A 10-year-old female patient with acute lymphoblastic leukaemia who just finished the third cycle of intrathecal administration of methotrexate, presented with acute onset of right hemiparesis.

**Imaging Findings:**

Eight hours after the beginning of symptoms, magnetic resonance (MR) depicts the presence of focal and symmetrical regions of restricted diffusion on DWI images and ADC maps, seen on both centrum semiovale and both corona radiata, as well as on the splenium of corpus callosum (Fig. 1). On T2-weighted images these lesions show high signal intensity, while on Flair there is mild ring hyperintensity (Fig. 2). Iso to hypointensity is seen on T1-weighted images. After intravenous administration of gadolinium there is no evident enhancement (Fig. 3).

Two months after the acute stage, follow-up images demonstrate no restriction on DWI and ADC maps on previously affected areas (Fig. 4). There is only slight hyperintensity on T2 and FLAIR, representing gliosis (Fig. 5). The patient was asymptomatic.

**Discussion:**

The use of intrathecal administration of methotrexate is an essential component in the chemotherapeutic treatment of acute lymphoblastic leukaemia [1, 2] to prevent and treat the affection of the central nervous system [2]. Renal toxicity is the most common and significant side effect of methotrexate; other side effects include: diarrhoea, mucositis, leukopaenia, hepatotoxicity, dry eyes, pleuritis, osteoporosis, and occasionally interstitial pneumonitis [3]. Acute leukoencephalopathy is observed in 5-18% of children undergoing this therapy [1, 4, 5], though some authors reported it as a rare manifestation, aseptic meningitis being the most frequent acute complication in this case [3]. Risk factors for this neurotoxic effect include: high dose treatment, intrathecal administration, young age, and associated cranial irradiation [1, 4, 5].

The pathophysiology of methotrexate-related neurotoxicity is unclear, but it is believed that it has a direct neurotoxic effect, generating cytotoxic oedema [2, 4]. Although this is seen on early MR as areas of altered signal intensity on DWI images [1, 2, 3, 4, 5], this acute cellular injury is not always irreversible [1, 3, 4, 5]. In patients undergoing cranial irradiation, this adverse effect may be more severe and irreversible [1]. Some authors reported fatal cases of methotrexate-induced neurotoxicity [2].

Clinical manifestations of acute neurotoxicity often include: seizure, transient ischaemic attack, encephalopathy,
ataxia, myelopathy [4, 5] and stroke-like focal deficits [3]. Nausea, vomiting, headache, somnolence and mental confusion have also been reported [2].

On MR images these lesions are not confined to typical vascular territories and usually appear as focal areas of restricted diffusion on DWI, with high signal intensity on Flair and T2-weighted images [1, 2, 3, 4, 5] and no gadolinium enhancement [1]. Generally they affect periventricular white matter, more often both centrum semiovale [4, 5] and both corona radiata [1]. It can also compromise the splenium of corpus callosum [1], as in our case, and the cerebellum [2, 3]. Many authors suggest that imaging findings change with time, with restricted diffusion seen only in the acute and subacute stages, followed by gliosis and encephalomalacia in the chronic phase [1, 4, 5]. So is the case of our patient.

Different reports demonstrate that the use of MR, and especially DWI images, is a helpful tool in the detection of early methotrexate white matter injury.

**Differential Diagnosis List:** Methotrexate-induced leukoencephalopathy, Infection (PML), Metastasis, Dural sinus thrombosis, Cerebral venous infarction, Ischaemic Infarction, PRES

**Final Diagnosis:** Methotrexate-induced leukoencephalopathy

**References:**


Figure 1

Description: There is restricted diffusion on both centrum semiovale (A) and both corona radiata (B). The splenium of corpus callosum is also involved (C). ADC maps confirm these findings (D, E, F).

Origin: Moliné T, Department of Neuroradiology, Fundación Científica del Sur, Buenos Aires, Argentina 2014.
**Description:** Lesions are hyperintense on T2-weighted images (A, B, C). Flair only shows mild ring hyperintensity on both corona radiata (D, E, F). **Origin:** Moliné T, Department of Neuroradiology, Fundación Científica del Sur, Buenos Aires, Argentina 2014.
Description: On T1-weighted images corresponding areas are iso to hypointense (A, B, C), with no evident enhancement after gadolinium administration (D, E, F). Origin: Moliné T, Department of Neuroradiology, Fundación Científica del Sur, Buenos Aires, Argentina 2014.
Description: Both centrum semiovale (A), corona radiatas (B) and splenium of corpus callosum (C) show mild T2-effect on DWI. ADC maps depict no evident restricted diffusion (D, E, F). Origin: Moliné T, Department of Neuroradiology, Fundación Científica del Sur, Buenos Aires, Argentina 2014.
Description: Areas of gliosis are seen on follow-up T2 (A, B, C) and FLAIR (D, E, F). Origin: Moliné T, Department of Neuroradiology, Fundación Científica del Sur, Buenos Aires, Argentina 2014.