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Letter to the Editor

LGI1-Associated Immune Encephalitis Requires a Comprehensive Search for Occult Malignancy

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We read with interest the article by Bounou *et al*. about a 71-year-old man with autoimmune encephalitis (AIE) associated with antibodies to leucine-rich glioma inactivated 1 (LGI1) who was eventually diagnosed with prostate carcinoma and monoclonal gammopathy of unknown significance (MGUS) [1]. The patient benefited from glucocorticoids, intravenous immunoglobulins and rituximab (RTX) [1]. The study is excellent, but some points should be discussed.

The first point is that SARS-CoV-2 infection (SC2I) has not been ruled out as a trigger of AIE [1]. Since AIE can be a complication of SC2I [2], it would have been mandatory to test the patient for SARS-CoV-2 on admission using RT-.PCR and during hospitalization. Since AIE can also be a complication of SARS-CoV-2 vaccination (SC2V), we should also know the vaccination status of the index patient.

The second point is that no results of a comprehensive viral panel have been reported [1]. Although it is reported that a film array was negative for the most common neurotropic viruses, a comprehensive viral panel is mandatory because viral encephalitis is the most common differential diagnosis of autoimmune encephalitis and both can coexist [3].

The third point is that current medication and comorbidities other than rheumatoid arthritis and leflunomide were not reported [1]. Since the patient was 71 years old, it is very likely that he suffered from other diseases in addition to rheumatoid arthritis, MGUS and prostate cancer. In particular, immune checkpoint inhibitors (ICI) have been reported in association with LGI1-associated AIE [4].

The fourth point is that the LGI1 antibody may have been produced in response to the emerging prostate cancer. It has been previously reported that LGI1 protein is involved in tumour cell invasion by regulating the ERK pathway [5]. There is also evidence that inactivation of LGI1 in prostate cancer cells is related to tumour progression [5]. We should know when the prostate-specific antigen (PSA) was first determined in the index patient, in particular whether the PSA was already elevated before the clinical manifestations of AIE occurred. Why was the PSA not determined on initial admission? In men >60 years of age, PSA determination should be part of routine screening for age-related diseases.

Some other points should be addressed. How can it be explained that the FDG-PET scan was normal but the bone marrow biopsy showed 7% plasma cells? What were the results of the second lumbar puncture? We should also know the values of light chains in serum and urine. It should be explained why the patient waited 10 days before presenting with confusion. How can it be explained that the first MRI with contrast was normal despite the CNS symptoms? The second malignancy that needs to be ruled out is multiple myeloma.

To summarize, this interesting study has limitations that put the results and their interpretation into perspective. Addressing these limitations could strengthen the conclusions and support the message of the study. As AIE is in most cases a paraneoplastic phenomenon, it is imperative to comprehensively screen patients with AIE for malignancy, although AIE can also be associated with immunologic diseases such as rheumatoid arthritis, viral infections and concomitant medications. Comprehensive screening for malignancy is critical to avoid missing time for early and appropriate treatment.

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References

1. Bounou L, Kaklamanos A, Androutsakos T, Kemanetzoglou E, Moustaka I, Protogerou A, *et al*. Anti-LGI1 Autoimmune Encephalitis in a Patient with Rheumatoid Arthritis and MGUS. Eur J Case Rep Intern Med. 2024; 11(7):004572. Doi: 10.12890/2024_004572
2. Valencia Sanchez C, Theel E, Binnicker M, Toledano M, McKeon A. Autoimmune Encephalitis After SARS-CoV-2 Infection: Case Frequency, Findings, and Outcomes. Neurology. 2021; 97(23):e2262-e2268. Doi: 10.1212/WNL.0000000000012931
3. Zhang JR, Zhuang S, Xu XD, Song WL, Li KR, Jiang Y, *et al*. Overlapping Epstein-Barr virus encephalitis and autoimmune glial fibrillary acidic protein astrocytopathy. J Neuroimmunol. 2023; 382:578174. Doi: 10.1016/j.jneuroim.2023.578174
4. Müller-Jensen L, Zierold S, Versluis JM, Boehmerle W, Huehnchen P, Endres M, *et al*. Dataset of a retrospective multicenter cohort study on characteristics of immune checkpoint inhibitor-induced encephalitis and comparison with HSV-1 and anti-LGI1 encephalitis. Data Brief. 2022; 45:108649. Doi: 10.1016/j.dib.2022.108649
5. Cowell JK, Head K, Kunapuli P, Vaughan M, Karasik E, Foster B. Inactivation of LGI1 expression accompanies early-stage hyperplasia of prostate epithelium in the TRAMP murine model of prostate cancer. Exp Mol Pathol. 2010; 88(1):77-81. Doi: 10.1016/j.yexmp.2009.09.008