described that would distinguish this variation of PLMT from the normal form of PLMT and researchers still do not know why some cases are painless. Since other similar processes were ruled out (including segmental spinal myoclonus, focal dystonia due to peripheral trauma, atypical forms of restless legs syndrome, tardive dyskinesias due to neuroleptic drugs, and focal forms of axonal hyperexcitability), these cases were included within PLMT syndrome. This leads us to believe that they are central in origin and often caused by peripheral trauma, although cases may of course be idio-pathic. In the first case, PLMT appeared after a soft tissue lesion with arthritis and cellulitis due to a gout flare-up. In the second case, the patient had suffered a spinal injury long before developing symptoms, and faint signs of post-traumatic myelopathy were revealed by the examination. However, we cannot provide a solid explanation for the onset of PHMF 25 years after that event. We were able to clinically observe a myoclonic component in the second case, which led us to consider segmental myoclonus due to spinal cord injury as an alternative diagnosis. Nevertheless, continuous movement of the fingers was the patient’s most noticeable symptom. Another alternative diagnosis could be an atyp-ical form of restless legs syndrome (restless hands in this case) based on patient using voluntary hand movements in an attempt to make involuntary movements disappear. However, we should not forget that restless legs syndrome is basically a sensory dysfunction that causes patients to move their limbs in order to relieve this perceived discomfort. The opposite situation exists in our case: the patient suffers an involuntary movement giving rise to discomfort (not pain) which the patient tries to relieve by moving her limbs. Therefore, no sensory component is involved in this process. Researchers have described patients with PLMT as responding poorly to treatment. There are so few cases of the painless variation of PLMT (P-LME) that we are unable to draw conclusions, except to state that in our experience, painless cases are easier to treat. The first case required no treatment, and in the second, the patient decided not to take any further medications after having tried several drugs and weighing their benefits against the adverse effects.

In conclusion, we wish to highlight that much remains to be learned about the mechanisms involved in this syndrome. It also remains to be seen whether or not the painless variation (PLME) can be classified as a subtype of PLMT or if it is actually another movement disorder that we have been unable to diagnose correctly.

References


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Primary cerebral lymphoma with spontaneous remission†

Linfoma cerebral primario con remisión espontánea


Dear Editor:

Primary central nervous system lymphoma (PCNSL) is a frequent type of non-Hodgkin lymphoma which affects the brain, eyes, spinal cord, and leptomeninges, with no evidence of other regions being affected at the time of diagnosis.1 PCNSL accounts for 3% of all primary brain tumours. The main signs and symptoms are papilloedema, headache, paresis, and convulsions.2 Spontaneous remission of PCNSL without administration of corticosteroids is rare3–5 and gives rise to diagnostic problems. We present the case of
an immunocompetent man aged 65 years with focal neurological signs and multiple cerebral lesions who experienced initial spontaneous remission of both clinical symptoms and pathological signs in MRI images, and whose final diagnosis of PCNSL was determined by autopsy.

A male patient aged 65 years visited the emergency department due to dizziness and vertigo with acute onset a week before the visit and progressively worsening symptoms which responded poorly to vestibular sedatives.

His personal history included a pulmonary thromboembolism 2 years before which required treatment with acenocoumarol for 6 months. Upon admission he was not taking any regular medications.

In the emergency department, neurological examination only showed mild gait instability. Cranial CT scan revealed a right frontal hypodense focus affecting the corpus callosum and reaching the contralateral hemisphere, with no enhancement after administration of intravenous contrast. T2-weighted/FLAIR images from the brain MRI showed a hyperintense right frontal lesion affecting the corpus callosum and extending to the left hemisphere, with patchy gadolinium-contrast enhancement; we also found hyperintense lesions in T2-weighted/FLAIR images with gadolinium contrast enhancement in both cerebellar hemispheres and thepons. During the first days of hospitalisation the patient’s neurological state worsened with more acute dysarthria and ataxia. Brain MRI was performed again. Apart from the previous lesions, it revealed a new right frontal lesion with gadolinium contrast enhancement and increased uptake of contrast in the lesion located in the splenium of the corpus callosum (Fig. 1A and B).

Based on a suspected diagnosis of primary cerebral lymphoma, we performed complementary blood testing, CT scan, CSF analysis, and PET scan. Blood tests: complete blood count, liver biochemistry, protein screen, electrolytes, beta-2 microglobulin, LDH, tumour markers, peripheral blood smear, autoimmunity, and serological tests for syphilis and HIV were all normal. Thoracic-abdominal-pelvic CT scan was normal. CSF was clear and acellular with normal opening pressure and normal protein and glucose levels; both flow cytology and cytometry were normal. Whole-body positron emission tomography (PET) with flurodeoxyglucose revealed malignant hypermetabolic lesions limited to the brain. Ophthalamological examination was normal.

Given a suspected case of cerebral lymphoma, we avoided use of corticosteroids since they might affect the biopsy reading. A brain biopsy of the right frontal lesion was performed and revealed non-specific gliosis and no evidence of malignancy. The patient was discharged with no treatment and monitored in neurology outpatient consults; doctors observed a gradual improvement of his neurological situation. Four months later, the patient was asymptomatic and leading a normal life. Doctors confirmed that the patient received no corticosteroids at any time. An MRI performed four months later showed nearly complete disappearance of the lesions and no contrast uptake in any of them.

Nine months after being admitted, the patient returned for a check-up due to symptoms of headache and vomiting which began a few days prior. Upon neurological examination, the patient was drowsy and presented time disorientation, moderate dysarthria, limited vertical gaze

Figure 1 (A) Brain MRI, axial FLAIR sequence. Hyperintense cerebral lesions in the frontal lobes reaching the corpus callosum (slight mass effect). (B) Brain MRI, T1-weighted sequence with gadolinium. Patchy areas of gadolinium contrast enhancement. (C) and (D) Brain MRI 4 months later showing a slight signal alteration in the corpus callosum and no areas with gadolinium enhancement.
with conjugate gaze palsy, and left faciobrachioocular hemiparesis. A new MRI revealed several lesions with contrast uptake in the cerebellum, mesencephalon, and right internal capsule. These lesions were treated with high doses of corticosteroids. However, a few days later, the patient presented dysphagia to liquids and the paresis evolved into left hemiplegia. The cerebellar lesion was biopsied, but showed no evidence of malignancy. The patient died a few days later.

Autopsy revealed a lymphoid neoplasm diffusely infiltrating the brain parenchyma and forming concentric perivascular cuffs (Fig. 2). We also observed significant astrocytic, histiocytic, and microglial responses. The immunological and histochemical study confirmed the tumour as a B-cell lymphoid neoplasm since it was strongly positive for B-cell markers (CD20 and CD79a). The Ki-67 proliferation index was high (70%). The anatomical pathology diagnosis was large B-cell lymphoma.

The suspected diagnosis of PCNSL is based on the brain MRI. This kind of lymphoma is most frequently located in the cerebral hemispheres, followed by the basal ganglia, corpus callosum, and cerebellum. Immunocompetent patients have multiple lesions in 20% to 40% of all cases and they usually present homogeneous uptake of contrast. Magnetic resonance spectroscopic imaging detects decreased N-acetyl aspartate concentration and elevated choline levels. When PCNSL is suspected, corticosteroids should be avoided, since they can hinder or prevent histological diagnosis. Resection of the lesion should also be avoided; any surgery should be limited to stereotactic biopsy. From a histological point of view, more than 95% of all cases present large B-cell lymphomas. Treatment for PCNSL in patients with an acceptable clinical state (Karnofsky Scale > 40) is mainly based on systemic chemotherapy with high doses of methotrexate (at least 3.5 g/m).2 Between 50% and 60% of the patients respond completely to treatment.7

Remission of PCNSL after treatment with corticosteroids is a well-known phenomenon, but cases of spontaneous remission are rare.1–5 Remission of the lesions and symptoms may give rise to diagnostic errors and lead doctors to wrongly suspect other processes such as inflammatory and demyelinating diseases. Relapses are typical and they usually occur some weeks or months later. However, doctors have described spontaneous remission periods lasting as long as 4 years.1 Immune theory is the most plausible explanation for this phenomenon. Some authors have found a higher percentage of natural killer cells in patients with spontaneous remission.1 In some such cases, this response was triggered by a situation in which there was a concomitant viral infection. Theoretically, this fact could lead to an increase in the percentage of natural killer cells, which are responsible for eliminating lymphomatous cells.

Spontaneous remission of PCNSL is an exceptional event, but this possibility should be considered so as to prevent diagnostic errors that may delay starting proper treatment.

References


Morbidity and costs associated with neurological disorders

Morbilidad y coste asociado a los trastornos neurológicos

Dear Editor:

Multiple illnesses are frequently present in elderly patients, and several different population studies have demonstrated that the number of illnesses per subject increases with age. This phenomenon and the ageing population as a whole, new diagnostic and therapeutic developments, and improved health education are some of the factors that have led to an overall increase in the consumption of healthcare resources. Studies have indicated that 24% of the population over 65 and 31.4% of the population over 85 have 4 or more chronic conditions. Neurological disorders (NDs) are a group of diseases affecting the central and peripheral nervous systems. They affect all ages, but consequences in elderly patients are more severe. As a result, neurological disorders comprise one of the groups of diseases that generate the highest costs, not only for the healthcare system (direct costs), but also for society at large (indirect costs). Care for NDs is frequently provided at the primary care level. The purpose of our study is to describe the association between the number of chronic comorbidities and the presence of NDs in patients older than 64 years in a normal clinical practice setting in multiple primary care (PC) clinics in Catalonia. The study also measures health costs associated with these patients.

We completed a retrospective multi-centre study based on medical records (digital medical histories) from patients treated in PC clinics. The study population was made up of subjects of both sexes in 13 PC clinics in Catalonia, administered by 4 providers (Badalona Serveis Assistencials, Consorci Sanitari Integral, GesClinic and La Roca del Vallés). These clinics provide service to a district containing approximately 313 500 inhabitants. The study population contained mainly lower-to-middle class residents from an urban industrial area. The study included all patients seeking medical care and registered at 1 of the 13 clinics in 2008. We excluded subjects referred from other PC clinics and subjects whose primary care doctors were in a different district. The study analysed the following variables: (a) general data with age and sex; (b) cases and comorbidities (diagnostic data); and (c) healthcare costs. Comorbidity was determined according to criteria defined by ICPC-2, the International Classification of Primary Care. The following groups were compared to the general population: (a) all NDs (Table 1) by major diagnostic groups or categories, and (b) certain specific NDs with high prevalence rates (peripheral polyneuropathy and neuritis; cerebrovascular accident [CVA], and vascular/Alzheimer-type dementias). The model used to calculate costs per patient was created by differentiating between semi-fixed costs (operational costs) and variable costs (depending on the activity of each patient creating costs). The main accounting items listed as fixed costs are as follows: staff, purchases, external services, and an array of costs pertaining to infrastructure maintenance and clinic management. The amount of semi-fixed costs assigned per patient was determined by that patient’s number of visits to the clinic. Variable costs were calculated according to diagnostic procedures ordered, treatment used (drug prescriptions), and referrals requested by medical personnel at the clinic. These items were listed in the study as laboratory, radiology, or complementary tests; consults with other services; and prescriptions (those paid for by the Catalan Public Health Service). Prices were taken from analytic accounting studies carried out in the clinics and from providers’ bills for intermediate products. Cost per patient was calculated as follows: CPP = (mean cost per visit × number of visits [semi-fixed costs]) + (variable costs). We completed a bivariate analysis using ANOVA, the chi-square test, and the Pearson correlation coefficient. Various forward stepwise logistic regression models (Wald statistic) were used to determine comorbidities associated with NDs in general, and neuropathies, CVA, and dementia in particular. They were corrected for age and sex. Healthcare costs (direct costs)