

Isolated multiple neuropathy as clinical manifestation of leukemia relapse

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Introduction. Neuroleukemia is a rare disorder of the peripheral nervous system due to leukemic cell infiltration.

Case report. We present the case of a 34-year-old patient with history of acute myelomonoblastic leukemia in remission that presented progressive paresis of the right median, bilateral facial, and left peroneal nerves. The electromyogram confirmed the diagnosis of multineuropathy. A PET-CT showed hypermetabolism of both sciatic, facial, and right median nerves. A bone marrow aspirate confirmed the leukemia relapse so a new round of chemotherapy was performed with improvement of the neurological deficit.

Conclusion. Peripheral nervous system infiltration by leukemic cells can mimic multiple syndromes depending on the structures involved. The nerve-blood barrier acts as a defense of leukemic cells against chemotherapy and the immune system. Thus, the peripheral nervous system constitutes a reservoir of leukemic cells. Neuroleukemia should be considered in patients with history of acute leukemia who have isolated symptoms of the peripheral nerve.

Key words. Leukemia. Leukemia relapse. Lymphoma. Multineuropathy. Multiple mononeuropathy. Neuroleukemiosis.

Introduction

Neuroleukemiosis is a rare affection of the peripheral nervous system by the infiltration of leukemic cells. One of its forms of manifestation is as isolated multineuritis. We present a case of multineuritis due to neuroleukemiosis in a patient with a treated mielomonoblastic acute leukemia.

Case report

A 34-year-old woman with history of mielomonoblastic acute leukemia treated with chemotherapy and allogeneic hematopoietic stem cell transplantation in remission phase for three months ago. She presented to the neurological service with progressive right-hand paresthesia, left facial numbness and gait impairment due to left feet palsy. Neurophysiological examination confirmed a multineuritis involving right median, left facial and both peroneal nerves. A first bone marrow aspirate and lumbar puncture ruled out a systemic or central nervous system leukemia relapse. A sural nerve biopsy was normal. It was oriented as an alloimmune phenomena in relation to hematopoietic transplantation and the immunosuppressive treatment was in-

creased. However, the patient presented a progressive clinical worsening.

On physical examination two months later, bilateral preauricular masses were noted. A facial MRI study showed large bilateral laterocervical masses that infiltrate the parotid glands, and a thickening of the left facial nerve. An ultrasound-guided parotid biopsy showed infiltration by monocytes morphologically suggestive of malignancy (Fig. 1). Virus varicela zoster, human herpes simplex virus 2, parotitis and parvovirus active infection were discarded. A PET-CT showed hypercaptation of sciatic nerves, facial nerves and right median nerve (Fig. 2).

A new bone marrow aspirate confirmed a systemic leukemia relapse. A new lumbar puncture ruled out central nervous system infiltration. The patient was treated with a new chemotherapy schema including cytarabine, fludarabine and mitoxantrone with an improvement of the neurologic deficit.

Discussion

Neuroleukemiosis can simulate multiple pathologies of the peripheral nervous system depending on the structure it affects. However, it has only been described in a few cases [1,2]. Neuroleukemiosis

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Figure 1. Bilateral laterocervical masses that infiltrate the parotid glands (a) with contrast-enhancing (b).

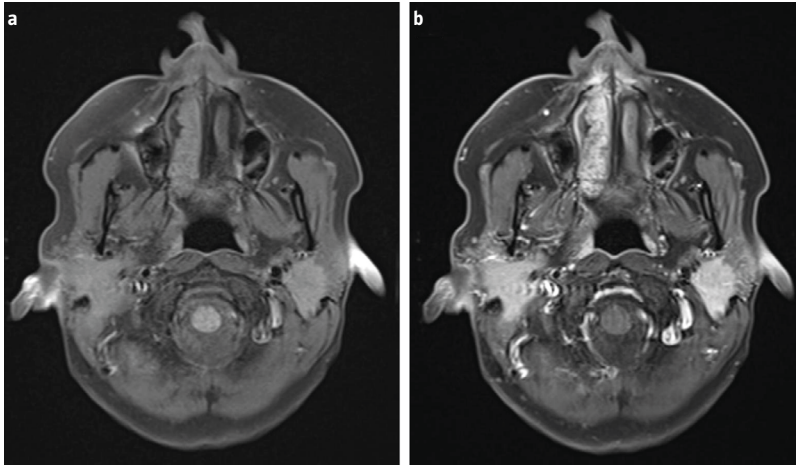
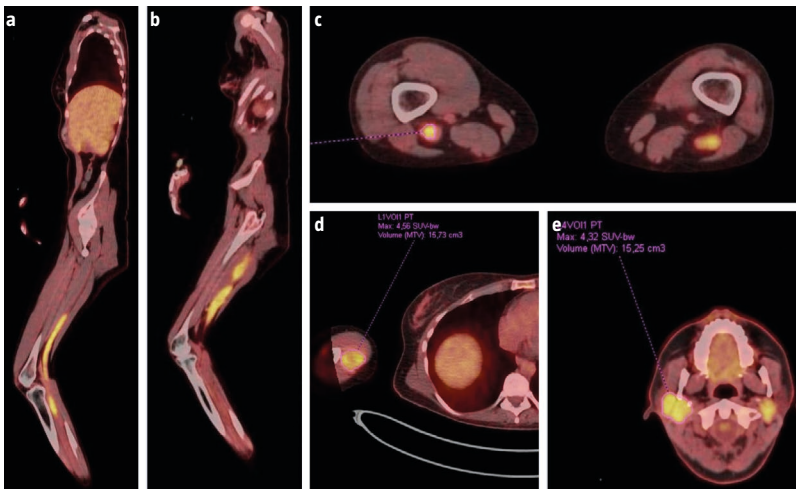


Figure 2. FDG uptake in the facial nerves (a), right median (b) and right (c), and left (d) sciatic-tibial nerves (e).



has been described in all types of leukemia, including some cases of lymphoma, in which case it is known as neurolymphomatosis [1]. It has been more frequently described in acute myeloid leukemia, especially monocytic or monoblastic.

It is suspected that the leukemic infiltration occurs because the blood-nerve barrier acts as a defense for leukemic cells against chemotherapy and immune system [1,2]. Since the peripheral nervous

system could act as a ‘reservoir’ for leukemic cells, neuroleukemiosis usually presents as a form of disease relapse months or years after remission. Nevertheless, it can also appear during the acute phase or even as the first manifestation [1,3].

Another theory suggests that it is produced by direct dissemination from the central nervous system through cerebrospinal fluid or the leptomeninges, since it rarely occurs without its involvement [2]. However, in this case two lumbar puncture ruled out central nervous system infiltration.

Neuroleukemiosis as a form of extramedullary leukemia relapse predicts a poor long-term prognosis although in the absence of bone marrow involvement it has a better short-term prognosis. In absence of systemic involvement, local treatment with radiotherapy can be performed with good response. In presence of systemic relapse, a chemotherapy regimen that contains agents capable of crossing the blood-nerve barrier is required [1,2]. Neurological prognosis is uncertain, with described cases of complete recovery after treatment [1,3].

Differential diagnosis of neuroleukemiosis is made with infectious complications, vasculitic neuropathy, chemotherapeutic neurotoxicity, Guillain-Barré syndrome and paraneoplastic neuropathies [1,4].

In patients who have received a hematopoietic stem cell transplant, the possibility that it is a manifestation of graft versus host disease could be taken into account. Peripheral nervous system involvement by graft versus host disease is very rare, affecting less than 5% of patients during the first year [4]. It often mimics other autoimmune diseases, including polyneuropathy, plexopathy, myasthenia gravis, or myositis [5,6]. Multineuritis has never been described as a form of graft versus host disease. If suspected, must take into account that neurological graft versus host disease can only be diagnosed if the patient has involvement of other organs and other causes of the pathology have been ruled out [4,5].

In conclusion, symptoms suggestive of peripheral neuropathy in leukemia patients should be considered as a ‘red flag’ even in the remission phase. If neuroleukemiosis is confirmed, central nervous system involvement and systemic relapse must be ruled out.

References

- Mau C, Ghali MGZ, Styler M, Malysz J, Specht CS, Rizk E. Neuroleukemiosis: diagnosis and management. *Clin Neurol Neurosurg* 2019; 184: 105340.
- Wang T, Miao Y, Meng Y, Li A. Isolated leukemic infiltration of peripheral nervous system. *Muscle Nerve* 2015; 51: 290-3.

3. Reddy CG, Mauermann ML, Solomon BM, Ringler MD, Jerath NU, Begna KH, et al. Neuroleukemiosis: an unusual cause of peripheral neuropathy. *Leuk Lymphoma* 2012; 53: 2405-11.
4. Barba P, Piñana JL, Valcárcel D, Querol L, Martino R, Sureda A, et al. Early and late neurological complications after reduced-intensity conditioning allogeneic stem cell transplantation. *Biol Blood Marrow Transplant* 2009; 15: 1439-46.
5. Grauer O, Wolff D, Bertz H, Greinix H, Köhl JS, Lawitschka A, et al. Neurological manifestations of chronic graft-versus-host disease after allogeneic haematopoietic stem cell transplantation: report from the Consensus Conference on Clinical Practice in chronic graft-versus-host disease. *Brain* 2010; 133: 2852-65.
6. Kraus PD, Wolff D, Grauer O, Angstwurm K, Jarius S, Wandinger KP, et al. Muscle cramps and neuropathies in patients with allogeneic hematopoietic stem cell transplantation and graft-versus-host disease. *PLoS One* 2012; 7: e44922.

Neuropatía múltiple como manifestación clínica de una recidiva de leucemia

Introducción. La neuroleucemiosis es una rara enfermedad del sistema nervioso periférico producida por la infiltración por células leucémicas.

Caso clínico. Presentamos el caso de una paciente de 34 años con antecedente de una leucemia mielomonoblástica aguda en remisión, que presentaba una parálisis progresiva del nervio mediano derecho, del facial bilateral y del peroneo izquierdo. El electromiograma confirmó el diagnóstico de una neuropatía múltiple. La tomografía por emisión de positrones-tomografía computarizada mostró un hipermetabolismo de ambos nervios ciáticos, facial bilateral y mediano derecho. La biopsia de médula ósea confirmó la recidiva de la leucemia, por lo que se inició un nuevo ciclo de quimioterapia con mejoría de los déficits neurológicos.

Conclusión. La infiltración del sistema nervioso periférico por células leucémicas puede simular múltiples síndromes neurológicos dependiendo de las estructuras afectadas. La barrera hematonerviosa actúa como defensa de las células leucémicas contra la quimioterapia y el sistema inmunitario, por lo que el sistema nervioso periférico constituye un reservorio de las células leucémicas. Por ello, la neuroleucemia debe considerarse en pacientes con antecedentes de leucemia que presenten síntomas aislados de afectación del sistema nervioso periférico.

Palabras clave. Leucemia. Linfoma. Mononeuropatía múltiple. Multineuropatía. Neuroleucemiosis. Recurrencia de leucemia.