 45% of NHL in all children. In contrast to the endemic regions of sub-Saharan Africa, in Europe and North America 70% of BL seen present as abdominal tumors [19]. In 20% of all cases, swollen lymph nodes are observed in the ovaries, in the kidneys and in the retroperitoneal areas [16]. Most patients are aged between 6 and 15 years. An association with EBV has been observed in 15% of all patients with immune deficiency (AIDS patients, transplant recipients, patients with congenital immune deficiency). Sporadic cases have been observed in Turkey [22] and in Japan. Fourteen per cent of the cases observed in Japan are associated with EBV [8].

When the central nervous system (CNS) was involved, cytological evidence of meningitis was most often identified. In the USA, Sariban found 15% of cases had CNS involvement [18]. In a study of 64 cases in Nigeria, Odeku observed spinal cord compression in 15% [12]. An intracranial localization of BL is extremely rare [20]. It is a complication that has been documented in a Japanese patient [9].

Usually, spinal cord compression appears in isolation without the other classic signs of BL. In all our cases, the clinical symptomatology indicated either an acute or a rapidly progressing spinal cord compression at the thoracic level. Paraplegia was observed within 7 days of the inception of symptoms. Before the occurrence of paraplegia, severe back pain was noted by Turkish authors [22]. In our series one half of the patients presented with back pain. Myelography regularly showed an extradural type of block caused by an epidural tumor. A high ESR was always documented. According to Turgut, spinal cord compression in association with a paravertebral mass appearing on the X-ray and backache in a child is suggestive of BL [22]. Our clinical observations did not confirm this suggestion.

The process whereby the epidural space is invaded is controversial. Different hypotheses have been put forward: invasion by contiguity starting from the paravertebral ganglia, or compression of the medullary arteries by retroperitoneal masses. A further controversial suggestion that has given rise to some discussion is de novo development from the epidural lymphoid system.

Primary spinal epidural NHL is rare [6]. In northern countries, neuroblastoma and sarcoma are the main causes of epidural malignancy with spinal cord compression in children [18]. In Africa, BL is routinely considered in the differential diagnosis of tumors in children. The AIDS pandemic and the frequent association of BL with HIV indicate the possibility that epidural tumors of the BL type will increase in frequency.

If untreated, the disease usually develops rapidly, resulting in death within a few months. The current treatment is a short and intensive poly-chemotherapy combining cyclophosphamide, methotrexate, vincristine and cytarabine [3, 14–17]. Because poly-chemotherapy is so effective, radiotherapy is no longer a therapeutic option.

The prognosis of the illness has been changed by modern chemotherapy. Thirty years ago, the mortality rate of BL was 90%. Currently, we achieve a cure rate of 80% of the regional forms and 60% of the diffuse forms of the disease. Meningeal involvement seems to be associated with a grave prognosis, as the survival rate does not exceed 30% [3, 14–17]. The initial involvement of the CSF seems to differ regionally in prognostic importance, being significant in Europe in contrast to Africa, where CSF involvement does not seem to influence the prognosis [17].

Relapses within the first 8 months following remission tend to be localized and are accompanied by neuro-meningeal invasion [17]. The treatment of relapses is rather aggressive, involving massive chemotherapy followed by autologous bone marrow transplantation. The results of such treatment seem encouraging [16]. By consensus, patients are considered to be cured if they remain in remission for over 8 months.

BL is primarily a non-surgical illness, but the neurological complications described in this paper presented as emergencies. Our series reveals a number of clinical situations that reflect the evolution of our therapeutic approach. The immunodepression, the origin of the patients (endemic region), the thoracic localization of the compression, and the high ESR all favored a diagnosis of BL. The diagnosis can be made through a needle biopsy of the peripheral lymph nodes or of the superficial tumor mass. In view of the effectiveness of chemotherapy, surgery should only be considered when rapid deterioration is observed or for the purpose of diagnosis, and laminotomy is the technique of choice.

In sub-Saharan Africa, one is often faced with the problem of relieving the obstruction as quickly as possible, especially as a histological diagnosis cannot be made early enough to start poly-chemotherapy. In addition, poly-chemotherapy takes some days or even weeks before clinically relevant decompression of the cord can be documented. This relief often comes too late for the patient. Against this background, laminotomy and exeresis of the

tumor followed by chemotherapy might well be considered.

However, more experience is needed to define the role of surgery for the relief of cord compression by a BL.

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