Acta Scientific Clinical Case Reports

Volume 2 Issue 12 December 2021

Case Report

Anti-NMDAR Related Autoimmune Encephalitis and Enteritis Associated with Ovarian Dermoid: A Case Report

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Received: October 20, 2021

Published: November 18, 2021

Abstract

Paraneoplastic limbic encephalitis is a component of the spectrum of Paraneoplastic neurologic disorders (PNDs). It is an immune-mediated neurological condition occurring in the presence of a known remote primary. PNDs have been reported in association with multiple malignancies, the most common one being bronchial carcinoma of lung, typically the small cell variant. Paraneoplastic autoimmune encephalitis (AE) which occurs secondary to the presence of anti-N-methyl D-aspartate receptor (NMDAR) antibodies, has been associated with ovarian teratoma. It has been described as a distinct subcategory of PNDs with a potentially lethal, however, treatment responsive course. Autoimmune enteropathy (AIE) is a rare cause of intractable diarrhea. It is considered as a probable rare complication of autoimmune anti-NMDAR encephalitis.

We present and discuss a unique case of paraneoplastic limbic encephalitis in a young woman with a small ovarian dermoid, who incidentally also presented with autoimmune enteropathy and tested positive for anti-NMDAR antibodies in serum and CSF.

Keywords: NMDA; Autoimmune; Encephalitis; Enteritis; Dermoid

Introduction

Paraneoplastic limbic encephalitis is a part of the spectrum of Paraneoplastic neurologic disorders (PNDs). The most widely accepted etiology is autoimmunity resulting in an inflammatory response, which has been proven by the demonstration of anti-neuronal antibodies in the CSF and serum of patients [1]. Clinically it is characterized by acute onset symptoms such as hallucinations, seizures, confusion and loss of short term memory. PNDs have been reported in association with multiple malignancies such as small cell lung cancer, ovarian teratoma, testicular germ cell tumor (GCT) [2], thymoma etc. [3].

We present a case of paraneoplastic autoimmune encephalitis (AE) in a young woman with a small ovarian dermoid who presented with acute onset symptoms characteristic of limbic encephalitis and autoimmune enteropathy.

Our case is unique because anti-NMDA receptor-related autoimmune enteropathy itself is rare. In addition, the synchronous occurrence of autoimmune enteropathy and AE is extremely rare in patients with an ovarian dermoid. On reviewing literature, no such case has been documented till date.

Case Report

A 17-year-old woman presented with fever, convulsions, irrelevant talk and decline in cognitive functions. She was admitted and underwent detailed neurological workup, including an MRI of the brain. MRI (Fig. 1d) revealed altered signal intensity areas in bilateral medial temporal lobes and hypothalamus, characteristic of limbic encephalitis. Cerebrospinal fluid analysis revealed no evidence of infection. During the course of her hospital stay, the patient also developed intractable diarrhea. An ultrasound of the abdomen showed diffuse edematous wall thickening involving the entire length of the large bowel, and a diagnosis of colitis was made. Stool cultures were however, negative for organisms. MR abdomen was advised for further evaluation of the bowel wall thickening which revealed T2W hyperintense edematous, diffuse, circumferential wall thickening involving the large bowel as well as the rectum (Figure 1 a, b, c). The MRI, in addition incidentally also re-

vealed a small 10x8 mm sized T1W hyperintense lesion in the right ovary, which showed complete suppression on the corresponding fat-saturated images, suggestive of a tiny ovarian dermoid. In order to link the findings, a possibility of a paraneoplastic process was raised secondary to the ovarian dermoid. A detailed serological work up subsequently performed revealed anti-*N*-methyl-D-aspartate (NMDA) receptor antibodies in the patient's serum and CSF. Thus a final confirmed diagnosis of right ovarian dermoid with anti-NMDAR associated autoimmune enteropathy and paraneoplastic limbic encephalitis was made. The patient was administered intravenous immunoglobulin (IVIg) at a dose of 2 gm/kg divided over 5 days along with oral Prednisolone (1 mg/kg). In addition, an anti-epileptic drug, injection Levipil (500mg BD) was also administered. The patient showed good clinical response to treatment, following which she underwent right oophorectomy for the ovarian dermoid. On subsequent follow up, patient showed resolution of the neurological and gastrointestinal symptoms.

Figure 1: Pelvic cuts of MRI (a, b, c) show diffuse circumferential edematous wall thickening involving the visualized large bowel loops as well as the rectum (yellow arrows). A tiny well defined T1W hyperintense lesion (red arrow in a) is also seen within the right ovary, which on corresponding fat-saturated images shows complete suppression (red arrow in b), suggestive of a small ovarian dermoid. Axial FLAIR image of the temporal lobes showing relatively symmetrical hyperintense signal in bilateral hippocampi.

Discussion

Autoimmune encephalitis (AE) is an immune-mediated neurological condition which is being increasingly recognized as a common cause of limbic encephalitis (LE). However, it is also known to affect other parts of the nervous system and thus is commonly known as "autoimmune" encephalitis rather than "limbic" encephalitis. The diagnosis is difficult clinically because AE may precede the detection of the primary. In addition, in patients with known malignancy, such symptoms may be attributed to other malignancy-related complications, like metastases, metabolic encephalopathy, infections (especially herpes simplex related encephalitis) or even toxic encephalopathy secondary to adverse reactions of chemotherapeutic agents [3].

AE is classified on the basis of the location of the antigen, i.e. whether the antigen is on the cell surface or intracellular [4]. Antibodies that target nuclear and cytoplasmic (intracellular) proteins such as Hu, Ma, and Ri are usually associated with malignancy [4]. LE in the presence of these antibodies is more commonly known as 'paraneoplastic LE.' These patients respond poorly to immunotherapy, and treatment of the cancer itself generally results in improvement of the neurological symptoms [1]. Anti-NMDA receptor antibodies are the most common cell-surface antibodies [4]. Anti-NMDA receptor antibodies have been found to be associated with ovarian teratoma [5]. NMDA receptors are important in transmission of impulses at the synapse. Anti-NMDAR antibodies act against the NR1 subunit of the NMDA receptor, resulting in a wide range of neuropsychiatric symptoms [5]. The tumors responsible for the symptoms may be very small in size[5], like a small ovarian dermoid in our case.

Imaging plays a fundamental role in clinically inexplicable cases. A characteristic pattern involving predominantly the medial temporal lobes and hypothalamus as seen on MR imaging, can aid in establishing the diagnosis of AE. Gultekin., *et al*. [6] reported that the typical MRI findings of PLE include unilateral or bilateral mesial temporal lobe abnormalities that are seen best on T2W and FLAIR images. On T1W images, these regions of the temporal lobes may appear hypo intense and atrophic, and may even show enhancement on post contrast images [6].

Autoimmune enteropathy (AIE) is a rare disease characterized by intractable diarrhea, villous atrophy of the small intestine, the presence of autoantibodies[7]. There are reports related to AIE in the setting of various types of autoimmune diseases, including rheumatoid arthritis, systemic lupus erythematosus etc[7]. When mucosal barrier function is destroyed, intestinal mucosa antigens are exposed to blood and induce an autoimmune response, which in turn induces an inflammatory response [7].

The treatment for PLE and AIE includes tumor removal and immunotherapy, with a complete resolution of symptoms.

Conclusion

The presence of autoimmune enteropathy in our case, in addition to autoimmune encephalitis due to anti-NMDA receptor antibodies highlights another paraneoplastic immune-mediated phenomenon in association with ovarian dermoid. Hence, we would like to conclude by reiterating the importance of keeping "paraneoplastic immune-mediated" etiology in mind in the presence of a known primary with unexplained imaging findings, and also searching for a primary in the presence of characteristic imaging findings.

Declaration of Patient Consent

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

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