Antibodies against contactin-associated protein 2 (CASPR2), a protein associated with the Voltage-Gated Potassium Channel Complex (VGKC) [1], represent an emerging cause of some old neurological manifestations; such as Morvan's and Isaacs' syndromes, as well as a variety of phenotypes encompassing limbic encephalitis, neuropathic pain, late onset epilepsy and dysautonomia [2,3].

Although the prevalence of anti-neuronal surface antibodies and their impact on clinical practice is not well-established [4-7], they represent an important etiology of autoimmune encephalitis and a curable cause of dementia and acute psychosis [8-10].

In a study by Baumgartner, et al. [11], 34% of the patients with autoimmune encephalitis were initially admitted to the psychiatry department. In addition, psychiatry disturbances represent the second most common presentation of autoimmune encephalitis after seizures [11].

When it comes to anti-CASPR2 psychiatric phenotypes, symptoms tend to present in a progressive manner (5-7 months); mostly with no fluctuations, and a tumor is present in 19% of the patients [2,10]. It affects mostly elderly man (Figure 1) [2,12] and clinical presentation ranges from cognitive decline, sleep disorders, depressive mood, global amnesia - especially when associated with anti-Leucine-rich, glioma inactivated 1 (anti-LGI1) antibodies - and psychotic episodes [2]. Other symptoms, such as seizures, peripheral nerve symptoms and dysautonomia may appear later in the disease, possibly being misdiagnosed as dementia or psychiatric disease [2].

It is important to highlight that most of the patients with anti-CASPR2 have either normal MRI image or hippocampal atrophy, which holds and association with anti-LGI1 antibodies; and therefore the diagnosis may be challenging when facing a case with this suspected etiology [13].

Figure 1: We summarized the profile of the patient that usually present with the anti-CASPR2 psychiatric phenotypes. Elderly man image acquired at http://smart.servier.com/.
In conclusion, antibodies against CASPR2 should be remembered as a cause of cognitive imbalance or psychosis, especially in elderly men, even with a normal MRI image. Also, if a tumor is not yet known, it is important to make a screening. Finally, anti-CASPR2 disorders respond well to immunotherapy, but may acquire a poor prognosis, especially when treatment is delayed due to misdiagnosis [12].

Author’s contributions
Performed data acquisition and data analysis as well helping with the writing in the text: André Ricardo Merkle, Leticia Caroline Breis, Marco Antônio Machado Schlindwein.

Made substantial contributions to conception and design of the study, as well as provided technical support: Marcus Vinicius Magno Gonçalves MD PhD.

References

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