Restricted diffusion delineated a short, very early phase of lesion evolution. While lesions progressed to the typical acute oedematous appearance (strong T2 hyperintensity and blood-brain-barrier disruption) the ADC increased in parallel to 'pseudo-normalisation' and increased values. Increased diffusion in acute lesions is in agreement with histological observations of widened extracellular spaces due to vasogenic inflammatory oedema.

In contrast to this there is no obvious explanation for restricted diffusion in early MS lesions. From experimental models of cerebral ischaemia and status epilepticus it is known that diffusion-weighted (DW) MRI can demonstrate restricted diffusion associated with shrinkage of the extracellular space and cytotoxic cell swelling induced by energy depletion (through an intracellular rise of lactate due to anaerobic glycolysis followed by depolarisation). In MS lesions the aggressive inflammatory milieu may cause energy depletion (e.g. through mitochondrial dysfunction induced by proinflammatory cytokines). We found pathological lactate peaks that may indicate a critical energy state in MS lesions. Lactate peaks could also be associated with hypercellularity, a recognised feature in early lesion development occasionally with prominent lymphocytic and microglial cell infiltrates and cell swelling in activated astrocytes. The slight changes of T2 and post-contrast MRI indicating increase of BBB permeability might have been sufficient for cell migration into developing lesions. It is conceivable that dense cellular infiltrates reduce the extracellular space and thereby restrict diffusion before this effect is counterbalanced by the development of inflammatory vasogenic oedema. Both mechanisms (disturbances of energy metabolism/hypercellularity) might act together.

Figure 1
A newly developing lesion with restricted diffusion on ADC map (arrows, row 2, middle), on follow-up strong T2 hyperintensity, increased ADC and prominent contrast enhancement.