Diffuse Large Cell Lymphoma, a different form of presentation

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1.Introduction

Diffuse large B cell lymphoma is the most common lymphoma and accounts for approximately 25 percent of all non-Hodgkin lymphoma. There is a male predominance with 55 percent of cases occuring in men; the median age presentation is 64 years old and incidence increases with age. Systemic "B" symptoms (fever, weight loss, drenching night sweats) are observed in 30 percent of patients, and the serum lactate dehydrogenase is elevated in over one-half.
Bone is the primary origin of the disease in only 1% of non-Hodgkin lymphoma, acounting for aproximatly 3% of all primary bone malignancies. Primary vertebral lymphoma presenting without sites of systemic involvement is exceedingly rare. Bony and epidural non-Hodgkin lymphoma has been described in small case series when it has involved the toracic and lumbar spine.

2.Case report

75-year-old white male.
Past medical history: arterial hypertension, type 2 diabetes mellitus, dyslipidemia, ischemic heart disease and chronic gastritis.

05/03/2013

Started with holocranial headache and right hemifacial hipostesia.
CT scan : frontal subcortical hypodensity compatibel with isquemic vascular disease not recent.

25/03/2013

Persistence of symptoms. Anorexia and vomiting not releted to food ingestion, weight loss of 4kg.
Diplopia:paresis of right V (V2 and V3) and left VI cranial nerve

In an atempted to make a lumbar punction, the patient had a vaso-vagal syncope. The ECG showed sinus bradicardia with 1st degree AVB and complet blocked of right bundle. He repeted 2 more episods of syncope and was diagnosed of central hypotiroidism.

Brain MRI showed infiltratives lesions, with replacement of bone marrow fat of clivus and probably the body of C2, characteresied by hipodensity in the sequence T1 and clival isointensity in T2 with enhancement after gadolinium administration. The hypophysis was enlarged and the left cavernous sinus tumescent.

08/04-19/04/2013
Admitted to Internal Medicine Department. He mainted headache aggravated with recumbency. Pain with distestesic characteristic in right V pair (V2 and V3), diplopia (VI left) and limitation of abduction of left eye. No other alteration in neurologic exame.
Physical examination:good general appearance. Hydrated and stained mucous. Afebrile. Normotensive. Cardiac and Pulmonary auscultation: no alteration. Abdomen: soft, pitting, painless. No organomegaly or palpable masses. No lymphadenopathy.

Hemoglobyn	11 g/dl (13.5-17)
VGM	83 fl (81,8-95,5)
HGM	29,7 pg (27-32,3)
LDH	259 U/L (87-241)
VS	41 (elevated)
BK cultural gastric aspirate	Negative
Tuberculin test	Negative
T4L	0,64 ng/dl (0,76-1,46)
TSH	0,219 uUI/ml (0,358-3,74)
Testosterone	105,24 ng/dl (241-827)
Cortisol	4,21 ug/dl (4,3-22,4)
B2 Microglobulin	2071 ng/dl (1090-2530)
Serum protein electrophoresis	No alterations
Total calcium	8,3 mg/dl (8,8-10,1)
ACE	7 U/L (8-55)
PSA	1,36 ng/ml (<4,0)
ANA	Nonreactive
ANCA	Negative
HIV, HVC and HVB	Negative

Upper gastrointestinal endoscopy	Normal
Lower gastrointestinal endoscopy	Normal
Gastric blind biopsy	Negative
Body CT	Normal
Lumbar punction	Spinal liquor showed no alterations
18-FDG PET	Exposed foci of hypermetabolism in the clivus, C2, D1, D4 and D9 vertebrae; right side pterygoid muscle; lateral aspect of the fourth left costal arch and proximal shaft of diaphysis of the right humerus, with suspicion of neoplastic etiology, although the hypothesis of granulomatous disease could not be excluded
Biopsy of the body of the 9th dorsal vertebra	Performed by an interventional neuroradiology team with histology confirming the diagnosis of diffuse lymphoma of large B cells, bcl2 negative with CD45+, CD3- CD20+ imunohistochemical profile
Myelogram	No changes in the three hematopoietic lines

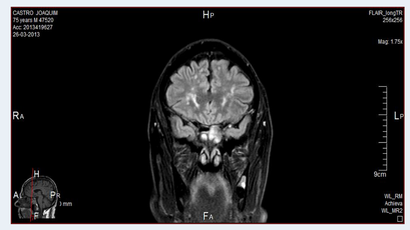

Figure 1: Brain MRI

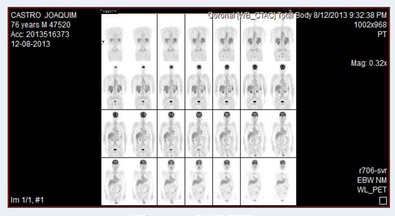

Figure 2: PET

During the hospitalization, at 15/04, his condition worsened with symptoms compatible with achieving cochlear's nerve with gait instability. He kept headache and neurological deficits with evidence of disease progression with involvement of V1 and possibly IX pair and altering proprioception.

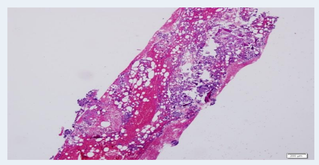
Figure 3: Histology Lymphoma diffuse large B cell

Diagnosis of primary bone lymphoma-diffuse large B cell, extended to CNS, in stadium: IVB IPI-High (weight loss,age, ECOG, Stadium, LDH and local extra-nodal)

Treatment : 6 cycles of R-CHOP-14 CNS and intrathecal prophylaxis of Central Nervous System with MTX and prednisolone
Proposed to consolidation with RT due to local bone foci positive in the evaluation of PET at the end of 3th cycle (Clivus, C2, D1, D4, D9 and right humerus).

Clinically at this time:
The patient showed improvement of neurological symptoms with reversal of diplopia and right hemifacial hypoesthesia improvement. He regained improving gait, moves alone without vertigo.

3. Discussion and Conclusion

- Almost 85% of NHLs are of B-cell origin. Although this type of lymphoma usually starts in lymph nodes, they may as well appear as extranodal disease, arising, most often, from the gastrointestinal tract. Primary bone lymphoma with neurologic presenting symptoms is rarely reported in literature. The site of the tumor only is a significant prognosis when the skull is afected, because of the risk of central nervous system lymphoma due to direct extension into the brain.
- The diagnosis is made by excisional tissue biopsy, most commonly a lymph node. This case shows the diagnosis challenge often posed by atypical forms diseases.
- The prognositic in this stadium and with this treatment at 30 months is 50% for event-free, 56% for progression-free and 59% of overall survival.
- Multidisciplinary assessment of this patient was essential for a rapid diagnostic and treatment intervention, ensuring the best clinical prognosis possible.

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