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Case report

Square-wave jerks and smooth pursuit impairment as subtle early signs of brain involvement in Langerhans' cell histiocytosis

Evangelos Anagnostou [a,b,*], Sokratis G. Papageorgiou [a], Constantinos Potagas [a], Theodoros Alexakis [a], Nikolaos Kalfakis [a], Dimitri Anastasopoulos [b]

[a] *Department of Neurology, Eginition Hospital, University of Athens, Greece*
[b] *Department of Physiology, Dizziness and Balance Unit, School of Nursing, University of Athens, Greece*

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Abstract

Central nervous system (CNS) involvement in Langerhans' cell histiocytosis (LCH) has been described as a progressive neurological disorder marked by motor and cognitive decline. Detailed analysis of ocular motor abnormalities is lacking. We report on a 60-year-old male with histologically confirmed LCH who developed oscillopsia and gait ataxia over a 1-year period. Eye movements recorded with infrared oculography revealed a high rate of square-wave jerks (SWJ) with frequencies of 41 min^{-1} on average and amplitudes between 1° and 7°, as well as marked impairment of smooth tracking of sinusoidally moving targets. Furthermore, static posturography disclosed increased body sway, with an abnormally high sway path. The initial brain MRI was unremarkable. Due to the presumed cerebellar dysfunction we performed a second MRI 1 year later that disclosed deep cerebellar lesions compatible with LCH relapse within the CNS. The abnormal high SWJ rate and the impaired smooth pursuit performance correctly heralded later involvement of the cerebellum anticipating lesion appearance in the MRI.

Keywords: Langerhans' cell histiocytosis; Square-wave jerks; Smooth pursuit; Early signs; Cerebellum; Neuroophthalmology

1. Introduction

LCH is a rare disease caused by uncontrolled clonal proliferation of Langerhans' cells. CNS involvement is even less common and less well studied [4]. The hypothalamic–pituitary manifestations usually expressed as diabetes insipidus are well known, whereas other CNS disorders are reported only anecdotally in small series [5]. The only published observation of ocular motor dysfunction in the presence of LCH refers to a circumscribed unilateral abducens nucleus lesion caused by a single tumour-like abnormality lying adjacent to the fourth ventricle [6]. However, this case was based on CT scans, leaving the possibility of further parenchymal lesions detectable on MRI open.

2. Case report

A 60-year-old man was referred with a mild unsteadiness of gait and slurred speech. The patient had presented 10 years ago with localized pain on the right portion of the skull, as well as with severe polyuria and polydipsia due to diabetes insipidus, without any neurological symptoms. Osseous cranial imaging revealed a solitary mass in the right temporal bone adjacent to the mastoid process. After surgical resection, histopathological examination established the diagnosis of LCH. In particular, the microscopical examination (Dr. Orlowska-Volk, Institute of Pathology, University of Freiburg, Germany) revealed granulamatous tissue containing numerous eosinophils, lymphocytes and mononuclear cells. Some of them were typical Langerhans' cells with a histiocytic appearance and reniform nuclei. Immunohistochemical stains were positive for the CD1a, CD68 and S100 antigens. Furthermore, all histiocytic elements were immunoreactive for MAC387. Low dose (30 Gy) radiation

* Corresponding author at: 8 Tetrapoleos Street, 11527 Goudi, Athens, Greece. Tel.: +30 2107489306; fax: +30 2107713366.
E-mail address: anevan@vivodinet.gr (E. Anagnostou).

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therapy was administrated for the following 6 months, and the patient remained asymptomatic thereafter.

On admission, a slight impairment of the articulation of consonants, and a slight difficulty in walking and occasional involuntary eye movements were noted. The latter were initially misinterpreted as "horizontal nystagmus". Finger-to-nose, heel-knee-shin as well as rapid alternating movements were unremarkable. Muscle strength and sensory examination were also normal. Deep tendon reflexes were brisk and symmetrical, whereas plantar responses were equivocal on both sides. The patient described momentary movements of the visual environment, occurring when he turned his head while driving a car.

Eye movement recordings were performed with the patient seated on a Barany chair in the center of a cylindrical screen of 160 cm radius. His head was stabilized by means of a dental bite-board attached to a head holder. A laser spot-target, subtending 0.2° of visual angle, was projected onto the screen. A laboratory computer controlled the Barany chair servomotor, as well as the laser spot mirror galvanometer (for details see [1]). Horizontal eye movements were recorded using an infrared corneal reflection device, A/D converted at 200 Hz with 12-bit resolution and a passband extending from dc to 70 Hz.

Equilibrium was quantified by means of static posturography. The patient stood quietly on a Kistler® platform mounted on four piezoelectric force transducers, each of which measured forces in three main directions. First, an "eyes open" condition was carried out, followed by an eyes closed condition, each lasting 60 s. Data were sampled at 50 Hz with 12-bit resolution and passed off-line through a 20 Hz low pass filter. Body sway was assessed in terms of the displacement of the center of pressure (COP), which is the point location of the vertical ground reaction force vector [2]. A special algorithm was written to calculate the sway path, i.e. the length of the path described by the COP in a given time interval (60 s in this case), which is derived from the sum of the planar distances between two consecutive sampling points [3].

Continuous SWJ were recorded during straight ahead fixation as well as after removal of visual cues (Fig. 1A). The average frequency of occurrence was 40.8 min^{-1} and remained unchanged after turning the fixation spot off. In the latter case, however, prolonged off-center fixation periods were demonstrated making square-wave intrusions appear wider. Moreover, a tendency for higher amplitudes was noted, giving rise to a small number of intrusions greater than 5°. Nystagmus was not present.

The second significant finding of the testing procedure was a marked disturbance of smooth pursuit eye movements in both directions (Fig. 1B). The deficit was obvious even at low-velocity sinusoidal target movement at 0.1–0.2 Hz. The waveforms consisted of intermingled catch-up saccades, short pursuit intervals of low gain, as well as continuously appearing SWJ. Visual suppression of the VOR was clearly pathological showing in phase eye and head movements. The rest of the oculographic examination, including visually guided saccades, VOR and head-shaking, did not reveal any abnormalities.

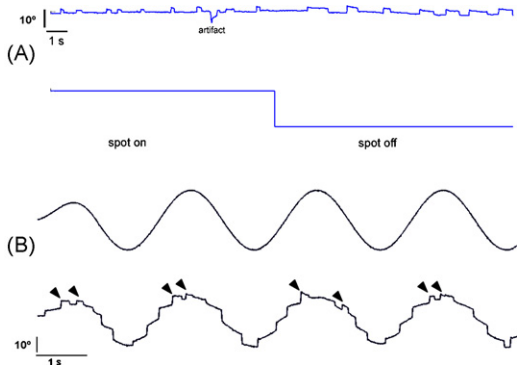

Fig. 1. (A) Continuous SWJ during straight ahead fixation as well as after removal of visual fixation. The average frequency of occurrence was 40.8 min^{-1} and remained unchanged after turning the fixation spot off. In the latter case, however, prolonged off-center fixation periods were demonstrated making square-wave intrusions appear wider. Moreover, a tendency for higher amplitudes was noted, giving rise to a small number of SWJ greater than 5°. (B) Smooth pursuit eye movements tested with sinusoidal target displacement (upper trace) at 0.4 Hz. Typical pathological staircase appearance of smooth eye tracking (lower trace) due to numerous catch-up saccades. The deficit was even more obvious at higher target velocities (not shown). Notably, SWJ continue to occur during smooth pursuit (arrowheads).

Posturographic testing disclosed a marked unsteadiness with increased fore-aft and lateral body sway reflected in pathologically increased values of sway-path scores (Fig. 2).

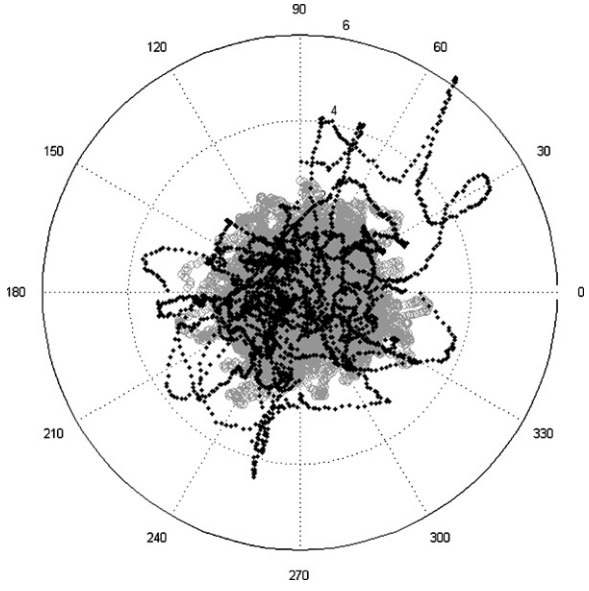

Fig. 2. One-minute force platform balance recording with eyes closed. Polar plot of COP excursions (anterior = 90°, right = 0°). Each point represents the head of a vector (corresponding to a COP excursion) starting from (0 cm, 0°). The black cloud (foreground) shows the patient's COP excursions during a 1-min recording, whereas the grey cloud is obtained from 1-min excursions of 25 healthy controls. The graph demonstrates the pathological body sway of the patient, more obvious in the anterior–posterior direction: total 1-min sway path = 229.536919 [normal values (mean ± 2 S.D.): 160 ± 30.08], lateral sway path = 117.720185 [92 ± 24.40], anterior–posterior sway path = 171.489066 [110 ± 22.20].