A Case of Recurrent Autoimmune Encephalitis Due to Homozygous TNFAIP3 Mutation

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INTRODUCTION

The A20 protein, encoded by the tumour necrosis factor alpha-induced protein 3 (TNFAIP3) gene, is involved in the negative regulation of the NF-κB signalling pathway. Loss-of-function mutations in TNFAIP3 cause A20 haploinsufficiency (HA20) which predisposes to autoinflammatory diseases such as Behçet's disease, juvenile idiopathic arthritis and SLE (1). Neurological involvement is quite rare in HA20.

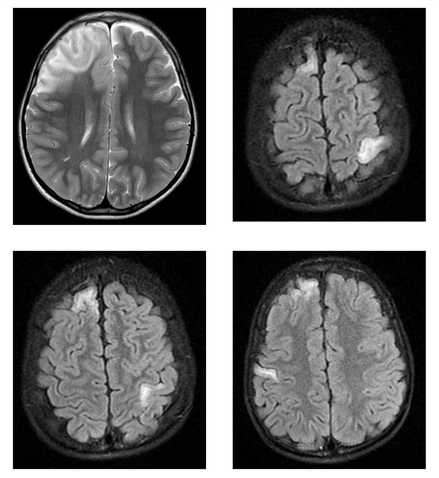

Figure 1. Brain MR images taken at three consecutive admissions. Hyperintense lesions and contrast enhancement in the right hemisphere frontal cortex, left hemisphere parietal cortex and right hemisphere parietal cortex on T2 enhanced images.

CASE PRESENTATION

An 11-year-old male patient was admitted to our hospital with complaints of headache, behavioural changes and decreased academic performance that started after he had COVID-19 infection at the age of 9 and recurrent seizures that started at the age of 10. His family history revealed that he walked at the age of 2 years and his routine vaccinations were incomplete. Morever, his parents were relative, one uncle had congenital mental retardation, and there was no other history of neurological disease in the family. Rheumatological symptom query was unremarkable. On neurological examination, left nasolabial sulcus was faint, DTRs were brisk and pathological reflexes were present, other system examinations were normal. Lumbal puncture (LP) could not be performed because of a lesion compatible with encephalitis causing oedema in the right frontal region and mild subfalsine herniation on brain MRI. He was hospitalized with a pre-diagnosis of autoimmune/viral encephalitis and received IVIG, antiedema treatment and antibiotherapy. He presented with seizures two more times at 6 months and 11 months after discharge. Newly developed cortical lesions were present on brain MRI at both admissions and he was hospitalized and treated with the diagnosis of recurrent autoimmune encephalitis. CSF examination was positive for oligoclonal band, viral, autoimmune encephalitis and paraneoplastic panels and serum MOG antibody test were negative. Immunological evaluation revealed reversal in CD4/CD8 ratio, low naïve T cells, high effector memory T cells and low RTE. WES examination performed for primary immune deficiencies with immunodysregulation revealed a homozygous mutation (c.607C>T) in the TNFAIP3 gene that was consistent with the patient's clinic. Over activation of the NF-κB signalling pathway was shown in functonal analyses. Monthly IVIG treatment and anti-IL-6 (Tocilizumab) were started and the patient was scheduled for bone marrow transplantaton.

CONCLUSION

Neurological involvement in A20 haploinsufficiency has been reported as CNS vasculitis in only a few cases to date (2). With this case with biallelic mutation, recurrent autoimmune encephalitis and autosomal recessive form of the disease were described for the first time in HA20 patients and thus the clinical spectrum of the disease expanded.

Laboratory	Test Results
Complete Blood Count	
Hemoglobin (g/dL)	13,8
Leukocyte (/mm³)	11240 (5200-11000)
Absloulte lymphocyte (/mm³)	2120 (2300-5400)
Absolute neutrophil (/mm³)	8310
Absolute eosinophil (/mm³)	50
Platelet (/mm3)	378000
Immunoglobulines (mg/dL)	
IgA	289 (57-282)
IgG	1280 (745-1804)
IgM	76,8 (78-261)
Lymphocyte subsets (%)	
CD3	63
CD4	34
CD8	23
CD16+56	19
CD19	15

Table 1. Immunological investigations of the patient

References

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