

LETTER TO THE EDITOR

Contrast-enhanced magnetic resonance imaging and perfusion-weighted imaging for monitoring features in severe CLIPPERS

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Sir, Pittock and colleagues (2010) recently defined a new clinical–radiological inflammatory entity prominently involving the pons, which they called ‘CLIPPERS’ (Chronic Lymphocytic Inflammation with Pontine Perivascular Enhancement Responsive to Steroids). The condition features the combination of a punctate and curvilinear pattern ‘peppering’ of the pons on post-contrast T₁-weighted magnetic resonance images, together with an initial responsiveness to corticoid therapy. The authors of this founding paper appropriately concluded that full evaluation using non-invasive and minimally invasive procedures should be made before considering at-risk brainstem biopsy, and that clinical–radiological criteria should be sufficient to initiate treatment without pathological examination. We observed a healthy 70-year-old female presenting with gait ataxia and dysarthria in whom initial magnetic resonance work-up demonstrated punctuate and curvilinear enhancement in the pons rapidly decreasing as distance from the pons increased (Fig. 1A), though the pattern was more easily recognized on delayed follow-up examinations (Fig. 1B and C). Additional perfusion-weighted imaging was performed, which demonstrated an increase in regional cerebral blood flow within involved areas, ranging from 200–300% of a reference region of interest placed within unaffected cerebellar white matter (Fig. 2A). The perfusion-weighted-derived regional cerebral blood flow-mapped images demonstrated a ‘trident-like’ pattern within pons, clearly suggesting relative sparing of the direct corticospinal tracts, contrasting with severe involvement of the adjacent white matter. This feature matched the clinical findings for extensor plantar responses and suggested more inflammation than tumour. Indication for biopsy was hardly debated by

multidisciplinary staff. A glucocorticoid treatment was initiated without biopsy and the patient underwent tight contrast-enhanced magnetic resonance monitoring (Fig. 1). Final diagnosis of an inflammatory disorder, matching the main features for the CLIPPERS entity, was considered after a 20-month treatment course. Some undescribed features in our patient are worth highlighting. The severity of pontine inflammation was extreme and unequalled when compared with images from the Pittock *et al.* (2010) study. Recognition of the so-called ‘punctuate/curvilinear pattern’ of contrast enhancement was more straightforward on post-treatment delayed magnetic resonance images (Fig. 1B and C) than on initial images (Fig. 1A). Perfusion-weighted maps at initial work-up demonstrated drastically increased regional cerebral blood flow values within diseased pontine areas (Fig. 2A). The relevance of this feature regarding discrimination between inflammation versus neoplasm was debated. In spite of intense treatment resulting in significant clinical improvement, contrast enhancement remained (Fig. 1A–G). Moreover, perfusion-weighted maps obtained 3 months after treatment initiation failed to reveal a significant decrease in regional cerebral blood flow values (Fig. 2B). These unexpected findings were interpreted as resulting from persistent leakage of contrast agent molecules through unrepaired blood–brain barrier of capillaries enlarged by a post-inflammatory ‘vasoplegic’ status. Another prominent feature of imaging monitoring was a rapid atrophy leading to severe parenchymal shrinkage of the pons (Fig. 1H–I), which we considered as the final retrospective demonstration for a non-malignant affection in spite of persistent contrast enhancement and increased regional cerebral blood flow values.

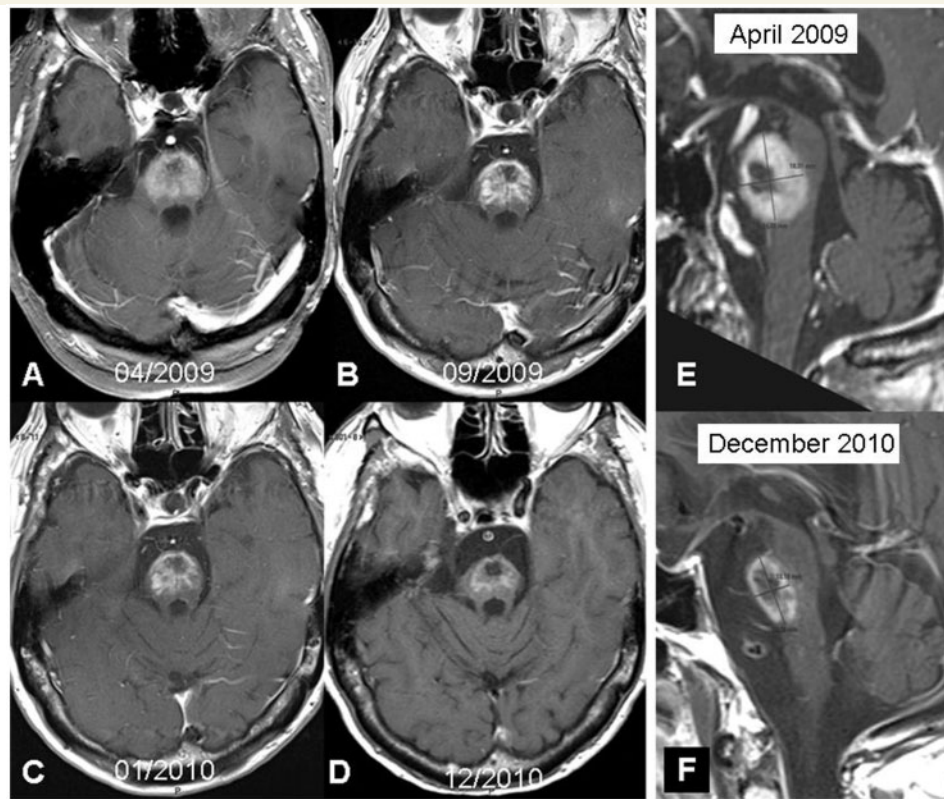


Figure 1 Contrast-enhanced T₁-weighted magnetic resonance monitoring throughout the 20-month treatment course. (A–D) Axial transverse images in similar slice location through mid-pons. (A) Initial pre-treatment work-up. Punctate and curvilinear pattern is suspected but not evident. Central antero-medial defect was thought to correspond either to necrotic focus or to cystic scar of a previous clinically silent inflammatory episode. (B) Five-month follow-up status. Only moderate regression of inflammatory signs are present but with subsequently more visible 'punctate and curvilinear peppering'. (C) Nine-month follow-up status. Strong contrast-enhancement is still present. Parenchymal atrophy has begun. (D) Twenty-month follow-up status. Contrast-enhancement is still present and atrophy has become obvious. (E and F) Mid-sagittal images through brainstem. (E) Mid-sagittal contrast-enhanced T₁-weighted view at initial phase showing intense contrast enhancement within pons, sparing adjacent medulla oblongata and mesencephalon. Central defect was similar to that in (A). (F) Mid-sagittal contrast-enhanced T₁-weighted view at 20-month time-point showing severe parenchymal shrinkage of the pons together with thinning of peripheral enhanced ring when compared with the previous image.

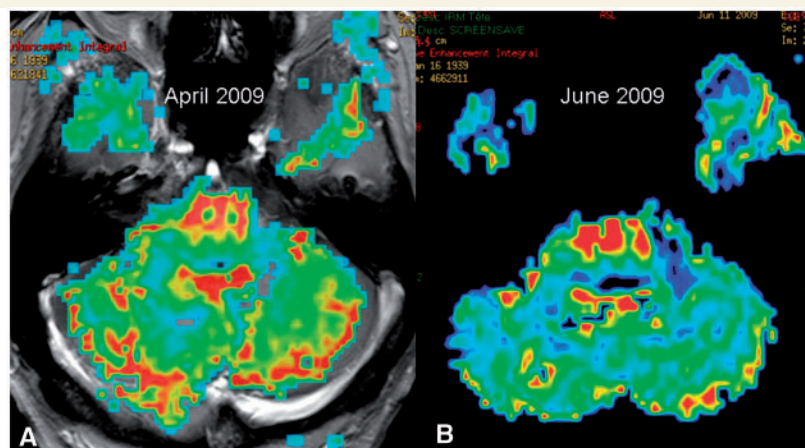


Figure 2 Early perfusion-weighted imaging follow-up. (A) Initial perfusion-weighted-derived regional cerebral blood flow map through the pons (with superimposition of contrast-enhanced T₁ image) showing increased regional cerebral blood flow with 'trident-like pattern'. 'Hottest' red areas reached a 300% increase in regional cerebral blood flow values when compared with unaffected cerebellar white matter. (B) Follow-up regional cerebral blood flow map 3 months later in corresponding slice location (superimposition with anatomical image not shown) failing to demonstrate significant subsidence of perfusion abnormalities in spite of near complete recovery of dysarthria and fairly good improvement of the cerebellar ataxia.

We believe that our patient suffered from a severe form of CLIPPERS syndrome. Her history confirmed the appropriateness of treating such patients without histopathological examination. Contrast-enhanced magnetic resonance monitoring and perfusion-weighted findings significantly added and acted as safety nets.

References

Pittock SJ, Debruyne J, Krecke KN, Giannini C, van den Aneele J, De Herdt V, et al. Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS). *Brain* 2010; 133: 2626–34.