Lymphome Hodgkinien révélé par un syndrome vestibulaire périphérique inhabituel

Hodgkin's lymphoma presenting with an unusual horizontal Nystagmus and vertigo

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RÉSUMÉ

Les syndromes neurologiques paranéoplasiques sont rares et difficiles à diagnostiquer du fait qu'ils précèdent souvent le diagnostic oncologique. Le lymphome hodgkinien est associé à plusieurs syndromes paranéoplasiques dont la dégénérescence cérébelleuse et la dermato/polymyosite. Le syndrome vestibulaire périphérique est exceptionnellement d'origine paranéoplasique. Nous rapportons le cas d'un patient de 52 ans sans antécédents notables ayant présenté un vertige avec nystagmus, nausées et amaigrissement. La recherche étiologique a révélé un lymphome hodgkinien (forme scléro-nodulaire) avec des anticorps onco-neuronaux négatifs, rendant le diagnostic un réel défi pour les cliniciens. La chimiothérapie, la radiothérapie et la rééducation vestibulaire ont permis l'amélioration du patient. Le syndrome vestibulaire périphérique peut être la seule manifestation paranéoplasique du lymphome hodgkinien entrainant ainsi un véritable défi diagnostique pour les cliniciens. La chimiothérapie et la radiothérapie comme traitement de la maladie sous-jacente est d'un grand bénéfice si celle-ci est démarrée le plus tôt possible.
Mots clés : vertige, paranéoplasique, syndrome vestibulaire périphérique, malignité, Lymphome d'Hodgkin.

SUMMARY

Neurological presentation of paraneoplastic syndromes is rare. They are often difficult to diagnose, especially when they precede the diagnosis of cancer. Hodgkin's lymphoma is associated with several paraneoplastic neurological syndromes such as cerebellar degeneration and dermato/polymyositis. Peripheral vestibular syndrome is uncommon presentation of these paraneoplastic syndromes. We report the case of a 52-year-old man with no prior medical history who presented to the otolaryngology clinic with vertigo precipitated by nystagmus, nausea and weight loss. Diagnostic workup revealed a nodular sclerosing variant of Hodgkin's lymphoma without paraneoplastic antibodies. The patient's symptoms resolved after institution of chemotherapy, radiotherapy and vestibular rehabilitation. Hodgkin's lymphoma has been reported to be associated with many paraneoplastic syndromes with neurological presentation in which peripheral vestibular syndrome is an uncommon one. Sometimes it can be the only presenting symptom of an unknown Hodgkin's lymphoma. This create a real diagnostic challenge for clinicians specially when paraneoplastic antibodies are negative. Chemotherapy and radiotherapy as treatment of the underlying disease is of a big benefit if started as early as possible.
Keywords: vertigo, paraneoplastic, peripheral vestibular syndrome, malignancy, Hodgkin's

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INTRODUCTION

Hodgkin's lymphoma is associated with multiple paraneoplastic neurological syndromes of which cerebellar degeneration is the most characterized one (1). Association with vertigo is exceptional and sometimes it can be the only presenting feature of an underlying Hodgkin's lymphoma posing a diagnostic challenge. We present a rare case of a 52-year-old Moroccan man who presented with a peripheral vestibular syndrome and was diagnosed after a thoroughly clinical workup with nodular sclerosing Hodgkin's lymphoma.

CASE REPORT

A 52 Years old man with no prior medical history presented to the otolaryngology department for progressive onset vertigo, vomiting, blurred vision and gait disturbance ongoing for 3 weeks with fever, fatigue, night sweats and weight loss. A physical examination revealed right jugular and supraclavicular lymph nodes measuring 2 cm for the larger one. The vestibular examination revealed spontaneous right-beating nystagmus with horizontal and torsional components in primary position and changing sense gaze to the right and the left. The oculomotor examination under videonystagmography revealed saccadic pursuit, abnormal saccades and optokinetic nystagmus contrasting with normal caloric test. Audiological examination was normal. Neurological examination revealed an ataxic gait and multidirectional Romberg without sensitive or motor deficits, compatible with a peripheral vestibular syndrome.

Cerebral magnetic resonance imaging (MRI) was normal and cerebrospinal fluid (CSF) analysis revealed a white count of 7, normal glucose level of 91mg/dL, discrete hyperproteinorachia (74mg/dL). CSF tested negative for malignant cells, oligoclonal bands, and viral titers. Paraneoplastic antibodies were negative in the serum. Additional laboratory testing revealed inflammatory anemia and negative infectious investigation including a complete blood count and serologic tests for hepatitis, VIH, Syphilis and Lyme disease. Complete metabolic panel including thyroid function, vitamin B12, folates was normal. Cervical Computed tomography (CT) scan revealed multiple cervical lymph nodes measuring 5.8 cm for the larger one. A computed tomography scan of chest and abdomen to search for any mediastinal or profound abdominal pathology revealed mediastinal lymphadenopathy measuring 1.7×1.3cm. An excisional cervical lymphadenectomy with histological examination was positive for nodular sclerosis Hodgkin's lymphoma with Reed-Sternberg cells and CD15, CD30 positivity (fig.1).

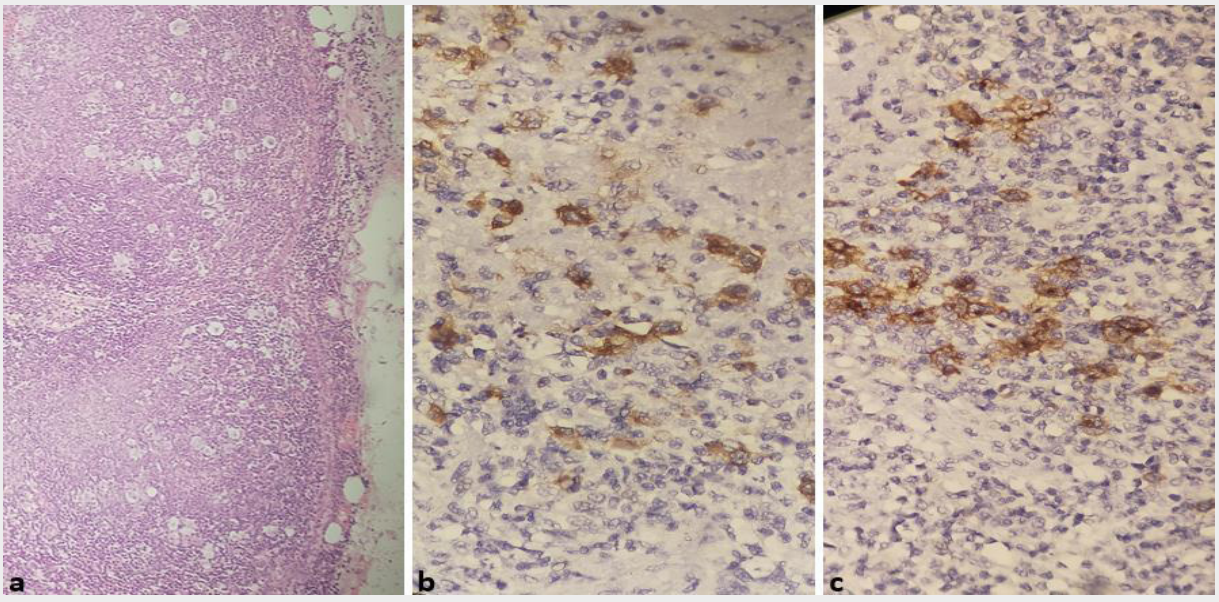

Figure 1. a- Microphotography showing Hodgkin Lymphoma, Nodular Sclerosis with Reed-Sternberg Cells and lacunar tumor cells in a background infiltrate composed of eosinophils, lymphocytes, plasma cells, and histiocytes.b- Immunohistochemistry: tumor cell are positive for CD 15 c- Immunohistochemistry: tumor cell are positive for CD 30

Bone marrow biopsy did not detect lymphoid infiltration. Stage IIB of Hodgkin lymphoma was confirmed. Repeated imaging with brain MRI was unrevealing. Patient was treated with ABVD protocol (Bleomycin-Dacarbazine, Doxorubicin and Vinblastine bleomycin, doxorubicin, vinblastine and dacarbazine) after implantation access device, achieving complete resolution of the presenting symptoms. Two months later, the vestibular syndrome progressively improved with vestibular rehabilitation and physiotherapy sessions. He progressively improved his neurological symptoms gaining independent and stable gait. He achieved complete haematological remission evaluated by positron emission tomography scan after completion of four cycles of chemotherapy and radiotherapy IF 30 Gy.

DISCUSSION

Our case illustrates the importance of considering a diagnosis of paraneoplastic syndrome in a patient with unexplained peripheral vestibular syndrome. Several malignancies, including small cell lung cancer, testicular germ cell tumours, adenocarcinoma, and pancreatic cancer have been associated with paraneoplastic vertigo and nystagmus (2). In fact, paraneoplastic syndromes are seen in association with 4% to 5% of solid cancers while they are rarely associated to Hodgkin and non-Hodgkin's lymphomas (1). Central nervous system involvement in Hodgkin's lymphoma is extremely rare with an incidence of approximately 0.02% (3). In Hodgkin's lymphoma, neurological paraneoplastic syndromes are dominated by cerebellar degeneration, acute inflammatory demyelinating polyneuropathy (Guillain-Barré), Chronic inflammatory demyelinating polyneuropathy, chorea and ataxia, subacute sensory neuropathy, motor neuron disease, myasthenia gravis, stiff person syndrome and brachial neuropathy (4). The most common neurological syndrome described in the literature is subacute cerebellar degeneration with more than 50 cases reported (4,5).

The pathophysiology of these paraneoplastic syndromes has been linked to antibodies production stimulated by tumor antigens that consequently target the neuronal antigens, causing several clinical syndromes. Antibodies associated with paraneoplastic nystagmus, vertigo and encephalitis include anti-Ta, anti-Ma, anti-Yo, anti-Hu anti-Purkinje cell antibody, and may be isolated from the serum and CSF (6). In some cases, antibody testing can be negative as in our case. Therefore, cerebrospinal fluid testing is recommended. Seronegativity of antibodies can be explained by the fact that there are antibodies not discovered yet (7).

Paraneoplastic vertigo and nystagmus have been reported but usually does not occur as an isolated finding. It mostly happens in association with other neurological syndromes such as cerebellar degeneration. The physiopathology of nystagmus or vertigo, even in the presence of autoantibodies, is unknown. In many cases of paraneoplastic syndromes, antibody testing is however negative (8,9,10,11).

In our case, vertigo and horizontal nystagmus were miming peripheral vestibular symptoms. The oculomotor abnormalities on videonystagmography and changing sense gaze nystagmus with ataxia were in favour of peripheral origin justifying complete neurological workup.

The presence of concomitant cancer and symptoms improvement after cancer treatment is consistent with paraneoplastic syndrome. Indeed, after the diagnosis of Hodgkin's lymphoma, the patient benefited from chemotherapy (Adriamycin, Bleomycin, Vinblastine and Dacarbazine) associated to radiotherapy IF 30 Gy as adjuvant. After completing four cycles of chemotherapy regimen with radiotherapy, neurological symptoms improved gradually. The patient is fully independent with stable gait and no handicapping symptoms. After 2 years follow-up, complete remission has been achieved with negative positron emission tomography scan.

The majority of neurological paraneoplastic syndromes are proven to be immune-mediated which justify that the treatment of the underlying tumour is the basis of symptoms treatment. Two general approaches to therapy are recommended: removal of the antigen source by treatment of the underlying malignancy and suppression of the immune response by introducing steroids and immunotherapy. Vetter et al stated that prompt oncologic treatment and immunotherapy can be beneficial, especially if initiated as earlier as the time of symptom progression rather than later when deficits have been fully installed (3). Prognosis is generally better in young patients with early stages tumours.

CONCLUSION

Many paraneoplastic neurological syndromes have been described in association to Hodgkin's lymphoma but peripheral vestibular syndrome is a very rare presentation. Seronegativity for paraneoplastic antibodies should not delay diagnosis and treatment of paraneoplastic neurological syndromes. Indeed, the cornerstone of treatment is adequate management of the underlying malignancy.

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