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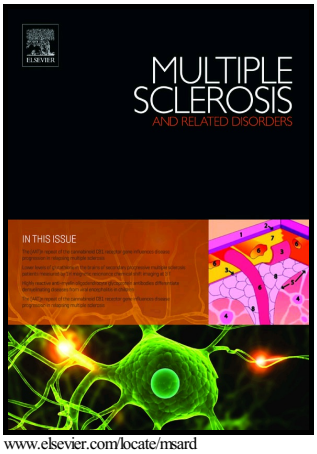

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Tatiana Koudriavtseva, Svetlana Lorenzano

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A possible role of impaired cell-mediated immunity in the pathogenesis of tumefactive demyelinating lesions

Tatiana Koudriavtseva[1*], Svetlana Lorenzano[2]

[1]Department of Clinical Experimental Oncology, Regina Elena National Cancer Institute, IFO, Via Elio Chianesi 53, 00144, Rome, Italy;

[2]Department of Neurology and Psychiatry, Sapienza University of Rome, Viale dell'Università 30, 00185 Rome, Italy

[*]**Corresponding author:** Tel.: +390652666580; fax: +390652665068; tatiana.koud@gmail.com

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We read with great interest the review on tumefactive demyelinating lesions (TDLs), i.e. lesions greater than 2.0 cm with "tumor-like" radiologic characteristics, recently published by Algahtani and colleagues (Algahtani et al., 2017). This is very interesting and attractive clinical theme due to challenges in differentiate diagnosis between TDLs and brain tumors, their poorly standardized therapy and ill-defined long-term evolution (Abdoli and Freedman, 2015).

TDLs may occur either as first clinical event in patients who could be subsequently diagnosed with multiple sclerosis (MS) or as relapse in MS patients often associated with use and/or suspension of disease-modifying therapies (DMT), or in other conditions including viral infections (e.g. HIV), autoimmune diseases (e.g. lupus erythematosis, Sjogren's syndrome, Behcet's disease), drugs (tacrolimus), and malignancy (e.g. renal cell carcinoma) (Algahtani et al., 2017).

To clarify the etiology and pathogenesis of TDLs, review's authors supposed that typical edema and macrophage activation might be consequent to a cytokine effect rather to the direct effect of T- or B-cell immunocytotoxicity, thus explaining the development of TDLs in course of fingolimod-related lymphopenia.

The hypotheses on the potential mechanisms underlying cases of TDL associated to MS treatments are conflicting (Algahtani et al., 2017). However, an immune condition characterized by an impaired adaptive and in particular cell-mediated immunity with relatively intact innate immunity may be recognized in several published cases. In fact, fingolimod, the sphingosine-1-phosphate