Isolated relapse in the central nervous system during cytologic and hematologic remission in a patient with acute promyelocytic leukemia

Recaída aislada en el sistema nervioso central durante remisión citológica y hematológica en paciente con leucemia promielocítica aguda

Dear Editor:

Acute promyelocytic leukaemia (APL) is characterised by the translocation between the PML gene (promyelocytic leukaemia) on chromosome 15 and the RAR-alfa gene (retinoic acid receptor-alpha) on chromosome 17. Therapy with all-trans retinoic acid (ATRA) in combination with chemotherapy regimes using anthracyclines has increased survival rates. An increase of extramedullary relapse has been observed in patients who received prior treatment with ATRA[1]. Isolated relapse of the central nervous system (CNS) after complete remission is an uncommon finding. We present the case of a patient suffering from APL with isolated CNS relapse and good clinical evolution after treatment.

Case report: 32-year-old male diagnosed with high-risk APL. He received induction therapy with idarubicin and ATRA, with which he achieved complete cytological and molecular remission. Subsequently, he received three well-tolerated cycles of consolidation with cytarabine, liposomal adriamycin and ATRA. Since then, the patient carried out maintenance treatment. Subsequently, a myelogram was performed, which confirmed cytological, cytogenetic and molecular response. After one month, he went to the emergency department for headache, lumbar pain, gait disturbance and diplopia. The physical examination revealed alternating VI cranial nerve paresis, cervical rigidity and ataxia. The analysis and peripheral blood smear showed no abnormalities. Cranial CT showed chronic ischemic injuries (complications of cardiac ischemic disease clinical picture shown at diagnosis). Lumbar puncture showed 478 nucleated cells with cytology showing massive infiltration of atypical promyelocytes, intensely positive myeloperoxidase and translocation of PML/RAR-alfa. Cranial MRI showed leptomeningeal thickening (fig. 1). Under the diagnostic guidance of isolated APL relapse in CNS, we began intrathecal chemotherapy treatment (liposomal cytarabine and dexamethasone) and then triple chemotherapy (methotrexate, ARA-C and hydrocortisone). Concomitantly, we administered systemic treatment with methotrexate and ARA-C, whole brain radiotherapy and arsenic trioxide until January 2008. Currently, the patient remains asymptomatic and in complete cytological and molecular remission in the bone marrow and CNS.

Previously, the occurrence of extramedullary disease as a presentation or a relapse in APL was considered a rare finding[1]. However, after the introduction of ATRA treatment and increased survival, numerous cases have been reported; the CNS and the skin are the most frequent locations[4]. The present case stands out as an isolated relapse in the CNS. Few cases have been described, without a consensus on treatment being reached and with different survival results[2,5-7]. One hypothesis proposed[1] is increased expression of adhesion molecules in malignant promyelocytes such as ICAM-1 and VCAM, which after treatment with ATRA may facilitate leukaemic infiltration in the cerebrospinal fluid (CSF). Of the associated risk factors, hyperleukocytosis at diagnosis (>10,000 leukocytes/Ìl) was associated with increased risk of CNS relapse and worse prognosis[3]. Since

Figure 1 Cranial magnetic resonance imaging with gadolinium showing leptomeningeal enhancement.

isolated extramedullary relapse may be followed by medullar relapse, all authors agree in treating local relapse as a systemic disease, with no consensus on the scheme to be followed. Intrathecal and systemic chemotherapy, and whole brain radiation therapy have been used with regimes that cross the blood-brain barrier, with different results[2-7]. In summary, when a patient with a history of APL presents neurological symptoms, extramedullary disease should be ruled out, even though the patient is in complete medullar cytological and molecular remission. Prospective studies are needed to determine whether treatment with ATRA *per se* increases the risk of developing extramedullary disease and to assess the need for a study on CSF and CNS chemoprophylaxis upon diagnosis for those at high risk of extramedullary relapse.

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Use of Spanish in scientific publications. Neurology in the context of clinical medicine and Spanish scientific journals

Utilización del español en las publicaciones científicas: la neurología en el contexto de la medicina clínica y las publicaciones científicas españolas

Dear Editor:

It is striking that from some areas such as neurological publications edited in Spain, there has been a defence of the interest and the need to publish in Spanish as opposed to in English[1-3], which has become the hegemonic *lingua franca* in the scientific field, especially in the field of natural and biomedical sciences[4].

To determine the weight and importance of the Spanish language in the scientific production of Spanish institutions in general, and in the area of clinical neurology in particular, as well as the potential impact of publication in Spanish in relation to the degree of citation, a study of the presence of this language in the Science Citation Index-Expanded (SCI-Expanded) has been conducted. The evolution of the impact factor of Spanish biomedical journals has also been studied; this is part of a broader line of research that attempts to characterise the role of non-Anglo-Saxon languages in different areas of knowledge, as well as the impact of certain publishing strategies related to language, including the translation into English of articles published in other languages.

The analysis of the diachronic evolution of publications (articles, letters, reviews and editorials) containing some SCI-Expanded-included Spanish institutional affiliation between 1979 and 2007 (fig. 1) shows that the language of Cervantes has dropped drastically. This is evidenced by the continued decline found, with values that have not exceeded 10% since the mid-nineties, and that represent only 6.29% of all the works produced by Spanish institutions in 2007. The dramatic reduction in Spanish is a fact, despite the increase in the number of source journals published in Spanish included in this database and, therefore, in the presence of this language in absolute terms. The same declining trend was noted in connection with articles published in journals of the different specialties which make up clinical medicine, even though the presence of Spanish is greater in the area, with values that have remained in any event below 20% since 2005 (fig. 1). However, a contrary trend is observed in clinical neurology, where the Spanish language is in relatively good health. Since the late nineties, the annual scientific production (which hovers around 30-40% of the total number of works produced by Spanish institutions) has remained stable (fig. 1). There are two clinical neurology journals published in this language (*Revista de Neurología* and NEUROLOGÍA) that were included in SCI-Expanded in 1997 and 2001, respectively; their editorial policy represents an important impulse in the use of Spanish as a language of scientific communication. Theirs is an edito-