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Reply:

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We thank Dr Ramantani and colleagues for their comments on our recent article discussing neuroradiologic findings in Aicardi-Goutières syndrome (AGS).[1]

The fact that they, too, report a relatively large series[2] adds weight to the idea that AGS may not be as rare as once thought. We entirely agree with their view that AGS shares more features with systemic lupus erythematosus than was previously believed to be the case[2] and also that clinical, genetic, and neuroradiologic findings should be considered together to achieve a better understanding of the complex pathogenesis of this disease. However, as recalled by Ramantani and colleagues, our work, prompted by the lack of a detailed description of neuroimaging in AGS, focused specifically on the neuroradiologic picture of the disease.

In our sample (see On-Line Table 1 in our article[1]), we found extra-neurologic involvement in 16 patients (44.4% of the sample) who presented with, among other manifestations, hypothyroidism, chilblain lesions, and celiac disease. As pointed out by Ramantani and colleagues, the prevalence of these features already highlighted in our sample, underlines the need to screen for autoimmune conditions because these can go undiagnosed. Indeed, we currently have a work in progress focusing on this very aspect. As we mentioned in the "Discussion" section of our article,[1] a precise correlation of neuroimaging with genetic and clinical data is needed to improve understanding of AGS and to interpret it as an autoimmune-mediated disorder.

We reiterate that cerebral calcifications are a key finding in the neuroradiologic picture of AGS, typically localized in the basal ganglia, in the deep white matter, and also in the posterior fossa[3-5]: as stated in our article, we found calcifications in the dentate nuclei in 11 patients (30.5% of our sample).[1]

Regarding the pathophysiologic mechanism responsible for the neuroradiologic picture of AGS, the microangiopathic hypothesis is generally accepted, especially in light of the studies of Barth et al.[6] As reported in our article,[1] the distribution of cerebral calcifications in AGS, mainly in the basal ganglia and the lobar white matter, may recall the finding of calcifications located along the walls of the arterioles,[7] thus supporting the hypothesis of a microangiopathic origin of the calcium deposition. However, the pattern of the leukodystrophy is not particularly typical of a leukoencephalopathy of inflammatory microangiopathic origin: in most of our sample, we observed a symmetric homogeneous distribution of the signal-intensity alteration rather than the patchy pattern usually found in microangiopathic autoimmune diseases.[8] In other words, the white matter signal-intensity alterations may not be interpreted simply as microangiopathic changes, and the microangiopathic mechanism could be limited to the first stages of the disease, when the autoimmune system mediated by interferon-α is still active. A more clearly defined and detailed follow-up study of a patient series, comparing the early and subsequent stages of the disease, is needed to obtain more information about the leukodystrophic process in AGS.

The lack of contrast enhancement found in our sample[1] simply confirms the integrity of the blood-brain barrier and does not necessarily conflict with the hypothesis that AGS has a microangiopathic pathophysiology. Furthermore, in our sample, no pathologic enhancement was noted in patients who underwent neuroradiologic examinations during the acute phase of the disease,[9] thus reinforcing the idea that the pathophysiology of AGS is probably more complex than that of a typical autoimmune-mediated disease.

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