



It is never a Good Syndrome

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Case History

A 65 year old man attended the emergency department for 10 days history of headache, fever, vomiting and visual hallucination. He had a history of thymoma with thymectomy (histology: minimally invasive thymoma) two years ago, and had been stable without recurrence. Upon arrival to the medical ward, he developed two episodes of generalized tonic clonic seizures. His urgent plain CT brain showed a 2.5 cm right parietal lobe round lesion with perilesional edema, which was rim enhancing on contrast scan. Urgent MRI brain favored cerebral abscess. Patient was started on phenytoin, intravenous ampicillin, metronidazole and ceftriaxone. Emergency craniotomy was performed. Brain biopsy confirmed herpes encephalitis. CSF was positive for herpes simplex virus 2 PCR. He was given 5 weeks of intravenous acyclovir, guided by CSF viral PCR, white cell and protein level (Figures 1-5 and Table 1).

Why is Underlying Immunodeficiency Suspected?

As HSV2 is a rare cause of adult-onset herpes encephalitis (over 90% being HSV1 infection [1]), it raised suspicion on the patient's immunity. In addition, he was found to have multiple pathogens in current admission as well as a past history of recurrent infections (Table 2-4).

Features of Good Syndrome

Based on the compatible immunological profile and history of thymoma, the diagnosis of Good Syndrome, i.e. thymoma with immunodeficiency, was established. It is a rare condition and is associated with poor prognosis (one study found mortality of 41% [2]). It is characterized by a combined B cell and T cell deficiency [3,4]. The classical immunological features compose of hypogammaglobulinemia, reduced B cells, reduced CD4 T cell, abnormal CD4 to CD8 ratio [3,4]. The most common cause of infection is sinopulmonary infection with encapsulated bacteria, e.g., *Haemophilus influenzae* and *Streptococcus pneumoniae* [2-4].

Management and Outcome

Patient was started on monthly intravenous immunoglobulin; he was vaccinated against *pneumococcus*, *haemophilus*, *meningococcus* and *influenzae*. His repeated CT thorax did not show recurrence of thymoma. He enjoyed good neurological recovery and was discharged. Unfortunately, he returned two months later with bilateral eye blindness, his vitreous aspirate was positive for HSV2 PCR. He suffered from bilateral acute necrotizing retinitis from HSV2 infection and was permanently blind. He was put on lifelong oral acyclovir since then. Upon his follow up two years from the first admission, he had been well without significant infective episodes.

Neurology and Good Syndrome

Rare CNS infections can occur in immunodeficiency. There are case reports [3] of cerebral toxoplasmosis, CMV encephalitis, and progressive multifocal leukoencephalopathy from JC

Table 1: Histology of brain biopsy.

Frozen Section: Atypical lymphoid proliferation
Formal Pathology: Nuclei with viral cytopathic changes including margination of chromatin and rare multinucleation are seen. Cells are positive for herpes simplex virus on immunohistochemical staining. Immunohistochemistry is in keeping with reactive lymphoid infiltrates. There is no evidence of malignancy

Table 2: Microbiological investigations.

Current admission	Previous history for past 2 years
<ul style="list-style-type: none"> Stool: Campylobacter and norovirus Nasopharyngeal swab: Enterovirus Buttock wound: HSV 2 	<ul style="list-style-type: none"> Recurrent labeled "herpes zoster" infection Recurrent Hemophilus influenzae chest infection

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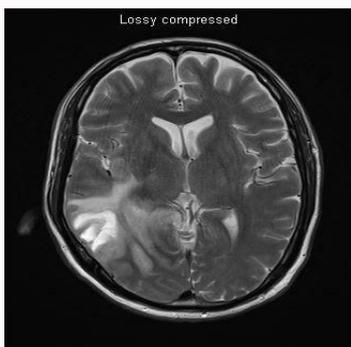


Figure 1: MRI T2 weighted image showing a T2 hyper intense right temporal lesion.

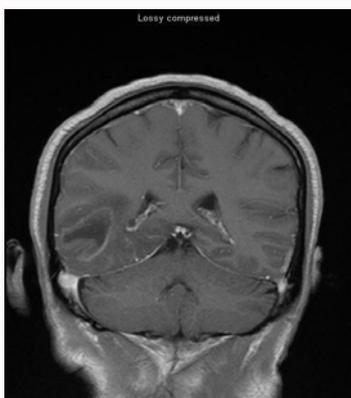


Figure 2: MRI with contrast showing a ring-shaped lesion with contrast enhancement.

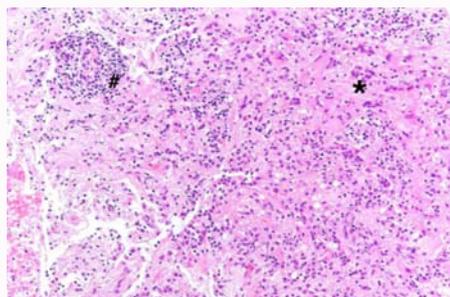


Figure 3: H&E staining showing reactive gliosis (*) and peri vascular lymphoid infiltrates (#).

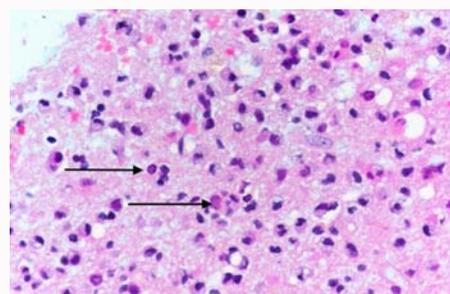


Figure 4: H&E staining showing viral cytopathic change including cells with viral inclusions and margination of chromatin (arrow).

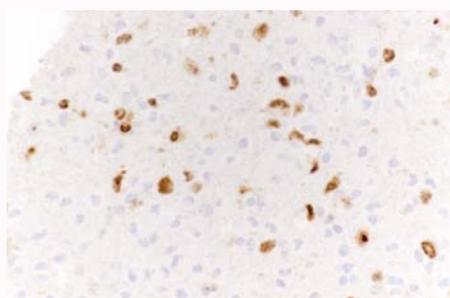


Figure 5: Immunohistochemical stain for herpes simplex virus highlights numerous viral inclusions (in brown).

Table 3: Haematological investigations.

Lymphocyte	0.6-0.8	N=1.0-3.2 × 10 ⁹ /L
Globulin	15	N=18-38 g/L
Anti-HIV antibody	Negative	

Table 4: Flow Cytometry of peripheral blood sample.

Marked B-cell lymphopenia
Mild CD4+ T cell lymphopenia
Low normal CD8+ T-cell count
Reversed CD4: CD8 ratio among T-cells
Mild NK-cell lymphopenia

virus in patients with Good Syndrome. 15% of Good Syndrome patients have myasthenia gravis [3]. Neurologists should be vigilant if myasthenic patients develop recurrent infections. This scenario creates diagnostic challenge as many myasthenic patients are being put on immunosuppressants. Microbiological profile, serum globulin level and lymphocyte count may give diagnostic clues. When in doubt, a peripheral blood flow cytometry, liaison with immunologists may be mandatory.

Treatment of autoimmune diseases e.g., myasthenia gravis, that require immunosuppressants, in patients with Good Syndrome who carry high risk of infections, is a clinical dilemma.

Conclusion

This is a case of Good Syndrome presented with HSV2 encephalitis. It should be reminded that over 90% of adult-onset herpes encephalitis

is caused by HSV1. Immunodeficiency should be suspected in HSV2 encephalitis. Good Syndrome is thymoma with immunodeficiency. It is rare and carries a poor prognosis. Clinicians should be alert about this syndrome in patients with recurrent unexplained infections, thymoma, and autoimmune diseases e.g. myasthenia gravis. Finally, more recognition, aggressive treatment and preventive measures may help to improve survival for these patients.

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