Case Report

Autoimmune Encephalitis as a Rare Paraneoplastic Syndrome in Adrenocortical Carcinoma

Abstract

Paraneoplastic neurologic syndromes (PNSs) are rare in pediatrics and are understood to be consequences of cross-reactivity against various neuroendocrine antigens expressed on cancer cells. Here, we report a case of autoimmune encephalitis, a type of PNS associated with a case of adrenocortical carcinoma (ACC), that had a clinical response to immunosuppressive therapy. ACC is a rare tumor with controversial tissue of origin but expresses various neuroendocrine antigens that could be the possible mechanism for this rare yet interesting association.

Keywords: *Adrenocortical carcinoma, paraneoplastic neurological syndrome, seronegative autoimmune encephalitis*

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Introduction

Paraneoplastic neurologic syndromes (PNSs) are rare in pediatrics and are reported in only a few pediatric malignancies such as Hodgkin lymphoma, neuroblastoma, and teratoma.[1] Opsoclonus-myoclonus, encephalitis, cerebellar syndrome, and encephalomyelitis are some of the reported paraneoplastic neurological syndromes. Paraneoplastic encephalitis is usually associated with neuroendocrine tumors and lymphomas.[2] We report a case of paraneoplastic encephalitis in a patient with adrenocortical carcinoma (ACC).

Case Report

A 6-year-old male, presented with left flank swelling along with excessive facial, axillary and pubic hair for 2 months. He also had history of increased apetite and weight gain. On examination, he had hypertension, flank mass, and virilization. Abdomen and chest computed tomography were suggestive of a left-sided adrenal mass with calcification and pulmonary metastasis. Serum dehydroepiandrosterone level was >1500.0 µg/dL leading to the diagnosis of ACC. Due to upfront unresectability, he was started on mitotane and cisplatin-etoposide-doxorubicin chemotherapy.

Two weeks after starting chemotherapy, he had multiple episodes of left focal seizure with secondary generalization. The patient also had behavioral alterations, frightfulness, and deterioration of the sensorium. On examination, he had dystonia and overall increased extremity tones. Magnetic resonance imaging (MRI) of the brain showed focal areas of T2 hyperintensity and diffusion restriction in the thalami, posterior parietal, subcortical, and insular cortex. Fluorodeoxyglucose-positron emission tomography (FDG-PET) of the brain was suggestive of hypermetabolism in the frontal-temporal lobe and basal ganglia with hypometabolism in parietal-occipital lobes bilaterally [Figure 1]. Electroencephalogram (EEG) was suggestive of left hemispheric near continuous discharges with occipital predominance [Supplementary Figure 1].

The patient was started on antiepileptics but had poor responses in EEG. Ultimately, the patient went on to require five antiepileptics: valproate, levetiracetam, topiramate, lacosamide, and lorazepam. Cerebrospinal fluid (CSF) analysis was suggestive of neutrophilic pleocytosis but normal protein and sugar. The rest of the CSF workup, including bacterial, tubercular, viral, parasitic, and known autoimmune-antibody panels, were negative. With the clinical possibility of seronegative autoimmune encephalitis (AIE), the child received intravenous immunoglobulin (IVIG) and pulse steroids.

Over a span of 3 days, child showed neurological improvement in the form of

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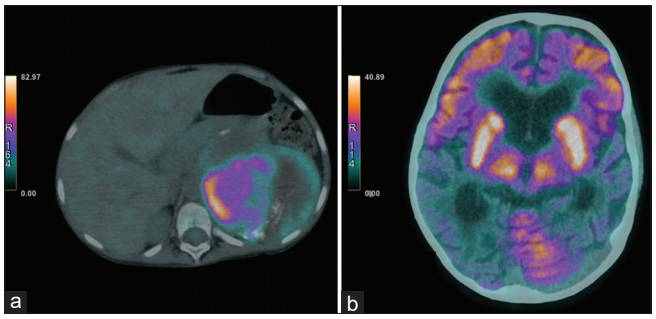

Figure 1: Axial FDG-PET/CT image showing left-sided adrenal origin calcified, solid, cystic mass with calcifications and FDG uptake in the solid component diagnosed as ACC (a) bilateral increased tracer uptake in frontal-temporal lobe and basal ganglia with decreased uptake in parietal-occipital lobes. (b) FDG-PET/CT: Fluorodeoxyglucose-positron emission tomography/computed tomography, ACC: Adrenocortical carcinoma

the improved sensorium, normalization of behavior, and seizure control. Gradually, a number of antiepileptics were tapered down from five to three. Unfortunately, the interim response for primary disease and the metastatic site was suggestive of tumor progression, and hence, parents opted for palliation.

Discussion

Malignancies usually reported with PNS include lung cancers, breast cancer, teratomas, lymphomas, neuroendocrine tumors, and malignant thymomas. Paraneoplastic encephalitis is one of the PNSs that are usually associated with tumors of neuroendocrine origin and has a debilitating course.[3] Although the exact mechanism of immune-tolerance breakdown that leads to paraneoplastic encephalitis is not known, cross reaction between tumor antigen and neural antigens is the most plausible explanation.[2] Although ACC is not of dierect neuroendocrine origin, it is positive for neuroendocrine markers like synaptophysin and neuron specific enolase.[4] This raises the possibility that some unknown neuroendocrine antigens could also be expressed over the ACC cells, which cross-react with neural antigens leading to AIE.

CSF autoantibody panel can be negative in paraneoplastic AIE;[5,6] like in the index case, due to previously unidentified antigens in some cases. In addition to CSF auto-antibody panel, MRI is an important modality, though it can be normal or nonspecific in a number of cases.[7] Multiple studies have reported increased sensitivity of FDG-PET over MRI in diagnosing AIE.[8-10] As paraneoplastic encephalitis is a form of AIE, the patterns of involvement in FDG-PET are often similar and include temporal, frontal, and basal ganglia hypermetabolism and occipital hypometabolism.[10,11] In an Indian study by Jha *et al*.,[12] it was found that while 41% of patients had isolated hypermetabolism and isolated hypometabolism each, another 18% had both. Verma and Ranjan[13] also observed a similar pattern of involvement in a cohort of 27 AIE patients, of which 10 were paraneoplastic and 7 were seronegative. The index patient had hypermetabolism in the frontal-temporal lobe and basal ganglia with hypometabolism in the parietal-occipital lobes.

First-line therapy of paraneoplastic encephalitis begins with high-dose methylprednisolone, IVIG, and plasmapheresis given individually or in combination.[14] Cases refractory to initial therapy are treated with second-line drugs such as cyclophosphamide and/or rituximab.[15]

To conclude, paraneoplastic encephalitis should be kept as a rare differential of unexplained encephalitis in a case of ACC. Exploration of the inciting antibody, which is currently unknown, will give more information on the exact antigen and the pathogenesis of this clinically interesting process.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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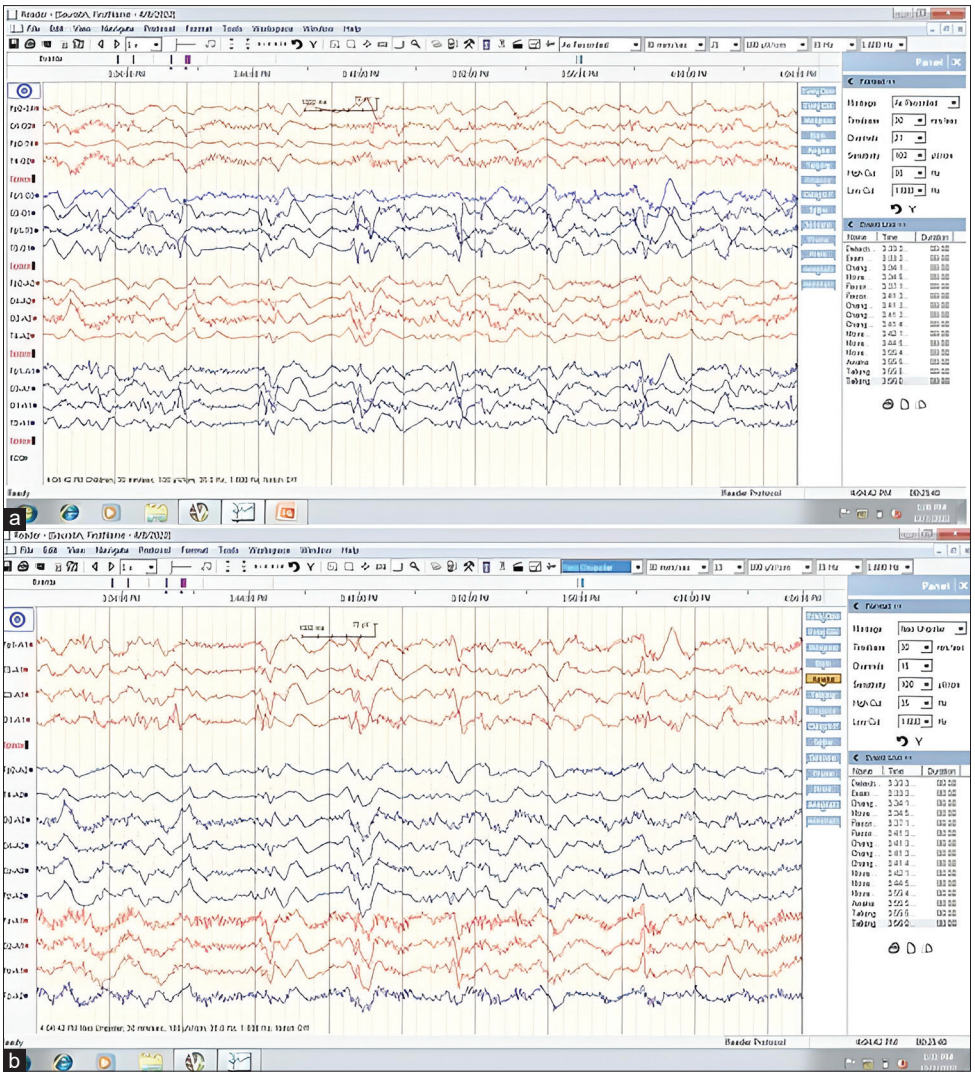

Supplementary Figure 1: Bipolar children montage epoch showing left hemispheric near continuous discharges with occipital predominance (a) unipolar montage showing the left occipital predominance of the discharges (b)