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Case Report

Differential Diagnosis of a Primary Vertebral Bone Lymphoma

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Abstract: Primary vertebral bone lymphoma is a rare malignant tumor, representing less than 5% of primary bone tumors and about 2-3% of all lymphomas [2-4]. It more commonly affects middle-aged and older adults (with a median age around 50-60 years), with a slight male predominance [1-5]. Its clinical and radiological presentation is non-specific and highly suggestive of other infectious, inflammatory, or tumoral pathologies of the spine, making it a true diagnostic challenge. Diagnostic delay is common and impacts prognosis. This review aims to synthesize the main differential diagnoses of vertebral lymphoma, focusing on the clinical, biological, and imaging elements that help guide the diagnosis. Histological analysis remains the cornerstone of the definitive diagnosis. An integrated multidisciplinary approach is essential for optimal management.

Keywords: Primary Bone Lymphoma, Spine, Differential Diagnoses, Magnetic Resonance Imaging, Positron Emission Tomography, Bone Biopsy, Osteomyelitis, Metastasis, Multiple Myeloma.

INTRODUCTION

Vertebral bone lymphoma often manifests as mechanical and nocturnal inflammatory pain, neurological signs due to medullary or radicular compression, and sometimes a decline in general health. On imaging, it typically appears as a lytic lesion, often invasive with a significant paravertebral soft tissue component that relatively spares the intervertebral discs [2, 3]. However, this presentation is shared by many other entities, requiring a rigorous diagnostic approach to avoid pitfalls.

CASE REPORT

A 73-year-old female patient, H.M., diabetic, hypertensive, presented with persistent nocturnal dorsal and lumbar pain, refractory to usual analgesics, evolving over several weeks. This was associated with asthenia, anorexia, gait weakness, and weight loss, in the absence of leg paresthesia or urinary difficulties. The patient underwent a CT scan of the chest, abdomen, and pelvis (Figures 1) revealing a lesion centered on the D12 vertebra, associated with deep adenopathies, initially suggestive of an infectious (tuberculosis) or tumoral (secondary) origin.

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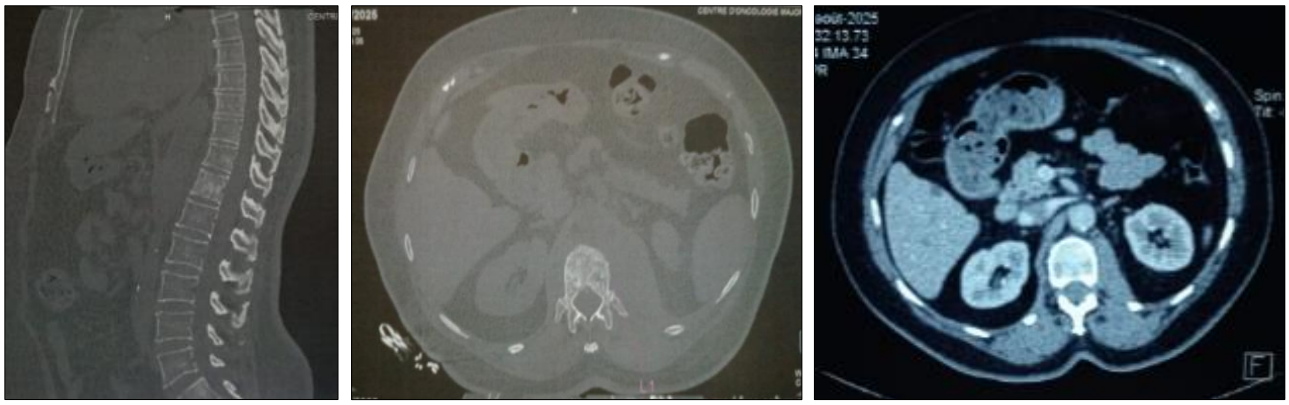
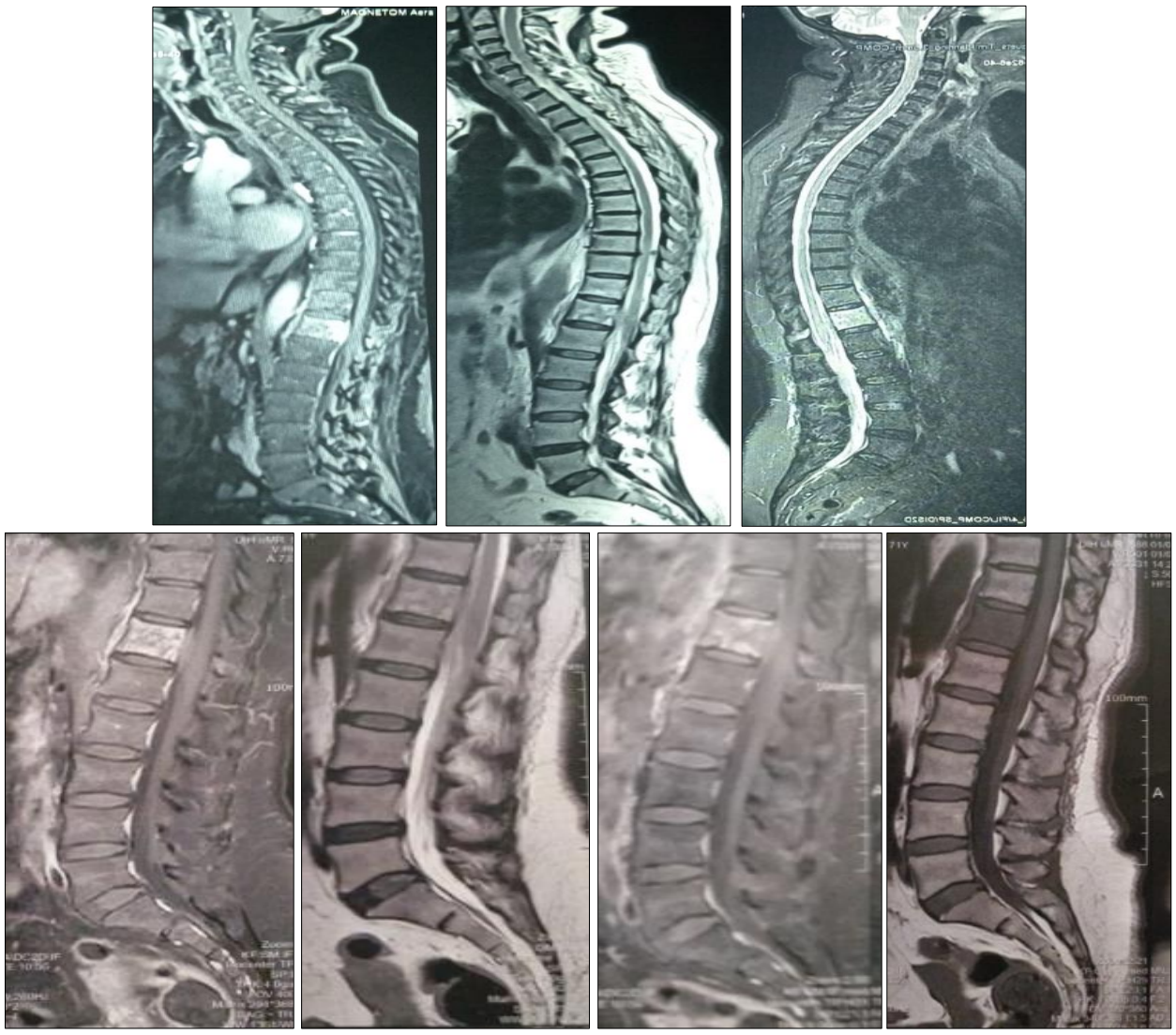
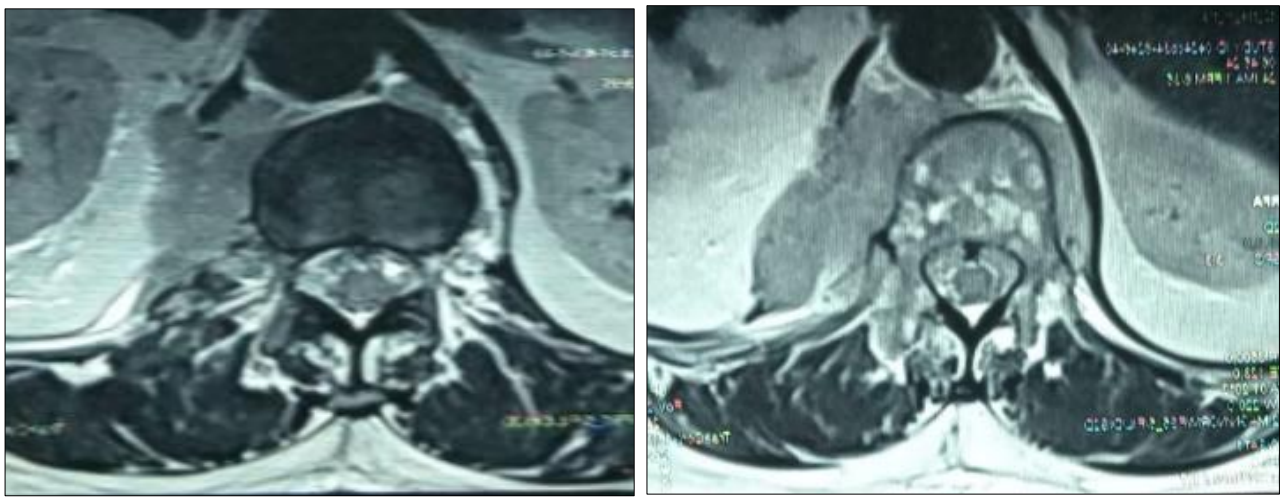


Figures 1

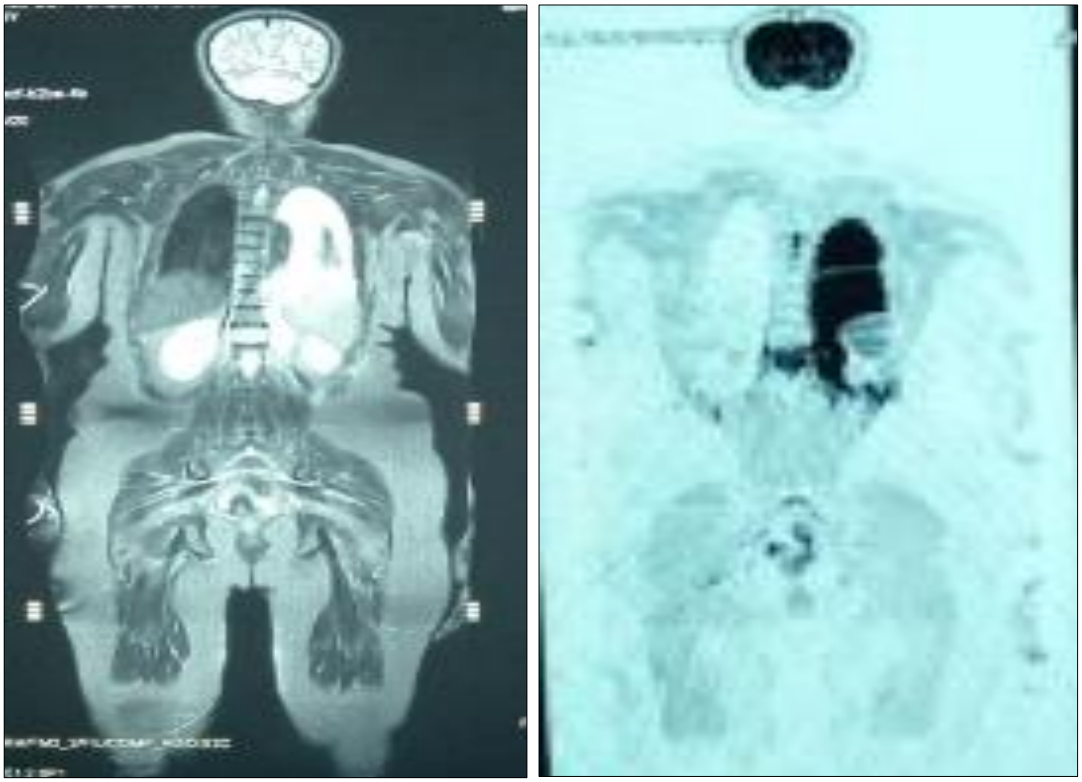
Spinal MRI (Figures 2) showed an infiltrating process of the D12 vertebra, with T1 hyposignal and T2 hypersignal, enhanced after gadolinium contrast injection, with preserved vertebral height, bulging of the posterior wall, and foraminal and endocanal extension, without signs of medullary suffering, associated with epiduritis. There was also infiltration of the paravertebral soft tissues, forming a pseudo-mass enhanced by contrast, measuring 62x47x80 mm (T x AP x CC). Topographically: Anteriorly: It reached the posterior wall of the abdominal aorta with loss of the separating fat interface over a 90° circumference. Laterally: It reached the right diaphragmatic pillars and invaded the left one. This mass also invaded the posterior arch of the left rib and the ipsilateral pleural space.





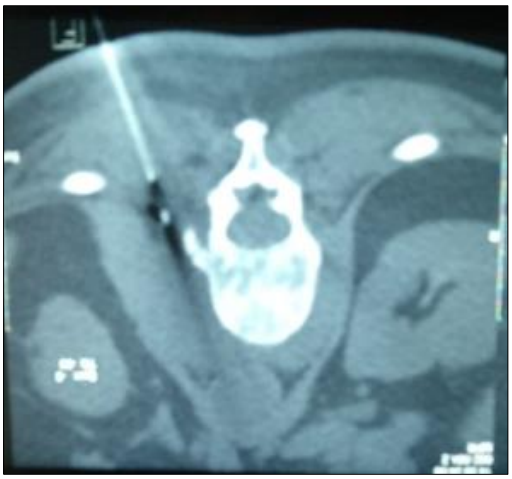
Figures 2

Whole-body MRI (Figures 3) additionally revealed grade 2 cerebral leukoaraiosis of the centrum semiovale, a moderately abundant left pleural effusion with pleural nodules, and a 14 mm celiac lymph node with diffusion restriction.



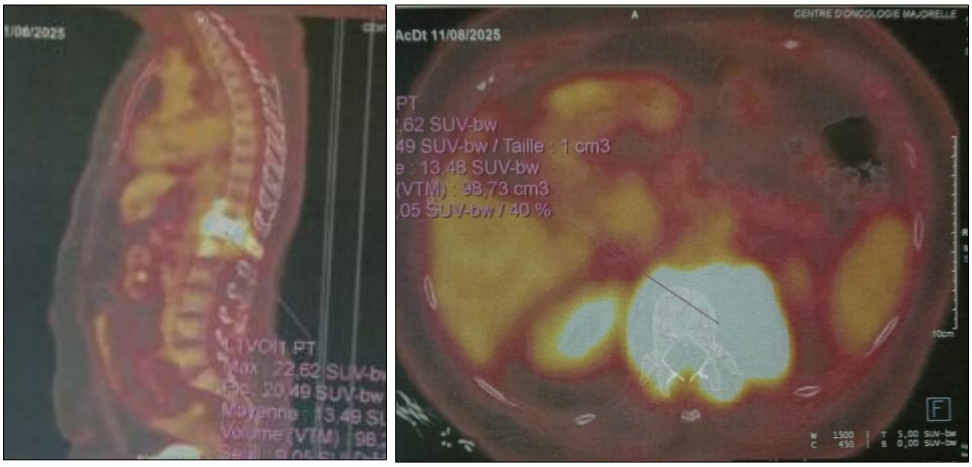
Figures 3

The biological workup showed an ESR of 70 mm/h, mild anemia with HB at 11.1 g/dl, negative syphilis, hepatitis, and HIV serology, with HbA1c at 8.4%. Myelogram cytology was suggestive of a multilineage myelodysplastic syndrome. Serum protein electrophoresis showed a normal profile. Sputum Genexpert was negative. An anatomopathological study with immunohistochemistry on a disco-vertebral biopsy (Figures 4) showed morphological and immunohistochemical profiles consistent with a disco-vertebral localization of a diffuse large B-cell lymphoma. Microbiological and bacteriological examinations of the biopsy specimen were negative.



Figures 4

A PET-CT scan (Figures 5) with 18-FDG showed a locally advanced hypermetabolic lesion at D12, associated with supra- and sub-diaphragmatic nodal involvement, with two hypermetabolic nodular foci projected in the ileal region.



Figures 5

The patient was started on chemotherapy. The protocol used was R-CHOP: 700 mg of Rituximab + 1400 mg of Cyclophosphamide, 90 mg of Doxorubicin, 2 mg of Vincristine, and 100 mg for 05 days of Prednisone. The patient received five cycles. A control PET-CT scan after the 5th cycle showed a complete metabolic response, Deauville score III, with disappearance of the D12 lesion, morpho-metabolic regression of the nodal foci and the right hilar adenopathy, and no appearance of new pathological hypermetabolic foci. A protocol extension of two cycles of 700 mg of Rituximab, spaced 21 days apart, was administered, followed by another control PET-CT scan. The follow-up of the cycles was marked by minor side effects.

DISCUSSION

Primary bone lymphoma represents about 1-2% of all lymphomas and 4-5% of primary malignant bone tumors [1, 2]. The spine is the most frequently affected bone site, accounting for about 50% of cases [5].

There is a bimodal age distribution. A first peak in adolescence and young adulthood (around 30-40 years) and a second peak in the elderly (60-70 years) [1]. There is a slight male predominance (male/female ratio of about 1.5:1 to 2:1) [1-5]. In our case, it is a 73-year-old patient, which does not correspond to the typical case of this pathology.

The thoracic region is the most frequently affected (≈60%), followed by the lumbar region (≈30%) and the cervical region (≈10%) [5]. The tumor most often affects the vertebral body (the anterior part), but it can extend to the pedicles, laminae, and even the spinal canal (epidural lymphoma) [2, 3]. Our patient presented with infiltration of the 12th thoracic vertebra with foraminal, endocanal, and paravertebral soft tissue extension, forming a pseudo-mass appearance.

The vast majority (>95%) of primary vertebral lymphomas are diffuse large B-cell lymphomas [1-4], an aggressive type of lymphoma, which is the case for our

patient. Other types (Burkitt lymphoma, T-cell lymphoma) are extremely rare at this site.

Immunocompromised patients (HIV infection, organ transplant recipients on immunosuppressants) have a significantly increased risk of developing lymphoma, including at the bone level [1]. Epstein-Barr Virus (EBV) is often associated with lymphomas occurring in an immunosuppressive context. In our case, syphilis, hepatitis, and HIV serologies were negative.

The Standard Clinico-Radiological Presentation of Vertebral Lymphoma

The clinical picture is often insidious and non-specific, which can delay diagnosis for several weeks or months.

Pain: The cardinal symptom. Present in nearly 80-90% of cases. It is typically nocturnal, sleep-disturbing, and mechanical (increased with movement, load). It may also have an inflammatory component (pain at rest). It is well localized at the affected spine level (dorsalgia, low back pain, cervicalgia).

Neurological Signs, constituting a Medical Emergency

- Neurological deficit: This is the most dreaded complication. It occurs in 30 to 70% of cases depending on the series, often due to medullary or radicular compression [5].
- Radicular pain (pain along the path of a nerve root).
- Paresis or paralysis of the limbs (lower limbs if thoracic or lumbar compression).
- Sensory disturbances (paresthesia, numbness, hypoesthesia).
- Sphincter disorders (urinary retention, incontinence) and erectile dysfunction. These signs are of poor prognosis and constitute an absolute emergency.

Constitutional Syndrome, present in about 20-30% of cases. It associates unexplained fever, profuse night sweats, and involuntary weight loss (>10% of body weight in 6 months). Its presence is often correlated with more advanced or aggressive disease.

Physical Examination Reveals

- Point spinal tenderness on palpation of the spinous processes.
- Motor deficit, sensory disturbance, abnormal osteotendinous reflexes (abolition of reflexes initially, then hyperreflexia with Babinski's sign in case of medullary suffering).
- Rarely, a palpable para-spinal mass may be detected.

Complications:

- Pathological vertebral fracture: Lymphoma causes bone osteolysis, which can lead to vertebral collapse and worsen neurological compression.
- Cauda equina syndrome: If the tumor compresses the nerve roots at the base of the spine.
- Paraplegia in the absence of urgent treatment.

Imaging plays a fundamental, multifaceted, and indispensable role in the diagnosis, staging, therapeutic follow-up, and surveillance of bone lymphomas; it is at the heart of the entire decision-making strategy. From initial suspicion to long-term follow-up, MRI and especially Positron Emission Tomography coupled with Computed Tomography (PET-CT) provide essential non-invasive information that guides biopsies, establishes prognosis, adapts treatments, and monitors responses, thus significantly improving patient management [2, 3].

Standard Radiography, a low-sensitivity exam, often performed first. May show a "moth-eaten" bone lysis (most common form, with blurred or sharp limits.), vertebral collapse ("ivory" or "phantom" vertebra in case of severe lysis), a sclerotic lesion with bone condensation (rarer), or mixed lesions (lytic and sclerotic), often without periosteal reaction. It may also show a significant associated soft tissue mass, often disproportionate to the visible bone destruction. This is a very suggestive element [2]. However, osteolysis of more than 30 to 50% of bone density is necessary to be visible. A purely medullary lesion may go unnoticed.

CT scan confirms bone lysis, assesses the extent of cortical destruction, and perfectly visualizes the often-bulky paravertebral soft tissue component. Excellent for guiding a biopsy. Less effective than MRI for assessing medullary involvement.

Magnetic Resonance Imaging (MRI): The reference exam for local evaluation. Primordial role for:

1. Precise delineation of tumor extent in the bone (medullary involvement) and soft tissues.
2. Tissue characterization: On T1, T2, T1 sequences with gadolinium.
3. Evaluation of treatment response.
4. Detection of sub-radiological lesions (not visible on other imaging modalities) [3].

Typical MRI appearance: The lesion appears as T1 hyposignal, T2/STIR hypersignal, and intensely enhances after gadolinium injection [2, 3]. Frequent involvement of the vertebral body and pedicles, extension to soft tissues, and disc sparing are characteristic but not pathognomonic. Infiltration of the epidural fat is highly suggestive.

Positron Emission Tomography coupled with Computed Tomography (PET-CT): is the key exam for extension workup [2, 3]:

- ✓ Crucial role: The tracer used during injection is a glucose derivative labeled with a fluorine-18

molecule (18-FDG), avidly taken up by hypermetabolic lymphomatous cells.

- ✓ Diagnosis: Reveals with very high sensitivity hypermetabolic bone and extra-osseous (nodal, visceral) foci.
- ✓ Extension workup/Staging: It is the most effective exam for searching for other locations, crucial for distinguishing a primary lymphoma (stage IE) from a secondary lymphoma (stage IV), which radically changes management.
- ✓ Biopsy guidance: Allows targeting the most accessible and active lesion for optimal sampling.

Biological diagnosis is an indispensable step complementary to imaging (MRI, PET-CT) and histological diagnosis (obtained by CT-guided vertebral biopsy). It is an essential pillar, not to establish the definitive diagnosis (which is histological), but to characterize the disease, assess its impact, guide treatment, and establish a prognosis. There is no specific biological marker for vertebral lymphoma. The workup combines standard tests, more specific lymphoma markers, and cerebrospinal fluid (CSF) analysis.

- Standard Biological Workup (Evaluation of General Condition and Impact): This workup is essential at admission and for follow-up.
- Complete Blood Count (CBC): May be normal in very localized forms (primary bone lymphoma). Looks for signs of diffuse medullary invasion: cytopenias (anemia, thrombocytopenia, neutropenia). Anemia is common in systemic disease or inflammatory syndrome. Lymphocytosis or the presence of atypical lymphocytes on morphological analysis can be a strong clue.
- Inflammatory Workup: Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP): Often very high, reflecting the inflammatory syndrome related to the tumor. A very high ESR is an orienting argument but is not specific.
- Liver and Kidney Function Tests: LDH (Lactate Dehydrogenase): A CAPITAL MARKER. Its elevation reflects tumor burden and cell lysis. It is a major prognostic factor integrated into prognostic scores (like the IPI - International Prognostic Index) [1]. It is frequently elevated in aggressive lymphomas. Alkaline phosphatases: May be elevated due to bone involvement. Creatinine: To assess renal function before administering potentially nephrotoxic chemotherapy (e.g., cisplatin) and for the risk of tumor lysis syndrome.
- Electrolyte Panel: Calcemia: Hypercalcemia can occur due to osteolysis and is a metabolic emergency. Phosphatemia, Kalemia, Uricemia: Essential for assessing the risk of tumor lysis syndrome, especially after initiation of effective chemotherapy.
- Specialized Biology and Tumor Markers: Serum Protein Electrophoresis: Looks for a monoclonal immunoglobulin (monoclonal peak) that could point to multiple myeloma, the main differential diagnosis of a lytic spinal bone lesion. Its absence is an argument against myeloma and supports lymphoma. Beta-2-Microglobulin: A non-specific marker of lymphoid proliferation and tumor burden. Its elevation is an unfavorable prognostic factor [1].
- Viral Serologies: HIV: Systematic, as immunosuppression is a major risk factor for lymphoma. Hepatitis B (HBV) and C (HCV) Viruses: Essential before any immunosuppressive treatment (chemotherapy). HBV reactivation under immunosuppressants can be fulminant and fatal. Screening and antiviral prophylaxis are mandatory if positive.
- Lumbar Puncture and Cerebrospinal Fluid (CSF) Analysis: To search for meningeal invasion by lymphomatous cells, even in the absence of neurological symptoms. Expected results: Cytology: Detection of lymphomatous cells (atypical large lymphocytes). Sensitivity is increased by cytocentrifugation technique. Biochemistry: Elevated protein levels; normal or decreased glucose. Immunophenotyping by flow cytometry: Detection of an abnormal B-lymphocyte population expressing specific markers (such as restricted kappa or lambda light chains), which is highly suggestive of meningeal involvement. Much more sensitive than cytology alone.
- Bone Marrow Biopsy (BMB): To rule out disseminated bone marrow invasion. This is crucial for disease staging. A primary vertebral lymphoma (Ann Arbor stage IE) is defined by involvement strictly localized to the spine without medullary invasion. The discovery of lymphomatous cells in the BMB changes the disease stage (stage IV) and therefore the therapeutic strategy and prognosis. It is usually performed at the posterior iliac crest.

Faced with a Destructive Vertebral Lesion, the Approach Must Be Systematic:

a. Initial workup: History, clinical exam, radiographs, spinal MRI, biological workup (CBC, ESR, CRP, LDH, serum protein electrophoresis).
b. Extension workup: PET-CT or thoraco-abdomino-pelvic CT scan to search for other locations or a primary.
c. Image-guided percutaneous bone biopsy: This is the key exam for a definitive diagnosis. It should be performed after ruling out spondylodiscitis (to avoid contaminating a healthy disc space). CT guidance ensures sampling in the most representative area.

d. Anatomopathological Analysis: Morphological analysis is complemented by immunohistochemistry (lymphoid markers: CD20, CD3, CD45, Ki67) which confirms the diagnosis of lymphoma (most often of B phenotype, CD20+) and excludes other diagnoses (cytokeratins for carcinomas, PS100 for melanomas, etc.).

Major Differential Diagnoses: The differential diagnosis is broad and can be categorized as follows:

1. **Infectious Pathologies:**

- Infectious Spondylodiscitis (Vertebral Osteomyelitis) (FIGURE 6) [2, 3, 4]**:**

Common Points: Inflammatory pain, fever, biological inflammatory syndrome, bone lysis on CT, enhancement on MRI, possible paravertebral collection.

Differentiating Elements:

Infection classically affects the disc space and adjacent vertebral endplates (disc space narrowing, disc hypersignal on T2). The paravertebral collection is often fluid/abscessed. The presence of a distant infectious focus is a clue. Guided biopsy for culture is diagnostic.

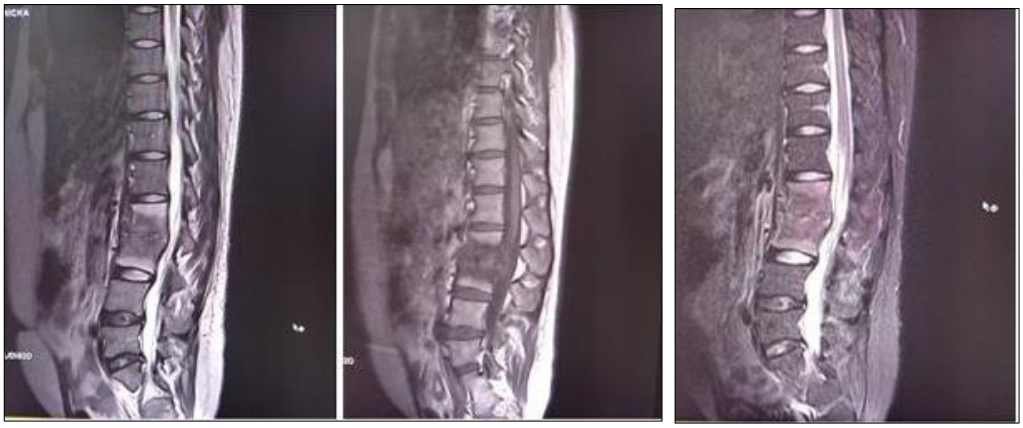


Figure 6: MRI in axial T1 gado, T2 and sagittal STIR and coronal T2 sequences showing an irregular L2-L3 pinching appearance, erosion of the vertebral endplates above and below, diffuse infiltration of the two L2-L3 vertebral bodies, with anterior epiduritis and a fine abscess of the anterior paravertebral soft parts

- Spinal Tuberculosis (Pott's Disease) (FIGURE 7):

Common Points: Vertebral lysis, formation of cold paravertebral and subligamentous abscesses that can extend distantly, soft tissue involvement.

Differentiating Elements:

Predilection for the thoracolumbar region. Significant destruction of vertebral endplates, multifocal and subligamentous involvement with distant extension. Presence of bone sequestra and a cold abscess with parietal calcifications. Disc involvement is more variable than in bacterial spondylodiscitis.

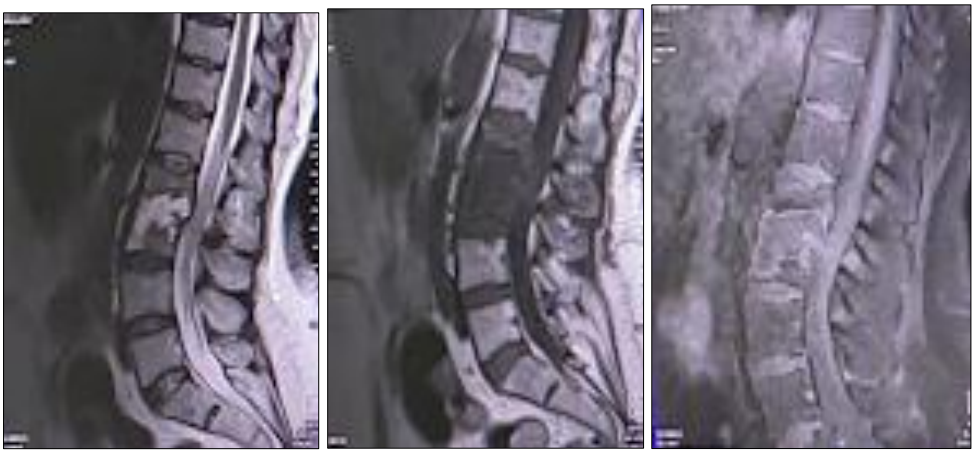


Figure 7: Tuberculous spondylodiscitis L2-L3 with disco-vertebral collections, destruction of L2-L3 vertebral bodies and retropulsion of the posterior wall without invasion of the epidural space

2. Primary Malignant Tumors

- **Vertebral Metastases (FIGURE 8)**

Common Points:

Bone lysis, vertebral collapse, pain, neurological compression. This is the most frequent differential diagnosis. Differentiating elements: Metastases are often multifocal. Searching for a primary (breast, lung, prostate, kidney, thyroid) is crucial. The "worm-eaten" appearance of the cortex is less frequent. MRI may show a more heterogeneous signal. Biopsy is often necessary to identify the origin.

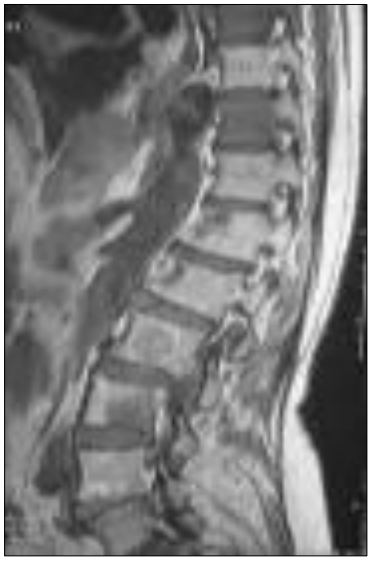


Figure 8: MRI in sagittal T2 sequence showing multiple osteolytic lesions in the context of spinal bone metastases

- **Multiple Myeloma (FIGURE 9):**

Common Points: Multiple "geographic map-like" lytic lesions without marginal sclerosis, bone pain, vertebral collapses.

Differentiating Elements:

Multifocal and diffuse involvement of the axial skeleton. Presence of a monoclonal gammopathy on serum and urine protein electrophoresis, renal failure, hypercalcemia. The tumor cells on pathology are dysplastic plasma cells.

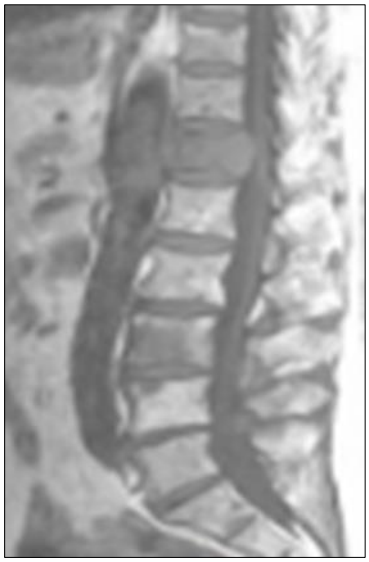


Figure 9: MRI in sagittal T1 sequence showing multiple osteolytic and nodular lesions on the spine in hyposignal, with diffuse involvement of D12 associated with retropulsion of the posterior wall without invasion of the epidural space

- **Ewing's Sarcoma / Primitive Neuroectodermal Tumor (PNET):**

Common Points: Small round blue cell tumor, bone lysis with a significant soft tissue mass, occurring in children and young adults.

Differentiating Elements: Frequent periosteal reaction (in "onion skin" or "spicules"). Age is a crucial factor. Diagnosis is confirmed by demonstrating the t(11;22) translocation in cytogenetics.

3. Benign Tumors and Pseudo-Tumoral Lesions:

- **Aggressive Vertebral Hemangioma (Figure 10):**

Common Points: Bone lysis, epidural or paravertebral extension, can cause neurological compression.

Differentiating Elements: Characteristic corduroy or polka-dotted appearance on radiography and CT (hypertrophy of vertical trabeculae). On MRI, frank T1 and T2 hypersignal (fatty and vascular content). Angiography may be useful.

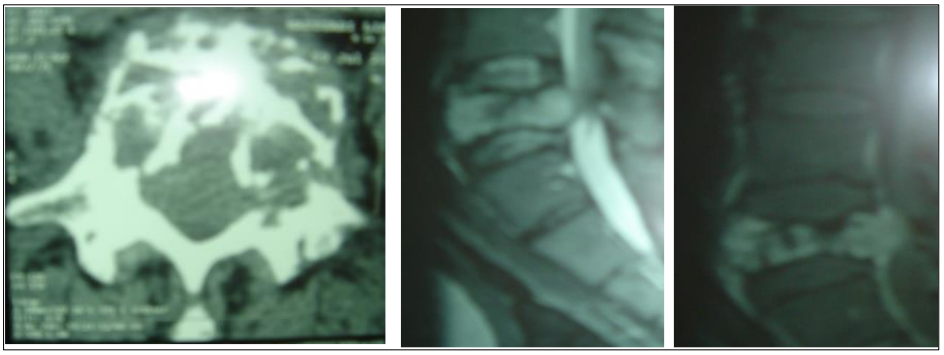


Figure 10: CT in axial section: L5 compression fracture with retropulsion of the posterior wall, honeycomb appearance. MRI in sagittal T2 and T1 gado sections: L5 compression fracture with hyperintense vertebra that enhances after gadolinium injection.

- **Eosinophilic Granuloma (Langerhans Cell Histiocytosis):**

Common Points: Geodic lytic lesion in children or young adults, can lead to complete vertebral collapse ("vertebra plana").

Differentiating Elements: Often a single, well-circumscribed lesion. Involvement of the vertebral body is typical, with disc preservation. The evolution is often benign.

The management of vertebral bone lymphoma is multidisciplinary (oncologists, radiotherapists, orthopedic or neurosurgeons) and depends on the patient's general condition, histological type, and local extent [1-5].

- Chemotherapy: This is the cornerstone of treatment. The most used protocol is R-CHOP (Rituximab + Cyclophosphamide, Doxorubicin, Vincristine, Prednisone), especially for DLBCL.
- Radiotherapy: Often used as a complement to chemotherapy, particularly to treat the vertebral lesion locally, consolidate the response, and relieve pain. It is also crucial in an emergency for spinal cord compression.
- Surgery: Its role is limited. It is mainly reserved for:
- Biopsy if percutaneous puncture is impossible or inconclusive
- Treatment of complications: nerve decompression in case of severe medullary compression and spinal stabilization (arthrodesis) in case of vertebral instability or fracture.
- Emergency treatment: Spinal cord compression is a medical-surgical emergency that may require high-dose corticosteroids, urgent radiotherapy, or surgical decompression.

The prognosis of vertebral lymphoma is generally better than that of other primary malignant bone tumors, as it responds very well to chemotherapy and radiotherapy [1-4]. Treatment response rates are high. The prognosis depends on factors such as age, general condition, precise histological type, the presence of B symptoms, and especially the existence or not of neurological signs at diagnosis. With modern protocols including Rituximab, 5-year survival rates can exceed 70-80% for localized disease.

CONCLUSION

Vertebral bone lymphoma is a great imitator whose diagnosis relies on a high clinical suspicion in the face of a destructive lytic vertebral lesion with a significant soft tissue component. Since no imaging sign is absolutely pathognomonic, the differential diagnosis is broad, including mainly metastases, infections, and myeloma. Percutaneous guided biopsy, with histological and immunohistochemical analysis, is the indispensable and unavoidable step to obtain a definitive diagnosis and initiate appropriate treatment, as primary bone lymphoma is a potentially curable pathology with chemotherapy.

Conflict of Interest: The authors declare that they have no conflict of interest.

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