Case 11006

Eurorad

PML-IRIS (ECR 2013 Case of the Day)

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ISSN: 1563-4086
Section: Neuroradiology
Area of Interest: Neuroradiology brain
Procedure: Diagnostic procedure
Imaging Technique: CT
Imaging Technique: MR
Special Focus: AIDS Case Type: Clinical Cases
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Patient: 38 years, female

Clinical History:

A 38-year-old woman in C3 stage of HIV infection, presenting symptoms of right hemiparesis and hemihypoesthesia. Patient abandoned antiretroviral therapy (ART) voluntarily, 2 years before.
Imaging Findings:

Initial unenhanced CT showed a focal hypodense lesion in the posterior limb of left internal capsule, basal ganglia calcifications and nonspecific signs of cortico-subcortical atrophy with secondary increased size of sulci and ventricular system (included within an HIV encephalopathy). MRI performed during hospitalisation (T1 FSE, T2 FLAIR, EPI and GE) revealed a focal lesion in the left internal capsule and multiple white matter lesions. Lesions have also been found in the left subcortical parieto-occipital area, and in right centrum semiovale. All of these were hypointense on T1w and hyperintense on T2w images, with peripheral diffusion restriction on DWI and no significant uptake of contrast or mass effect. Patient was diagnosed with progressive multifocal leukoencephalopathy (PML). Four weeks after starting ART, the patient's condition deteriorated. MRI revealed increased size of previously observed lesions and new ones, with the same imaging features.
Discussion:

IRIS (Immune reconstitution inflammatory syndrome) is a clinical condition, in HIV+ patients undergoing the ART therapy. The restored immune system causes tissue damage leading to clinical worsening [1]. IRIS occurs in about 16% of patients starting ART therapy [2] affecting CNS (CNS-IRIS) in 0.9%. In HIV patients with PML who start ART, estimated frequency of IRIS is 19% [3-4].
Our patient developed right hemiplegia and hemiparesis, in relation with the larger lesion in left internal capsule. Clinical presentation of PML is nonspecific. Symptoms like hemiparesis or hemiplegia may be indistinguishable from HIV encephalopathy. It can also cause sensory or cognitive impairment, depending on the brain area affected. IRIS-PML is clinically characterised by a worsening of PML symptoms within 4-8 weeks after initiation of ART.
In PML, demyelinating lesions are asymmetrically distributed, without inflammation. Usually lesions are multiple and typically affecting subcortical white matter rather than periventricular or deep white matter. MRI show hypointense lesions in T1w sequences/ hyperintense in T2w sequences, usually without significant mass effect or gadolinium enhancement. In DWI the pattern of ring diffusion restriction could be explained by the distribution of infected oligodendrocytes in the advancing margin of the lesion.
Typically, in patients with IRIS-PML, MRI scans show signs of inflammation, usually manifested with gadolinium

enhancement and/or mass effect (60% of cases [5]). In this case, one month after starting treatment, the patient's condition deteriorated and both enlargement of pre-existing lesions and appearance of new lesions were observed on MRI. No gadolinium enhancement or mass effect was observed. Currently, specific CSN-IRIS biomarkers that allow accurate diagnosis are not known. The diagnosis is usually based on the presence of multiple factors: HIV infection with recent onset of ART, positive response to therapy with reduced virus count and/or increased CD4 inflammatory manifestations in the MRI, and exclusion of other pathology [2, 6]. The definitive diagnosis, however, has to be based on histopathological criteria.
Conclusions: PML is the most common diagnosis for HIV+ patients with lesions of demyelinating pattern. It should be noted, that after initiation of ART therapy, paradoxical clinical worsening may occur (IRIS). Currently, in the absence of specific criteria for IRIS diagnosis, it is mostly based on MRI findings like new inflammatory lesions or enlargement of pre-existing ones. Recent studies of spectroscopy - the mIns peak (associated with severe inflammation) specifically, seem to indicate that there is a specific PML-IRIS elevation [7-8], but further research is needed to confirm this finding.
Differential Diagnosis List: PML-IRIS (Progressive multifocal leukoencephalopathy-Immune reconstitution inflammatory syndrome), Natural history of PML, AIDS-dementia complex + PML, Lymphoma, Primary demyelinating disease

Final Diagnosis: PML-IRIS (Progressive multifocal leukoencephalopathy-Immune reconstitution inflammatory syndrome)

References:

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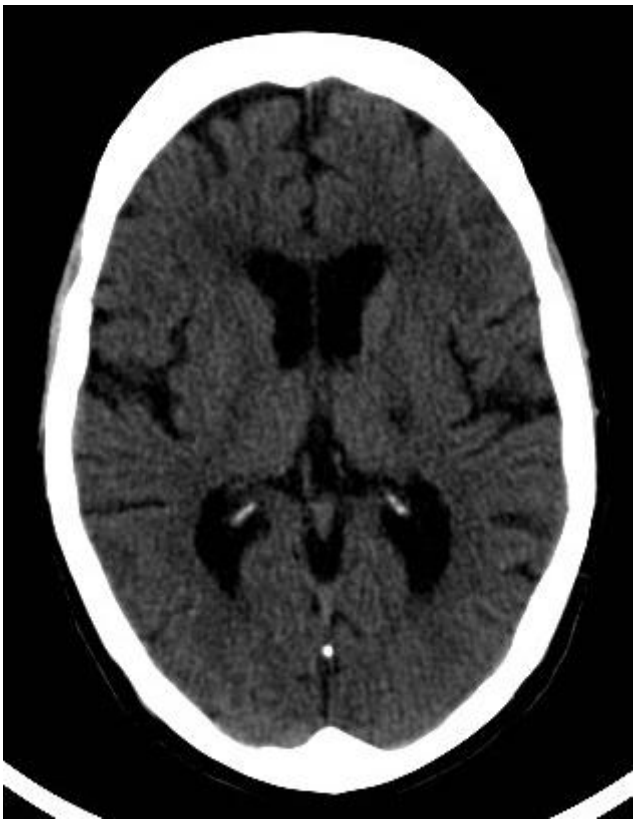
Cuvinciuc V, Martin-Blondel G, Marchou B, Bonneville F. (2010) Proton MR spectroscopy of progressive multifocal leukoencephalopathy-immune reconstitution inflammatory syndrome. AJNR Am J Neuroradiol 2010 Sep;31(8):E69-70; author reply E71. (PMID: 20538829)

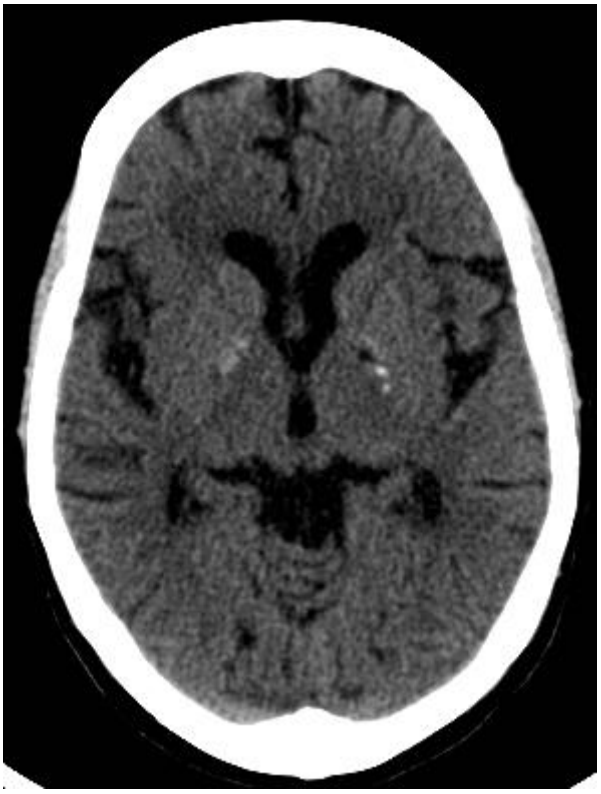
Figure 1

a



Description: Focal hypodense lesion in the posterior limb of left internal capsule **Origin:** Department of Radiology. U y P. La Fe Hospital, Valencia, Spain

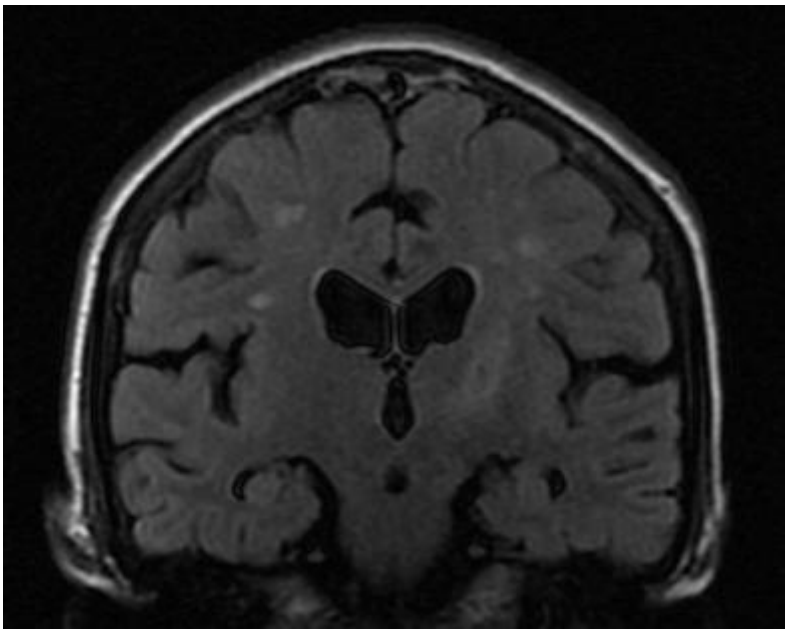
b



Description: Basal ganglia calcifications and nonspecific signs of cortico-subcortical atrophy with secondary increased size of sulci and ventricular system (included within an HIV encephalopathy)
Origin: Department of Radiology. U y P. La Fe Hospital, Valencia, Spain

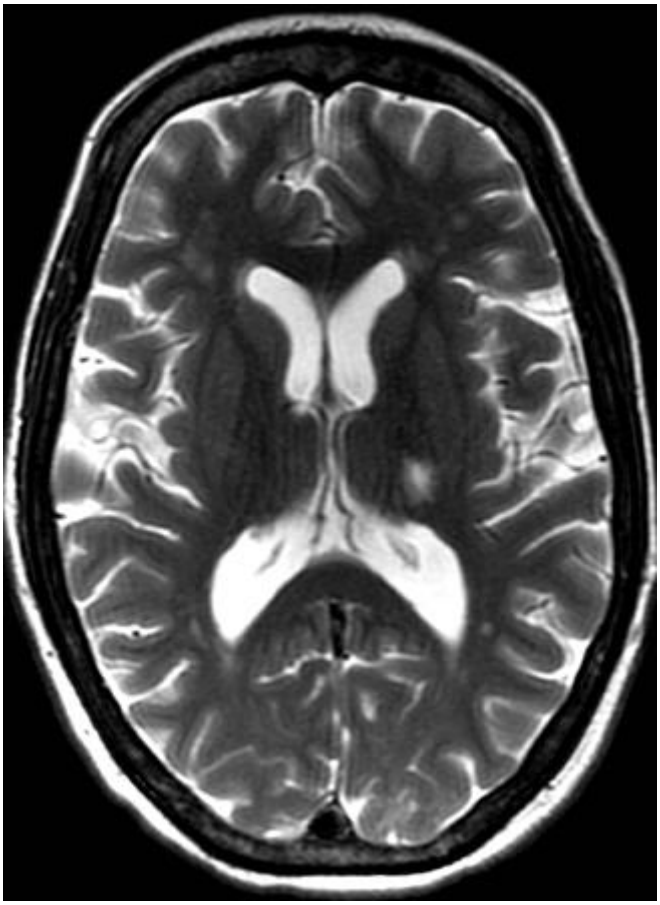
Figure 2

a



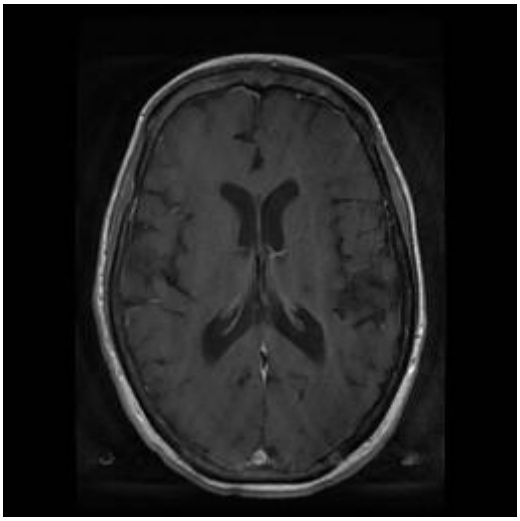
Description: Coronal FLAIR. Demyelinating lesion in the left internal capsule and multiple white matter lesions. **Origin:** Department of Radiology. U. y P. La Fe Hospital, Valencia, Spain.

b



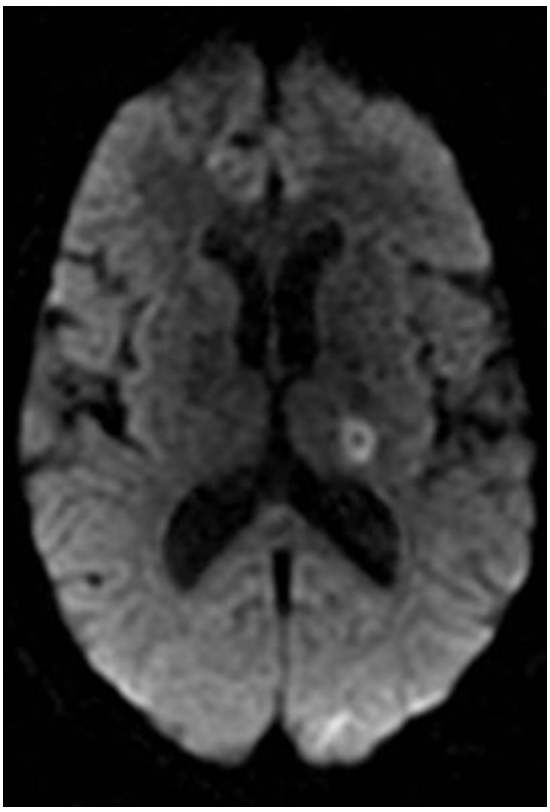
Description: Axial T2 FSE. Focal lesion in the left internal capsule shows hyperintensity on T2WI.
Origin: Department of Radiology. U. y P. La Fe Hospital, Valencia, Spain.

c



Description: Axial T1 with contrast. Lesion shows hypointensity on T1 and no enhancement after administration of contrast. **Origin:** Department of Radiology. U. y P. La Fe Hospital, Valencia, Spain.

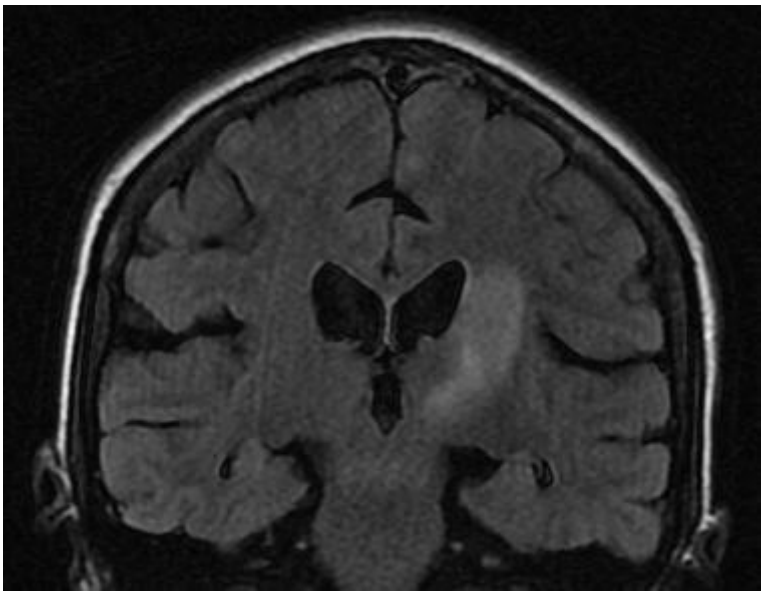
d



Description: DWI. Peripheral diffusion restriction on DWI **Origin:** Department of Radiology. U. y P. La Fe Hospital, Valencia, Spain.

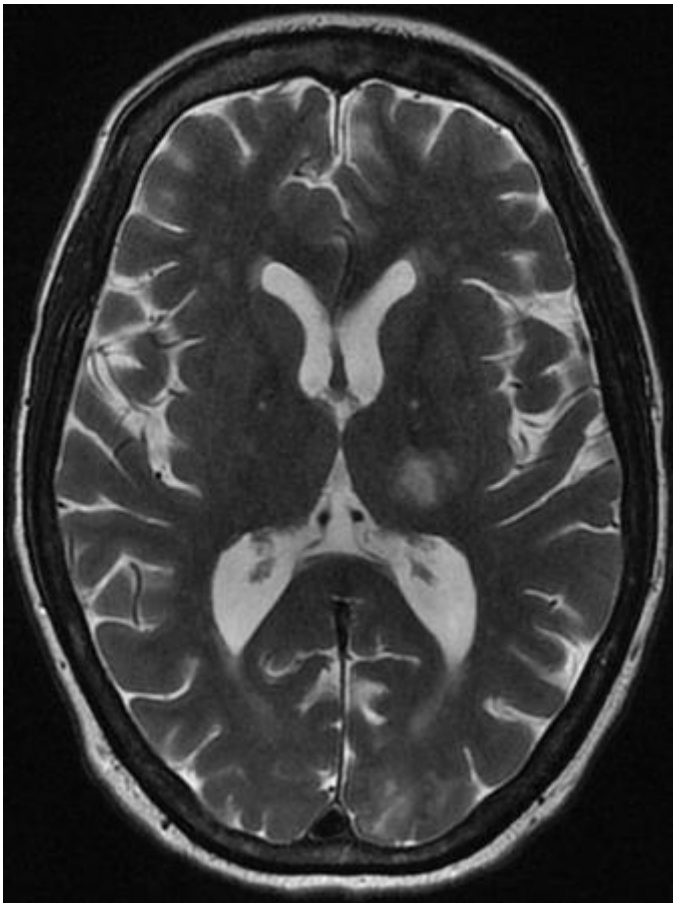
Figure 3

a



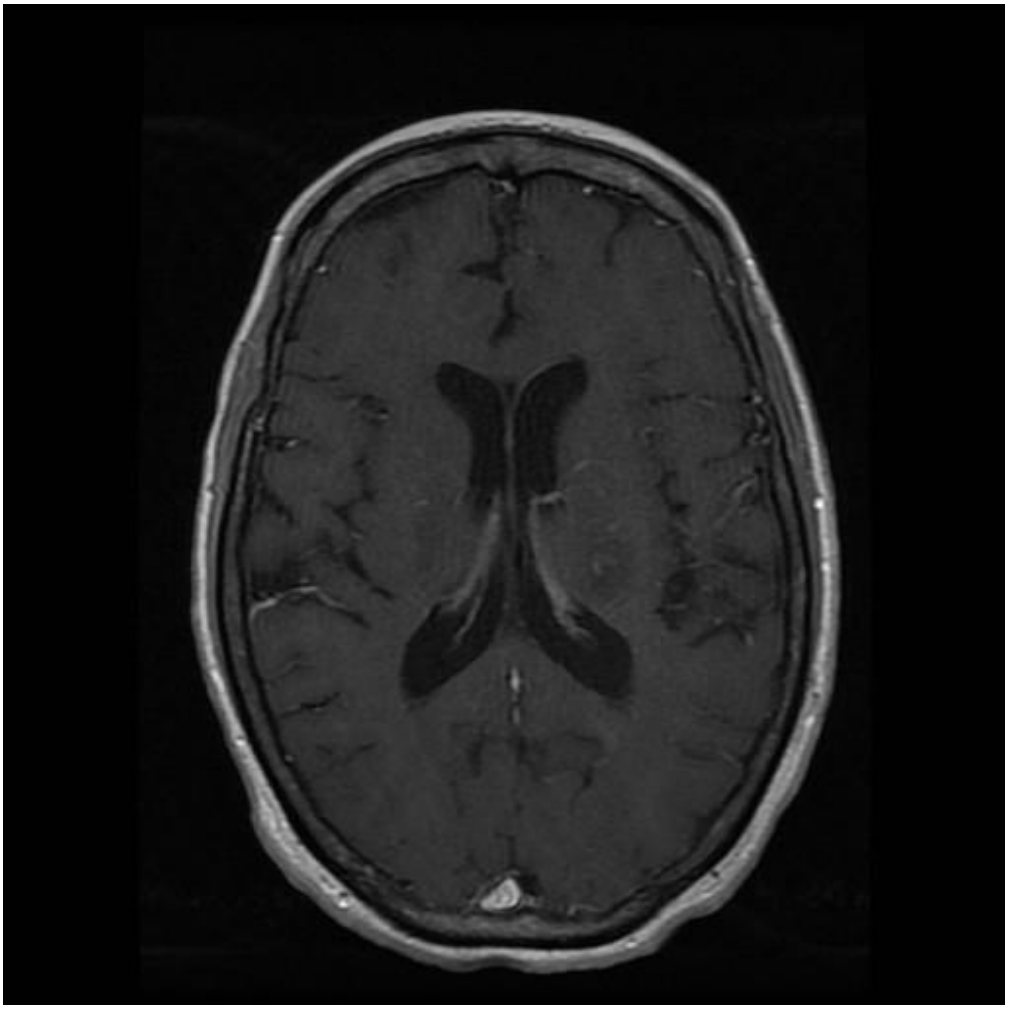
Description: Coronal FLAIR. Increased size of the previously observed lesions and new ones. **Origin:** Department od Radiology. U. y P. La Fe Hospital, Valencia, Spain.

b



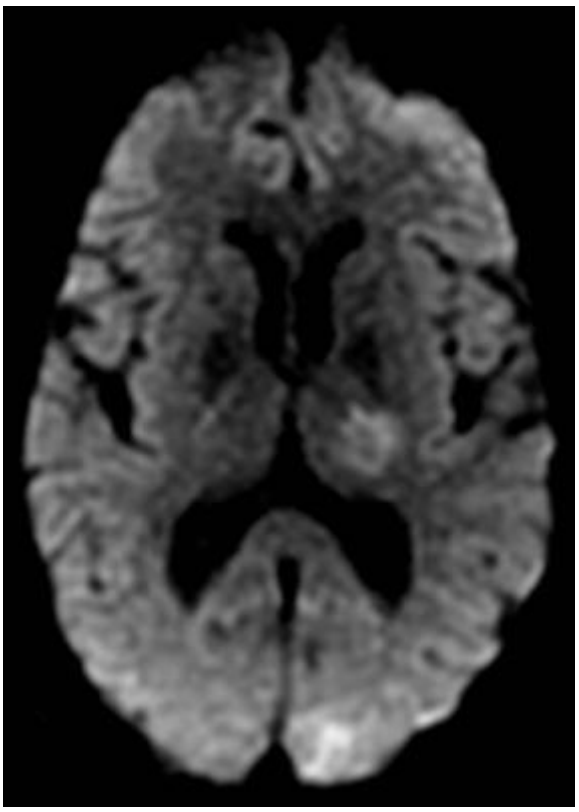
Description: Axial T2 FSE. **Origin:** Department od Radiology. U. y P. La Fe Hospital, Valencia, Spain.

c



Description: Axial T1 with contrast. Despite increasing size lesions shows no enhancement with contrast. **Origin:** Department od Radiology. U. y P. La Fe Hospital, Valencia, Spain.

d



Description: DWI. Lesion showed increased peripheral diffusion restriction on DWI compared to previous MRI. **Origin:** Department od Radiology. U. y P. La Fe Hospital, Valencia, Spain.