

## LETTERS TO THE EDITOR

## Whipple's disease: Presentation of an unusual case with isolated cerebral involvement<sup>☆</sup>

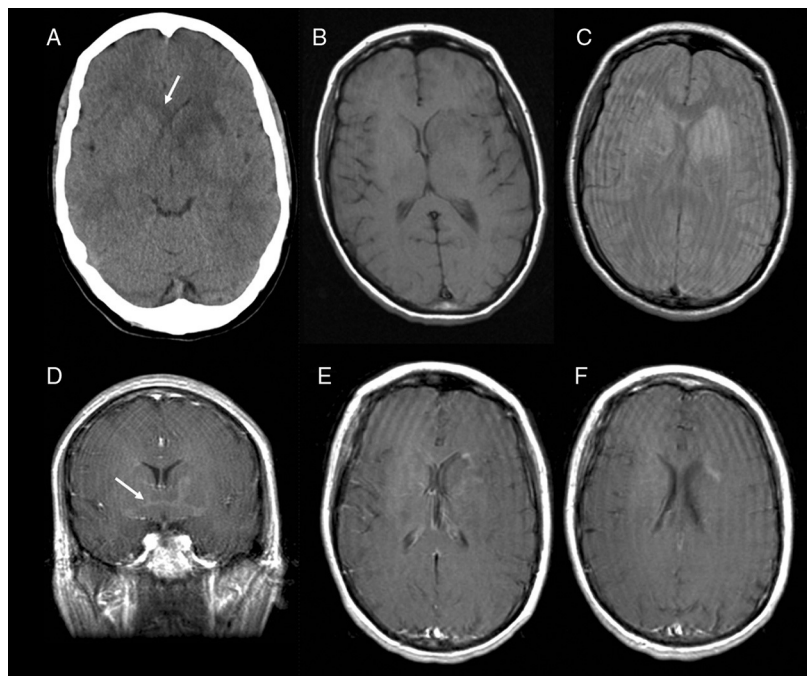
### Enfermedad de Whipple: Presentación de un caso infrecuente de afectación cerebral aislada

Dear Editor:

Whipple's disease (WD) is a multisystem infection caused by *Tropheryma whipplei* (*T. whipplei*). Associated neurological

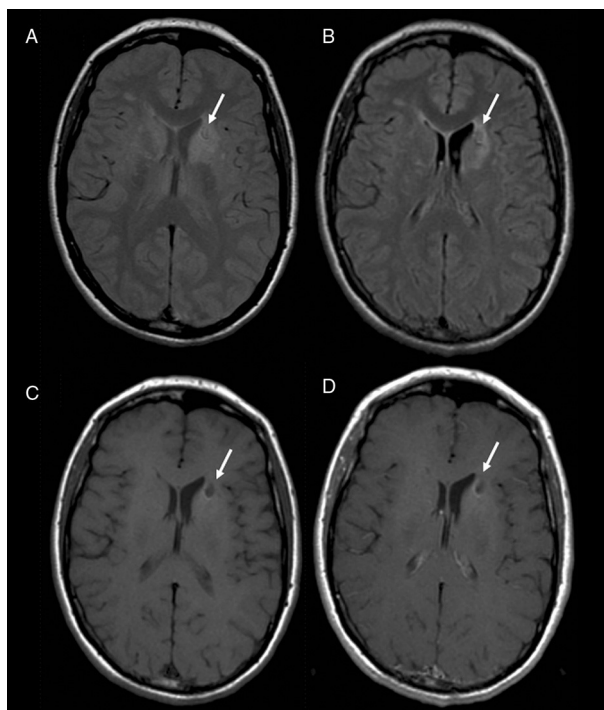
symptoms are common, although they rarely appear as the initial manifestation of the disease. They are often related to disease limited to the CNS.<sup>1</sup>

We present a case of a 30-year-old woman who presented at the emergency department with neck pain accompanied by frontal headache and tingling and clumsiness in the left arm and left side of the face. The patient attributed symptoms to a motor vehicle accident with no head trauma that had taken place 2 weeks before. Additionally, she reported some drowsiness and difficulty speaking. The patient's medical history was not relevant except for her residence in a rural area. Physical examination revealed dysarthria, minimal claudication in the upper left limb, and paraesthesia



**Figure 1** CT without contrast (A) performed upon arrival of the patient shows a hypodense area affecting the left caudate and lentiform nuclei and the internal capsule. Note the hypodense area extending contralaterally along the edge of the corpus callosum. MR images taken 18 hours later revealed hypointensities in the same regions described by the CT scan in T1-weighted sequences and hyperintensity in DP-weighted sequences. Administration of paramagnetic contrast (D–F) yielded distinct, heterogeneous and mainly peripheral areas of enhancement clearly showing the lesion's contralateral extension through the anterior commissure (arrow in D).

<sup>☆</sup> Please cite this article as: Lombardo Galera S, et al. Enfermedad de Whipple: presentación de un caso infrecuente de afectación cerebral aislada. Neurología. 2013;28:317–9.



**Figure 2** Routine MRI study completed at the 1-month mark shows the change in residual signal that causes retraction of the anterior horn of the lateral ventricle in DP-weighted (A), FLAIR (B) and T1-weighted sequences without contrast (C). No areas showing pathological enhancement were seen after administering contrast (D). All sequences show a nodular hypointense/isointense feature corresponding to the biopsy lesion (arrow).

of the left hand without loss of sensitivity. Complete blood count, biochemical analysis, and other conventional laboratory tests yielded normal results.

Doctors performed an emergency cranial computed tomography without contrast that showed a hypodense area affecting the caudate nucleus and globus pallidus, the anterior limb of the left internal capsule, and the anterior part of the left external capsule (Fig. 1).

Cranial MRI scans performed with and without contrast 12 hours after the patient was admitted showed signal alterations in both caudate nuclei, left lentiform nucleus, genu of the corpus callosum, and anterior commissure; changes were more pronounced on the left side. Lesions showed expansile tendencies and faint, irregular enhancement after administration of contrast (Fig. 1).

During the hospital stay, the patient was studied using thoracic, abdominal, and pelvic CT with both oral and intravenous contrast. Scans did not reveal any relevant findings. Lumbar puncture was used to extract cerebrospinal fluid for analysis, and all results from both cytology studies and serology studies (for the most common pathogens) were normal.

Given the patient's progressively worsening condition (abulia, hypersomnia, urinary incontinence, Babinski sign, and claudication of the lower limbs), doctors decided to perform a stereotaxic brain biopsy of the lesion adjacent to the right caudate nucleus. The anatomical pathology study of the sample showed areas of gliosis and hypercellularity

caused by numerous macrophages with clear cytoplasm and granular PAS-positive structures that suggested CNS impairment due to WD. Tissue and serum samples were analysed using the polymerase chain reaction method; serum was negative for *T. whipplei*.

In light of these results, doctors performed a lower gastrointestinal series and digestive tract endoscopy with a duodenal biopsy. Tests revealed no signs of extracranial Whipple disease.

The patient was treated with 2 g IV ceftriaxone every 12 hours; treatment was tolerated well and the patient's status improved. The patient continued to be treated with 800/160 mg co-trimoxazole every 12 hours for 1 year.

A routine MRI scan 2 months later clearly showed a reduction in the size of the lesions described by previous images. No expansile effect or contrast uptake was detected in the lesions. The patient remained asymptomatic, without abulia, and with normal plantar reflexes and sphincter control; claudication in lower limbs also improved (Fig. 2).

Since WD is rare, it is frequently diagnosed late, especially in cases presenting with neurological signs and none of the digestive symptoms characteristic of that condition. Conventional laboratory studies reveal non-specific changes. PCR is regarded as the diagnostic technique of choice because it has higher sensitivity and specificity than other techniques. Nevertheless, negative PCR findings do not rule out the diagnosis of WD, as seen in this case.

Although findings from CT and MRI scans are non-specific, these techniques provide the most information. Cranial CT shows cerebral atrophy and single or multiple focal hypodense lesions that predominantly affect the white matter, cortex, and hypothalamus. Lesions present contrast enhancement.<sup>2</sup> The most common MRI finding is that the lesions described above are hyperintense in T2-weighted and hypointense in T1-weighted sequences.<sup>3</sup> Additionally, expansile lesions showing enhancement after administration of paramagnetic contrast may appear. Perfusion/diffusion-weighted MRI and spectroscopy may be useful, but few studies have been performed to date and typical patterns have not yet been described.<sup>2</sup> Reports indicate that these techniques are valuable in cases of recurrent cerebral WD in which lesions may be smaller, even though restricted diffusion may be indicative of areas of active infection.<sup>3</sup> Acute ischaemic lesions may produce similar imaging findings, but it is possible to distinguish between them based on their continuity and presence or absence of a fully evolved infarct.

PET studies with <sup>11</sup>C-methionine may be used in differential diagnosis to rule out tumours; in WD, hypermetabolic regions may be present in cortical and subcortical areas including the brainstem.<sup>4</sup> However, other studies employing <sup>99m</sup>Tc-HMPAO SPECT have described decreased cerebral blood flow in affected areas.

## References

1. Peters G, Du Plessis DG, Humphrey PR. Cerebral Whipple's disease with a stroke-like presentation and cerebrovascular pathology. *J Neurol Neurosurg Psychiatry*. 2002;73:336–9.
2. Bermejo P, Burgos A. Enfermedad de Whipple y sistema nervioso central. *Med Clin (Barc)*. 2006;127:379–85.

3. Raheja AA, Lui YW, Pinzon-Ardila A, Lim RP, Sparr SA. Use of diffusion-weighted imaging in recurrent central nervous system Whipple's disease: a case report and review of the literature. *Clin Imaging*. 2010;34:143–7.
4. Galdicks N, Burghaus L, Vollmar S, Cizek J, Impekoven P, Thomas A, et al. Novel neuroimaging findings in a patient with cerebral Whipple's disease: a magnetic resonance imaging and positron emission tomography study. *J Neuroimaging*. 2004;14:372–6.

S. Lombardo Galera\*, E. Roldán Romero, F. Bravo Rodríguez  
*Sección de Neurorradiología Diagnóstica y Terapéutica,  
 Servicio de Radiodiagnóstico, Hospital Universitario Reina  
 Sofía, Córdoba, Spain*

\*Corresponding author.

E-mail address: [mslombgalera@hotmail.com](mailto:mslombgalera@hotmail.com)  
 (S. Lombardo Galera).

## Plexiform neurofibroma in an 8 year-old patient<sup>☆</sup>

### Neurofibroma plexiforme en paciente de 8 años

*Dear Editor:*

Neurofibromatosis type 1 (NF1) is caused by a mutation of the NF1 gene, which is located in chromosome 17q11.2.<sup>1,2</sup> Neurofibromas account for 90% of all cases, with plexiform tumours appearing less frequently. While neurofibromas are benign nerve sheath tumours, up to 10% of all plexiform neurofibromas may undergo malignant transformation.

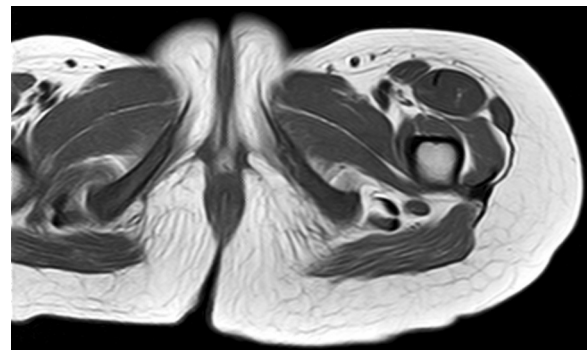
We present the case of a girl aged 8 years and 4 months who was diagnosed with NF1 at the age of 2 years. Four days after surgical tonsillectomy and adenoidectomy, she presented inability to walk, associated with paraesthesia (cramps) in the left leg and foot. Examination revealed loss of strength in the left foot, inability to perform dorsiflexion, inadequate eversion/inversion, and positional talipes. The patient was unable to walk whether with normal or abnormal gait. Babinski sign was absent. Deep tendon reflexes were present without an increase in the reflexogenic area. Positive Lasègue's sign on the left side.

Complementary tests were as follows: radiographies of both hips, and the left foot and leg; ultrasound of the popliteal fossa and proximal third of the left leg that ruled out vein thrombosis; and a complete blood count in which coagulation, autoimmunity, and CPK readings were normal. The electroneurogram and electromyogram showed signs compatible with partial axonal mononeuropathy (axonotmesis) of the left common sciatic nerve mainly affecting the peroneal component. The patient was also studied using lumbosacral spinal, pelvic, and lower limb MRI, which showed a well-defined soft tissue lesion in the theoretical path of the left sciatic nerve, which was visible from the sciatic notch caudally to the popliteal fossa. This finding was compatible with neurofibroma (Figs. 1 and 2).

Plexiform neurofibromas are tumours that affect nerve structures (plexus, fasciculus, or nerve branches).<sup>3</sup> The

incidence of NF1 type 1 is estimated to be about 17%.<sup>2</sup> The imaging study used to detect and characterise this disorder was MRI. We completed a general exploration of the 3 spatial planes with a T1-weighted sequence, fat-suppressed T2-weighted sequence, and fat-suppressed T1-weighted sequence after administration of intravenous gadolinium. Neurofibromas are usually hyperintense in the T2-weighted sequence. They show enhancement after administration of intravenous contrast, they are anatomically related to a nerve, and they may present a target pattern.<sup>3–6</sup> Twelve percent of these lesions undergo malignant transformation and they generally present rapid growth or sustained pain. Positron emission tomography may be useful for studying these lesions in cases of suspected malignant transformation; some studies have calculated sensitivity and specificity levels as high as 90% and 87%, respectively.<sup>7–9</sup> Symptomatic and/or malignant lesions are treated surgically. Chemotherapy and radiotherapy are employed in cases of malignant transformation. Angiogenesis inhibitors or cell-differentiation-inducing agents have also been used, given the vascular origin of these lesions.<sup>10</sup>

Our patient was referred to the hospital's rehabilitation department and treated with gabapentin for 2 months. We performed a neuropsychological study which revealed normal results, as well as an MRI showing no new lesions. Two years after the episode, she was pain-free and gait was normal. The neurological examination showed no deficits.



**Figure 1** T1-weighted axial MRI of the sciatic notch. Well-defined soft tissue lesion at the left sciatic nerve (hypointense in T1-weighted sequence), lateral to the semimembranosus tendon.

<sup>☆</sup> Please cite this article as: Pérez Villena A, et al. Neurofibroma plexiforme en paciente de 8 años. *Neurología*. 2013;28:319–20.