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Research Paper

Medullary invasion in Hodgkin's lymphoma: the value of medullogram

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Abstract: *Hodgkin's lymphoma is a disease characterized by abnormal tumoral proliferation of lymphoid cells in one or more lymphoid organs. It can sometimes spread to extra-ganglionic sites, and is highly metastatic during its course, particularly in bone marrow. Diagnosis is based on histopathological analysis of an excised lymph node biopsy, which shows the presence of Reed-Sternberg cells.*
Bone marrow studies are a crucial step in the management of malignant solid tumors in children, as they determine the therapeutic attitude and response to treatment. The presence of bone marrow metastases darkens the prognosis of these tumors.
Some pediatric tumors always require careful bone marrow exploration at the time of diagnosis. Other pathologies, notably Hodgkin's disease, only warrant it in the presence of certain warning signs.
In this work, we report a rare case of a child with Hodgkin's disease and bone marrow invasion, which we will discuss in the light of the literature

Keywords: *Hodgkin's lymphoma, sternbeirg tumour cells. Immunohistochemistry .*

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I. Introduction

Hodgkin's lymphoma (HL) is a malignant form of lymphoproliferative cancer, characterized by the presence of reed-sternberg cells (SRC) and their infiltration of lymph nodes. It accounts for around 8.2% of all diagnosed lymphomas [1]. LH has an annual incidence of around 3 new cases per 100,000 population [2]. Initial symptoms often manifest themselves as painless peripheral lymphadenopathies (70%), most often in the cervical lymph nodes (60-80%).extra nodal localization of HL is less frequent than in non-Hodgkin's lymphoma (NHL), accounting for only 5% to 10% of cases [3].

The diagnosis of Hodgkin's lymphoma is based on histopathological analysis of a biopsy excised from a lymphatic adenopathy, which shows the presence of Reed-Sternberg cells (large binucleated cells), within a characteristic heterogeneous cellular infiltrate composed of eosinophils, histiocytes, lymphocytes, plasma cells and monocytes. The standard imaging work-up includes a chest X-ray and a cervico-thoraco-abdomino-pelvic CT scan. Positron emission tomography (FDG-PET) can improve the staging of lymph node or extra-lymph node involvement by complementing the data from other imaging tests. Magnetic resonance imaging (MRI) and bone marrow biopsy are performed only if neurological symptoms are present.

For children, adolescents and young adults, treatment protocols have been developed on a European scale and are mainly based on chemotherapy. The duration of chemotherapy depends on tumor volume, stage of disease extension, presence of inflammatory syndrome and general impact. Disease response to treatment is assessed by CT scan for volumetric measurements, and PET scan for metabolic measurements.

Radiotherapy to initially invaded lymph nodes is now used in only a quarter of patients.

Hodgkin's lymphoma has a good prognosis, with a 5-year relative survival rate of 84% for all forms of the disease, but it is also highly metastatic, particularly in the bone marrow.

This case is one of the exceptional cases of massive medullary Hodgkin's disease in a 12-year-old child.

The aim of this observation is to highlight the importance of medullogrames in the positive diagnosis of extensive forms of the disease, where bone marrow involvement is present.

II. Patient and observation

This 12-year-old child, with no notable pathological history, was admitted to the paediatric ward with a right laterocervical mass. His symptoms dated back to 1 year before his admission, with the appearance of a swelling in the right laterocervical region, progressively increasing in volume, with fever and weight loss of 4 kg.

Physical examination on admission revealed a child in fairly good general condition, with bilateral right-predominant laterocervical ADPs, the largest of which was 5 cm in diameter, painless and without inflammatory signs. On abdominal examination, splenomegaly was noted at 2 fingerbreadths.

A thoracic-abdomino-pelvic CT scan revealed cervical-mediastinal, axillary, susclavicular, intra-retroperitoneal and inguinal adenopathies, homogeneous pleomegaly and a secondary pulmonary localization (Figure 1).

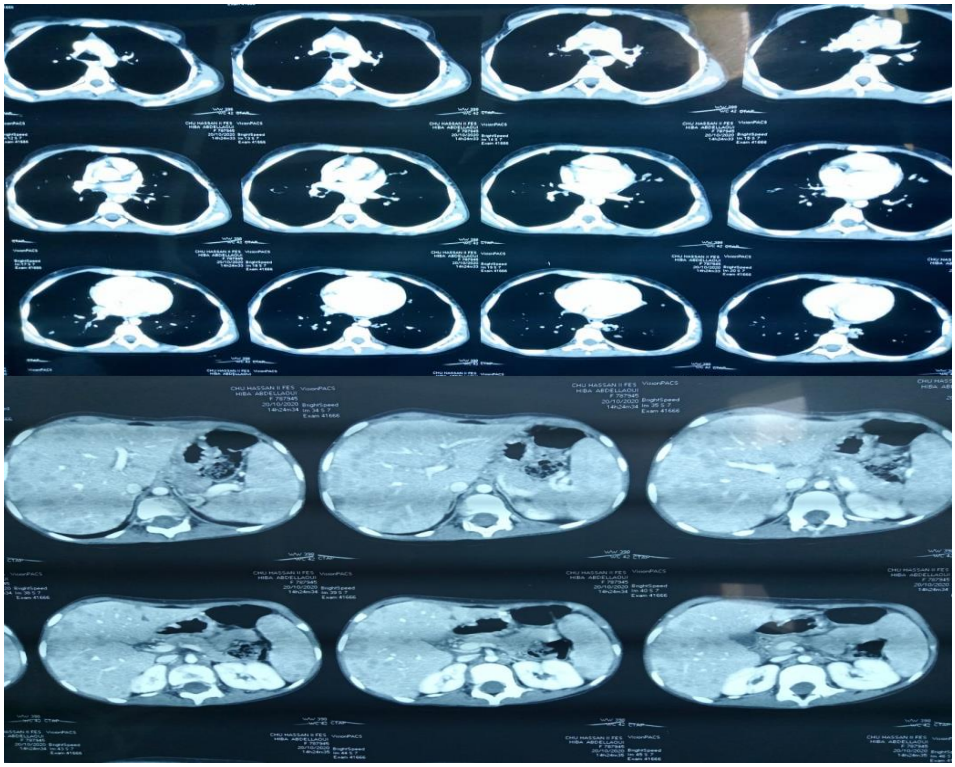

Figure 1: A thoraco-abdomino-pelvic CT scan.
Carried out in the radiology department of the CHU-Hassan II in Fez.

Histological study showed hyperplasia of lymphoid follicles in the cortical lymph nodes. The paracortical zone is also hyperplastic, with a diffuse infiltrated appearance in some areas, with numerous large cells, possessing poly-lobed nuclei, sometimes taking on a mirror-like appearance, irregular and containing large eosinophilic nucleoli. (Figure 2 A/B) .

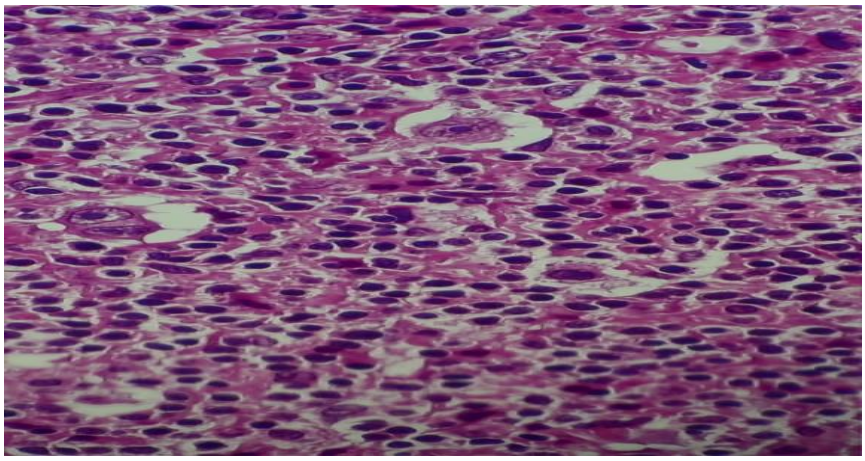

Figure 2/A: Histological section showing Hodgkin cells of reed SternbeirgCarried out in the anapathy lab at CHU-Hassan II, Fez

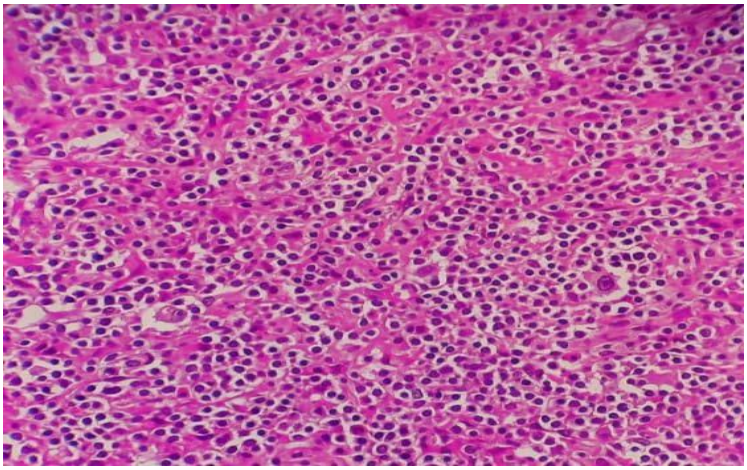

Figure 2/B: Histological sections showing lymph node parenchyma with a few reed sternbeirg tumour cells, Carried out in the anapathy lab at CHU-Hassan II, Fez.

Immunohistochemistry showed intense and diffuse positivity of tumor cells to anti-CD20, anti-CD15, EMA and CD30 antibodies, expressed by some tumor cells.
The lymphoid population is essentially made up of CD3-expressing T lymphocytes, arranged in diffuse sheets, sometimes in a crown around the tumour cells.
Histological and immunohistochemical findings were consistent with lymphocyte-predominant Hodgkin's lymphoma.
The patient had been subsequently classified as Stage IV according to the Ann Arbor classification, belonging to the unfavorable groups according to the criteria of the German Hodgkin Lymphoma Study Group (GHSG). The initial extension work-up showed no other localization .
Therapeutically, the patient had initially received 2 courses of OPEA chemotherapy, 4 courses of COPDAC, then 3 courses of IEC. She was then referred to the radiotherapy department, where she underwent a series of external radiotherapy treatments, first supra-diaphragmatic =20 Gy in 10 sessions, then sub-diaphragmatic at 1-month intervals.
After a remission of 3? years, the patient reconsulted with asthenia, pallor, anorexia and weight loss, with inguinal ADP on clinical examination.
The extension work-up, including a cervico-thoraco-abdomino-pelvic CT scan, showed a secondary hepatic localization of classic scleronodular Hodgkin's lymphoma, with lateral pulmonary-bilateral parenchymal micronodules, the largest measuring 13 mm in diameter.
The PET scan showed active pathological involvement of the supra- and subdiaphragmatic lymph nodes, associated with hepatic, pulmonary, splenic, peritoneal and osteomedullary involvement.
Bone scintigraphy was performed to detect secondary bone involvement.
Osteomedullary biopsy showed no lymphomatous infiltration.

The bone marrow biopsy showed a normo-cellular, hemodiluted, heterogeneous marrow, with 04% blasts and some extra-hematopoietic cells with a chromophilic cytoplasm, a bilobed, "carnival mask" nucleus, and loose chromatin revealing one or two enlarged nucleoli: Sternberg reed cells (Figure 3).
Hodgkin cells (HRS) are dispersed in a non-tumoral background, in which polynuclear cells, histiocytes, plasma cells and fibroblasts are mixed in variable proportions.
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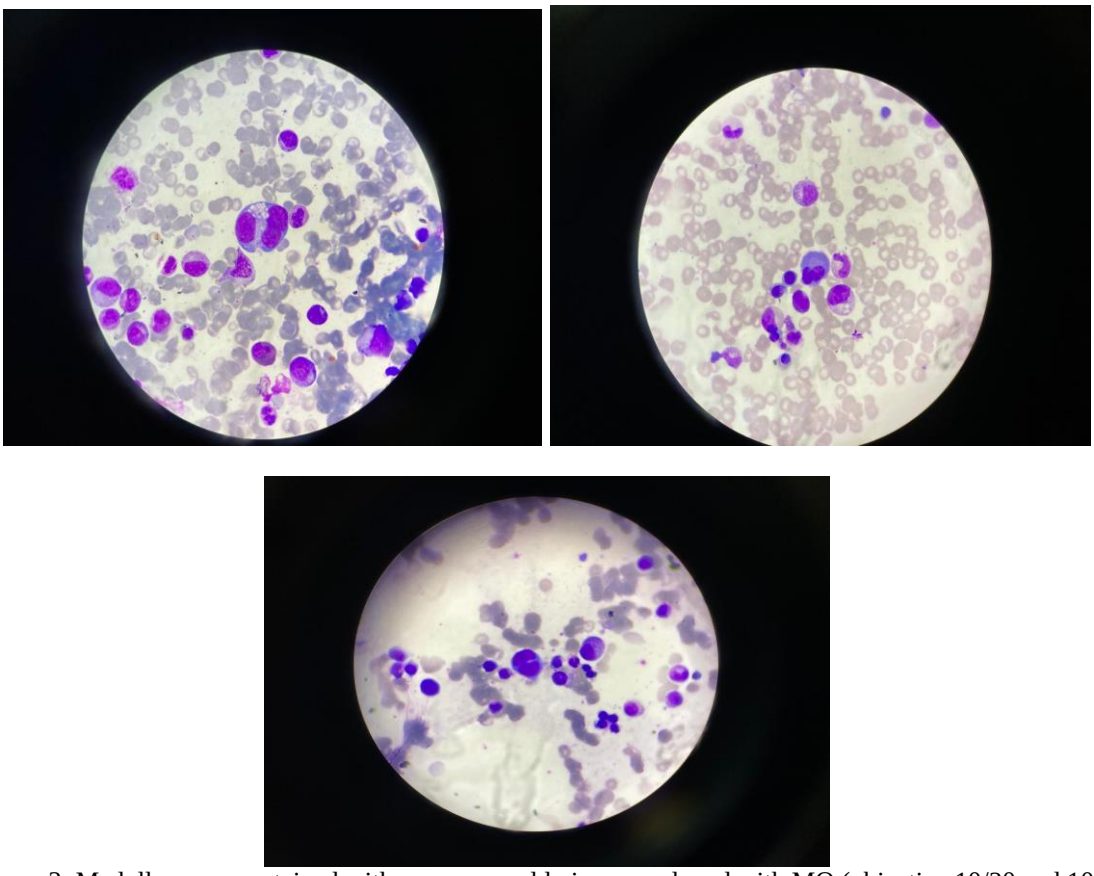

Figure 3: Medullary smear stained with may crunwald giemsa and read with MO (objective 10/20 and 100) showing descereed Sternberg cells, binucleated cells.
Performed in the hematology laboratory -LCAM -CHU Hassan II, Fez.
The patient was missous protocol MIED, for relapse of his disease without clinical or radiological improvement.

III. Discussion

Hodgkin's disease is a hematological malignancy characterized by the presence of Reed-Sternberg cells, in a varied, reactive inflammatory tissue. Reed-Sternberg cells are unique to this disease and are surrounded by a complex cellular environment. The disease accounts for 10% of all lymphomas and 1% of all cancers.
The positive diagnosis of childhood Hodgkin's lymphoma is based on a combination of clinical, biological, radiological and pathological findings.
Invasion of the bone marrow by Hodgkin cells is rarely reported, and most published data come from individual case studies.
The search for bone marrow invasion in Hodgkin's lymphoma plays an important role in the prognosis and extension of this tumor. It conditions the therapeutic attitude and the evaluation of the response to treatment.
In 1979, Duhamel et al. were the first to report 10 cases of massive medullary disease. The constant feature was febrile pancytopenia with major inflammatory signs. Bone marrow biopsy (BOM)
reveals very dense, collagen-enhanced reticulin fibrosis, which raises the problem of differential diagnosis with primary myelofibrosis. However, in this series, the diagnosis of MDH was easy in the presence of superficial and/or retroperitoneal adenopathies accessible to biopsy. [5]
Fenaux et al. reported 2 cases of medullary form revealed by febrile pancytopenia, in a context of severe alteration of general condition without superficial or deep tumor syndrome and accompanied by an inflammatory syndrome. Histological study of the marrow showed non-specific myelofibrosis. The secondary appearance of superficial adenopathies led to the diagnosis of mixed-cellularity MDH. [6]

In our case, the diagnosis of MDH was based on biopsy of the right latero-cervical adenopathy and medullary invasion confirmed by bone marrow aspiration.

At present, the prognosis of Hodgkin's disease or Hodgkin's lymphoma is generally good to very good. For localized forms of Ann Arbor stages I and II, around 95% of patients can be cured. For the more advanced stages III and IV, cure is achieved in around 70% of cases[7].

The rapid evolution and severity of the massive medullary forms of MDH contrast with the usual forms of the disease, which have a poor prognosis.

The results of the Polish study by A. Kolda showed a dismal prognosis, with a 90% death rate in patients with medullary metastases at diagnosis, despite chemotherapy [4].

The most commonly used treatment for cancer is the ABVD (Adriamycin, Bleomycin, Vinblastine, Deticene) protocol, administered in cycles spaced 3 to 4 weeks apart. The regimen adopted by EORTC (European Organisation for Research and Treatment of Cancer) and LySA (Lymphoma Study Association) comprises: in forms without risk factors: 3 cycles of ABVD followed by radiotherapy at a dose of 30 Gy; in forms with risk factor(s): 4 cycles of ABVD followed by radiotherapy at a dose of 30 Gy[8, 9].

In the majority of cases, radiotherapy complements the action of chemotherapy by treating localized areas, notably groups of lymph nodes, initially affected by the disease[10].

The final stage is the treatment of relapses, based essentially on chemotherapy, radiotherapy and stem cell autotransplantation[11-12].

Our patient benefited from the same chemo-radiotherapy treatment protocol, with a good initial clinical and radiological response. After a 3.5-year remission, The patient was readmitted due to a relapse of her disease, and despite treatment according to the MIED protocol, there was no clinical or radiological improvement. Tragically, the patient died during her hospitalization.

IV. Conclusion

Hodgkin's disease is a relatively rare malignant tumor. It is diagnosed histopathologically. Diffuse stages remain the most common. It is a curable disease, but therapeutic trials are ongoing to better understand and cure it. Bone or medullary involvement is associated with an increased risk of relapse in patients with the classic form of the disease.

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