

Encephalomyelitis with retinopathy in common variable immunodeficiency (CVID)

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Abstract - CVID is the most common primary immunodeficiency and rarely causes neurological manifestations since the introduction of IVIg but here, the authors present a case of a 31-year-old Afro-Caribbean man who after short non-adherence to his immunoglobulins, develops encephalomyelitis with retinopathy. To the authors' knowledge, this is the first case presented with retinal photographs, OCT, CT, MRI and brain biopsies.

Keywords: encephalomyelitis; mri; ophthalmology; immunodeficiency; case report

Introduction

Encephalitis, myelitis and encephalomyelitis have previously been described in patients with primary immunodeficiency in association with unexplained retinopathy and in the absence of an identifiable infectious aetiology.¹ We report the first case with retinal photographs and ocular coherence tomography in conjunction with MRI and brain biopsies.

Case Report

A 31-year-old African-Caribbean man with CVID was referred with headache. He described an acute-onset, constant headache for one month without fever, meningism, seizures nor any preceding illness. He was diagnosed with CVID as a teenager and managed with three-weekly IVIg administered at home by his mother, who was a nurse. However, he later revealed he had missed his last few infusions. The neurological and

systemic examinations were unremarkable except for bilateral drusen-like retinal abnormalities which persisted on follow-up a year later (figure 1).

An urgent CT brain scan revealed a hyperdense lesion within the right callosal body (figure 2A). There was restricted diffusion and contrast-enhancement on MRI (figure 2B) with several smaller lesions around the lateral ventricles. CSF examination showed 68 lymphocytes and 1.31g/L protein. Gram stain, cultures, cytology and viral PCR screen were negative. Repeat CSF examination revealed a type 2 pattern of oligoclonal bands (previously known as unmatched oligoclonal bands). Screening for infective, autoimmune and neoplastic causes, including whole body CT, was negative. Repeat MRI one month later showed resolution of the initial lesions. New bilateral, confluent T2-weighted hyper-intensity through the periventricular and deep white matter (figure 2C) was associated with subtle restricted diffusion and perivascular enhancement. There was diffuse intramedullary signal change within the entire spinal cord (figure 2D).

The patient developed a sixth nerve palsy and erectile dysfunction. A third CSF examination was uninformative and frontal lobe biopsy showed a non-specific leptomeningitis and encephalitis, predominantly affecting white matter (figure 3). There was no evidence of granulomatous inflammation, vasculitis, infection or neoplasia. A tissue PCR screen was negative.

Results

The patient resumed regular IVIg and his symptoms spontaneously resolved without treatment (no steroids given). The retinal findings are unchanged and the MRI abnormalities resolving.

Discussion

CVID is the commonest symptomatic primary immunodeficiency syndrome and characterized by reduced levels of IgG, IgA and/or IgM with reduced or absent specific antibody production.² Neurologic complications are rare; CNS infections and autoimmune disorders are described and chronic enteroviral encephalitis was frequently seen before the introduction of IVIg in 1982.^{3,4}

Rudge *et al* described encephalitis, myelitis or encephalomyelitis in six CVID and seven X-linked agammaglobulinaemia patients in whom enteroviruses were confirmed in a minority.¹ MRI findings were variable; periventricular and deep white matter lesions were mentioned in two cases and atrophy in others. Three CVID patients developed an unexplained retinopathy interpreted as similar to retinitis pigmentosa or chorioretinitis (images unavailable). A recent series describes 14 patients on IVIg for various primary immunodeficiencies that developed a progressive neurodegeneration of unknown cause.⁴ Five developed a retinopathy.

A novel form of autoimmune meningoencephalomyelitis, glial fibrillary acidic protein (GFAP) astrocytopathy, has recently been described.⁵ The clinical, CSF and MRI findings were similar; however, a quarter of the patients described had a hypergammaglobulinaemia, as opposed to the underlying hypogammaglobulinaemia in our case. Unfortunately we were not able to check for these antibodies as this was not described at the time of presentation.

The encephalomyelitis with retinopathy in our case has a striking similarity to those in previous series but there is a possibility that the retinal abnormalities are an incidental finding and the initial contrast-enhancing lesions remain unexplained. In contrast to previous cases, the retinal abnormalities were more drusen-like, a pattern previously described in a single patient with CVID.⁶ Similar to Rudge *et al* we maintain

a viral cause is most likely; however, the novel autoimmune GFAP meningoencephalitis may also be a possibility.

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Disclosure of Interest

The authors report no conflict of interests

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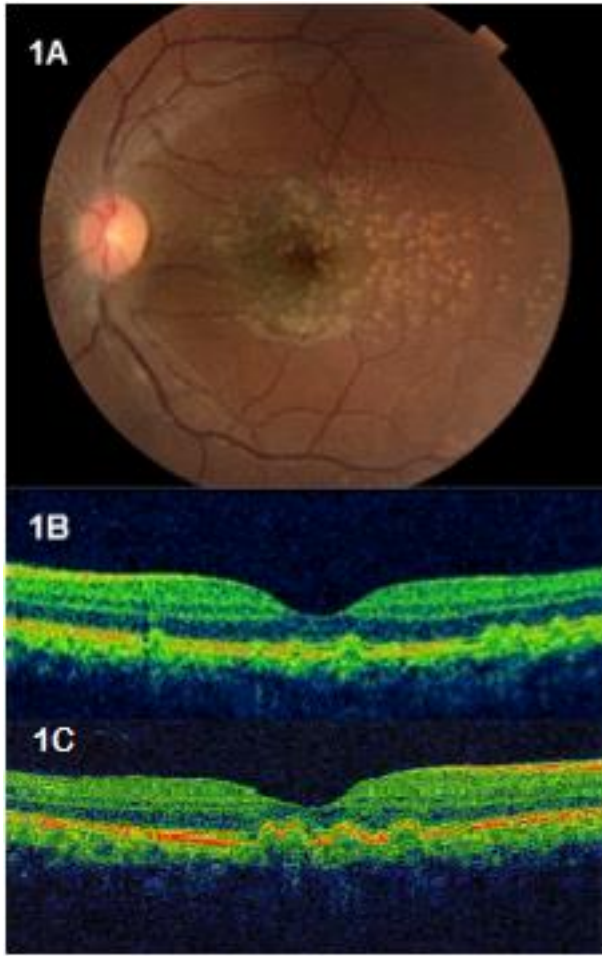
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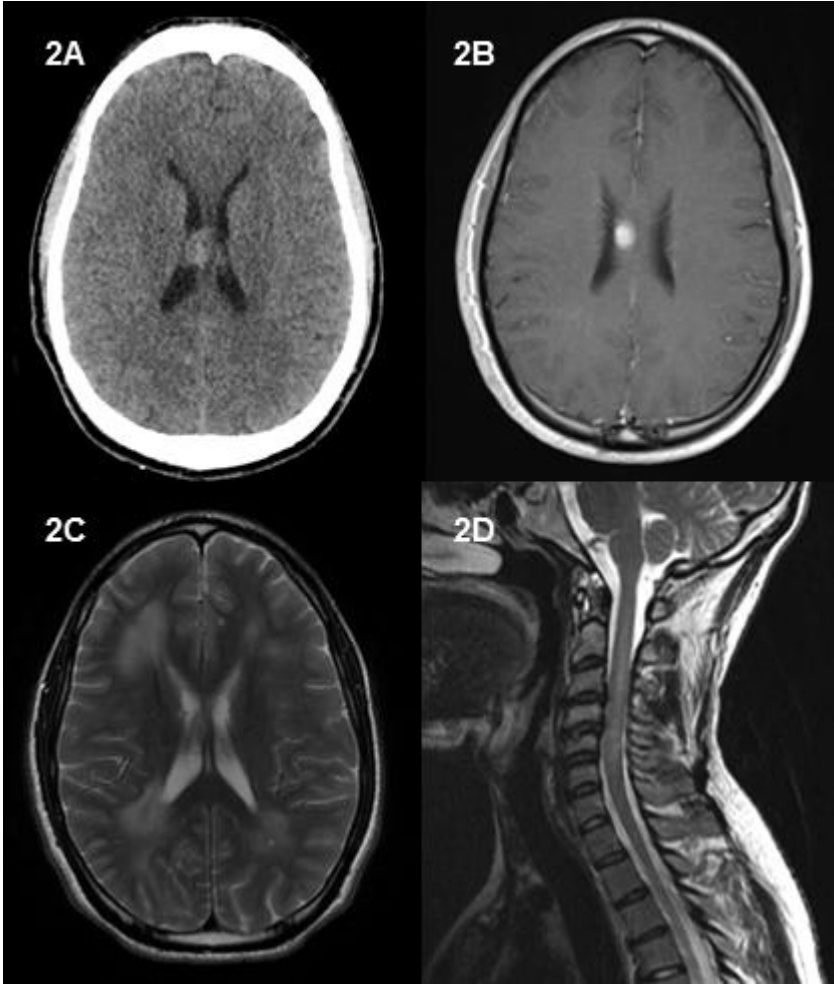
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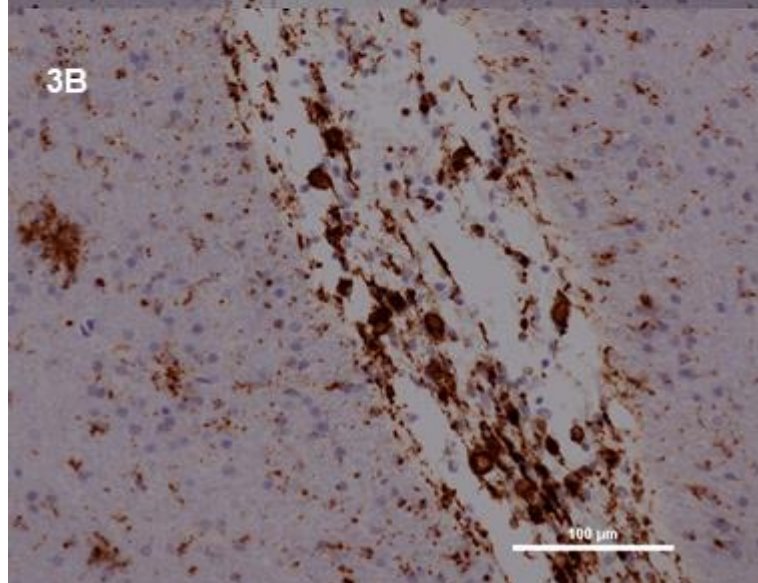
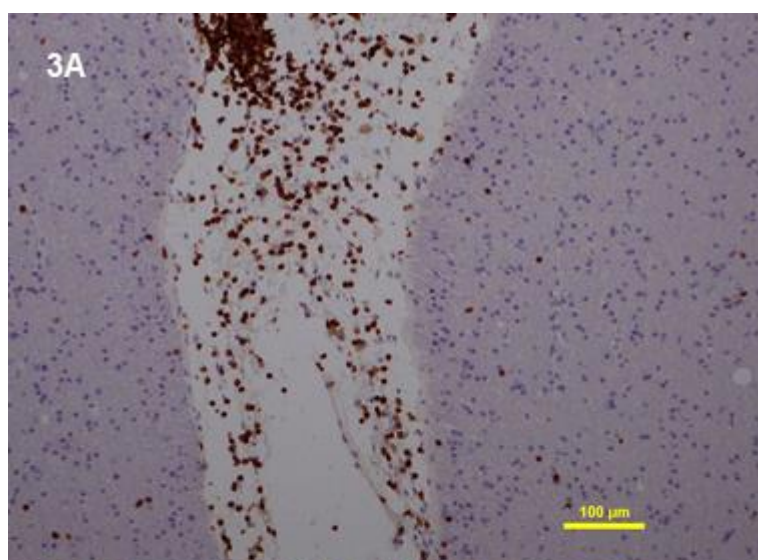


Figure 1. (A) Retinal photograph of the left fundus showing drusen-like abnormalities in the macula. (B) Ocular coherence tomography of the left eye macula showing drusen-like deposits just below the level of the retinal pigment epithelium. (C) Ocular coherence tomography of the left eye macula 12 months later showing persisting drusen-like deposits.

Figure 2. (A) Unenhanced axial CT Brain image showing a hyperdense mass within the right callosal body. (B) Axial T1-weighted MRI Brain post-gadolinium demonstrating a contrast enhancing mass within right callosal body. (C) Axial T2-weighted MRI Brain image showing bilateral, confluent hyperintensity through the periventricular and deep cerebral white matter. (D) T2-weighted sagittal MR image showing diffuse intramedullary signal change within the cervical cord.

Figure 3. Right frontal lobe biopsy. The white matter shows dilated Virchow-Robin spaces with mild perivascular infiltration by lymphocytes and macrophages. An occasional microglial nodule and scattered apoptosis is seen. There is mildly increasing glial cellularity and pleomorphism consistent with reactive gliosis. Adjacent cortex shows mild gliosis and an occasional perivascular lymphocyte. (A) Immunostaining for CD3 shows moderate numbers of perivascular T-cells and scattered parenchymal T-cells. Immunostaining for CD20 shows no B-cells. (B) Immunostaining for CD68 shows moderate numbers of perivascular macrophages and moderate parenchymal microglial activation.