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Contents

Thrice Monthly Volume 9 Number 19 July 6, 2021

OPINION REVIEW

- 4881** Fear of missing out: A brief overview of origin, theoretical underpinnings and relationship with mental health
Gupta M, Sharma A

REVIEW

- 4890** Molecular pathways in viral hepatitis-associated liver carcinogenesis: An update
Elpek GO
- 4918** Gastroenterology and liver disease during COVID-19 and in anticipation of post-COVID-19 era: Current practice and future directions
Oikonomou KG, Papamichalis P, Zafeiridis T, Xanthoudaki M, Papapostolou E, Valsamaki A, Bouliaris K, Papamichalis M, Karvouniaris M, Vlachostergios PJ, Skoura AL, Komnos A
- 4939** Enhancing oxygenation of patients with coronavirus disease 2019: Effects on immunity and other health-related conditions
Mohamed A, Alawna M

MINIREVIEWS

- 4959** Clinical potentials of ginseng polysaccharide for treating gestational diabetes mellitus
Zhao XY, Zhang F, Pan W, Yang YF, Jiang XY
- 4969** Remarkable gastrointestinal and liver manifestations of COVID-19: A clinical and radiologic overview
Fang LG, Zhou Q
- 4980** Liver injury in COVID-19: Known and unknown
Zhou F, Xia J, Yuan HX, Sun Y, Zhang Y
- 4990** COVID-19 and gastroenteric manifestations
Chen ZR, Liu J, Liao ZG, Zhou J, Peng HW, Gong F, Hu JF, Zhou Y
- 4998** Role of epithelial-mesenchymal transition in chemoresistance in pancreatic ductal adenocarcinoma
Hu X, Chen W
- 5007** Insights into the virologic and immunologic features of SARS-COV-2
Polat C, Ergunay K

ORIGINAL ARTICLE**Basic Study**

- 5019** SMAC exhibits anti-tumor effects in ECA109 cells by regulating expression of inhibitor of apoptosis protein family

Jiang N, Zhang WQ, Dong H, Hao YT, Zhang LM, Shan L, Yang XD, Peng CL

Case Control Study

- 5028** Efficacy of Solitaire AB stent-release angioplasty in acute middle cerebral artery atherosclerosis obliterative cerebral infarction

Wang XF, Wang M, Li G, Xu XY, Shen W, Liu J, Xiao SS, Zhou JH

Retrospective Study

- 5037** Diagnostic value of different color ultrasound diagnostic method in endometrial lesions

Lin XL, Zhang DS, Ju ZY, Li XM, Zhang YZ

- 5046** Clinical and pathological features and risk factors for primary breast cancer patients

Lei YY, Bai S, Chen QQ, Luo XJ, Li DM

- 5054** Outcomes of high-grade aneurysmal subarachnoid hemorrhage patients treated with coiling and ventricular intracranial pressure monitoring

Wen LL, Zhou XM, Lv SY, Shao J, Wang HD, Zhang X

- 5064** Microwave ablation combined with hepatectomy for treatment of neuroendocrine tumor liver metastases

Zhang JZ, Li S, Zhu WH, Zhang DF

- 5073** Clinical application of individualized total arterial coronary artery bypass grafting in coronary artery surgery

Chen WG, Wang BC, Jiang YR, Wang YY, Lou Y

Observational Study

- 5082** Early diagnosis, treatment, and outcomes of five patients with acute thallium poisoning

Wang TT, Wen B, Yu XN, Ji ZG, Sun YY, Li Y, Zhu SL, Cao YL, Wang M, Jian XD, Wang T

- 5092** Sarcopenia in geriatric patients from the plateau region of Qinghai-Tibet: A cross-sectional study

Pan SQ, Li YM, Li XF, Xiong R

- 5102** Medium-term efficacy of arthroscopic debridement *vs* conservative treatment for knee osteoarthritis of Kellgren-Lawrence grades I-III

Lv B, Huang K, Chen J, Wu ZY, Wang H

Prospective Study

- 5112** Impact of continuous positive airway pressure therapy for nonalcoholic fatty liver disease in patients with obstructive sleep apnea

Hirono H, Watanabe K, Hasegawa K, Kohno M, Terai S, Ohkoshi S

Randomized Controlled Trial

- 5126** Erector spinae plane block at lower thoracic level for analgesia in lumbar spine surgery: A randomized controlled trial
Zhang JJ, Zhang TJ, Qu ZY, Qiu Y, Hua Z

SYSTEMATIC REVIEWS

- 5135** Controversies' clarification regarding ribavirin efficacy in measles and coronaviruses: Comprehensive therapeutic approach strictly tailored to COVID-19 disease stages
Liatsos GD
- 5179** Systematic review and meta-analysis of trans-jugular intrahepatic portosystemic shunt for cirrhotic patients with portal vein thrombosis
Zhang JB, Chen J, Zhou J, Wang XM, Chen S, Chu JG, Liu P, Ye ZD

CASE REPORT

- 5191** Myelodysplastic syndrome transformed into B-lineage acute lymphoblastic leukemia: A case report
Zhu YJ, Ma XY, Hao YL, Guan Y
- 5197** Imaging presentation and postoperative recurrence of peliosis hepatis: A case report
Ren SX, Li PP, Shi HP, Chen JH, Deng ZP, Zhang XE
- 5203** Delayed retroperitoneal hemorrhage during extracorporeal membrane oxygenation in COVID-19 patients: A case report and literature review
Zhang JC, Li T
- 5211** Autologous tenon capsule packing to treat posterior exit wound of penetrating injury: A case report
Yi QY, Wang SS, Gui Q, Chen LS, Li WD
- 5217** Treatment of leiomyomatosis peritonealis disseminata with goserelin acetate: A case report and review of the literature
Yang JW, Hua Y, Xu H, He L, Huo HZ, Zhu CF
- 5226** Homozygous deletion, c. 1114-1116del, in exon 8 of the *CRPPA* gene causes congenital muscular dystrophy in Chinese family: A case report
Yang M, Xing RX
- 5232** Successful diagnosis and treatment of jejunal diverticular haemorrhage by full-thickness enterotomy: A case report
Ma HC, Xiao H, Qu H, Wang ZJ
- 5238** Liver metastasis as the initial clinical manifestation of sublingual gland adenoid cystic carcinoma: A case report
Li XH, Zhang YT, Feng H
- 5245** Severe hyperbilirubinemia in a neonate with hereditary spherocytosis due to a *de novo* ankyrin mutation: A case report
Wang JF, Ma L, Gong XH, Cai C, Sun JJ

- 5252** Long-term outcome of indwelling colon observed seven years after radical resection for rectosigmoid cancer: A case report
Zhuang ZX, Wei MT, Yang XY, Zhang Y, Zhuang W, Wang ZQ
- 5259** Diffuse xanthoma in early esophageal cancer: A case report
Yang XY, Fu KI, Chen YP, Chen ZW, Ding J
- 5266** COVID-19 or treatment associated immunosuppression may trigger hepatitis B virus reactivation: A case report
Wu YF, Yu WJ, Jiang YH, Chen Y, Zhang B, Zhen RB, Zhang JT, Wang YP, Li Q, Xu F, Shi YJ, Li XP
- 5270** Maintenance treatment with infliximab for ulcerative ileitis after intestinal transplantation: A case report
Fujimura T, Yamada Y, Umeyama T, Kudo Y, Kanamori H, Mori T, Shimizu T, Kato M, Kawaida M, Hosoe N, Hasegawa Y, Matsubara K, Shimojima N, Shinoda M, Obara H, Naganuma M, Kitagawa Y, Hoshino K, Kuroda T
- 5280** Infliximab treatment of glycogenosis Ib with Crohn's-like enterocolitis: A case report
Gong YZ, Zhong XM, Zou JZ
- 5287** Hemichorea due to ipsilateral thalamic infarction: A case report
Li ZS, Fang JJ, Xiang XH, Zhao GH
- 5294** Intestinal gangrene secondary to congenital transmesenteric hernia in a child misdiagnosed with gastrointestinal bleeding: A case report
Zheng XX, Wang KP, Xiang CM, Jin C, Zhu PF, Jiang T, Li SH, Lin YZ
- 5302** Collagen VI-related myopathy with scoliosis alone: A case report and literature review
Li JY, Liu SZ, Zheng DF, Zhang YS, Yu M
- 5313** Neuromuscular electrical stimulation for a dysphagic stroke patient with cardiac pacemaker using magnet mode change: A case report
Kim M, Park JK, Lee JY, Kim MJ
- 5319** Four-year-old anti-N-methyl-D-aspartate receptor encephalitis patient with ovarian teratoma: A case report
Xue CY, Dong H, Yang HX, Jiang YW, Yin L
- 5325** Glutamic acid decarboxylase 65-positive autoimmune encephalitis presenting with gelastic seizure, responsive to steroid: A case report
Yang CY, Tsai ST
- 5332** Ectopic opening of the common bile duct into the duodenal bulb with recurrent choledocholithiasis: A case report
Xu H, Li X, Zhu KX, Zhou WC
- 5339** Small bowel obstruction caused by secondary jejunal tumor from renal cell carcinoma: A case report
Bai GC, Mi Y, Song Y, Hao JR, He ZS, Jin J
- 5345** Brugada syndrome associated with out-of-hospital cardiac arrest: A case report
Ni GH, Jiang H, Men L, Wei YY, A D, Ma X

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Four-year-old anti-N-methyl-D-aspartate receptor encephalitis patient with ovarian teratoma: A case report

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Abstract

BACKGROUND

A population-based comparative study in United States shows that the prevalence and incidence of autoimmune encephalitis are comparable to those of infectious encephalitis and its detection is increasing over time. Some patients are complicated with ovarian teratoma. The younger the patient is, the less likely a tumor will be present.

CASE SUMMARY

This case report describes the successful treatment of anti-N-methyl-D-aspartate-receptor (NMDAR) encephalitis by early laparoscopic ovarian cystectomy and immunotherapy in a 4-year-old female child. And to the best of our knowledge, this detailed case report describes the youngest patient to date with anti-NMDAR encephalitis who underwent laparoscopic ovarian cystectomy.

CONCLUSION

Although the younger the patient is, the less likely a tumor will be detected, we still emphasize that all patients with suspected or confirmed anti-NMDAR encephalitis should be screened for ovarian tumors if possible. Prompt initiation of immunotherapy and tumor removal are crucial for good outcomes.

Key Words: Anti-N-methyl-D-aspartate receptor encephalitis; Childhood; Laparoscopic surgery; Ovarian teratoma; Case report

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Core Tip: In this case report, we describe the successful treatment of anti-N-methyl-D-aspartate-receptor (NMDAR) encephalitis by early laparoscopic teratoma removal and immunotherapy in a 4-year-old female child. And to the best of our knowledge, this detailed case report is about the youngest patient to date with anti-NMDAR encephalitis who underwent laparoscopic ovarian cystectomy. We intend to increase awareness about the importance of early identification of anti-NMDAR encephalitis and once the disease is diagnosed, it should be screened for tumor, especially ovarian teratoma, and surgical intervention should be adopted as soon as possible.

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INTRODUCTION

A population-based comparative study in the United States shows that the prevalence and incidence of autoimmune encephalitis are comparable those of infectious encephalitis and its detection is increasing over time. The prevalence of anti-N-methyl-D-aspartate-receptor (NMDAR) encephalitis was 0.6/100000[1]. This disorder is observed in patients of all ages but most often in young adults and children with or without teratomas[2,3]. Approximately 80% of patients with anti-NMDAR encephalitis are women[4]. In an observational cohort study, patients with ovarian teratoma accounted for 44.2% of all female anti-NMDAR encephalitis patients (207 of 468)[5]. However, in a single-center prospective study in China, patients with ovarian teratoma accounted for 26.9% of all female patients (29 of 108)[6]. Previous reports have demonstrated that the prevalence of tumors in this disease is associated with age, sex, and race[2,3]. Patients typically present with acute behavioral changes, psychosis, and catatonia that evolve to seizures, memory deficits, dyskinesias, speech problems, and autonomic and breathing dysregulation[2]. The optimal management of anti-NMDAR encephalitis includes immunotherapy and removal of the tumor[7,8]. Despite the severity of the disease, patients often improve after intensive care support, immunotherapy, and prolonged hospitalizations that require multidisciplinary care[5]. We report a case of ovarian mature cystic teratoma in a 4-year-old female child with anti-NMDAR encephalitis who received laparoscopic ovarian cystectomy and immunotherapy. To the best of our knowledge, this detailed case report describes the youngest patient to date with anti-NMDAR encephalitis who underwent laparoscopic ovarian cystectomy.

CASE PRESENTATION

Chief complaints

A 4-year-old girl was admitted to the pediatric intensive care unit (PICU) of Peking University First Hospital as an emergency (day 1) with intermittent fever, convulsions, and abnormal mental behavior over 15 d of evolution.

History of present illness

Fever (In China, fever is diagnosed when a body temperature is ≥ 37.3 °C) occurred 15 d ago with the highest body temperature of 37.5 °C and without obvious inducement. The symptoms were accompanied by headache. The girl developed convulsions 10 d after the initial symptom onset, lasting a few seconds to 3 min with spontaneous remission occurring 2-3 times a day. Her parents sent her to a local hospital for treatment first. Routine blood tests were normal, and the serum immunoglobulin M antibodies against coxsackie virus and adenovirus were positive. Electroencephalogram (EEG) indicated a small number of low-medium amplitude spikes in the left parietal and central regions and midline during the sleep period. Brain magnetic resonance imaging (MRI) was performed without obvious pathological findings. The patient was diagnosed with viral encephalitis and treated with antiviral drugs at the

local hospital. During admission, the condition of the patient worsened on day 13 of symptom onset with intermittent psychiatric symptoms and behavioral changes, including agitation, pressured speech, and dyskinesias of the arms and legs. Thereafter, her parents took her to the outpatient department of pediatrics at our hospital, and she was admitted to the PICU as an emergency.

History of past illness

The patient had a free previous medical history.

Personal and family history

There was no special personal or family history.

Physical examination

After admission, physical and neurological examinations were unremarkable except for a slightly higher temperature at 37.5 °C.

Laboratory examinations

Routine laboratory tests were unremarkable. Tumor markers and autoimmune profiles were within normal limits. Blood and urine cultures revealed no findings of bacteria or other microorganisms. The detection of thyroid function was also normal.

Imaging examinations

Brain MRI was performed without obvious pathological findings. Brain MRI was re-examined on day 9 and demonstrated small flaps of T2 fluid-attenuated inversion recovery hyperintensity in the right frontal lobe. On day 12, abdominal-pelvic ultrasound revealed a 3.4 cm × 3.1 cm × 2.8 cm cystic tumor in the left adnexal region, suggesting ovarian teratoma.

MULTIDISCIPLINARY EXPERT CONSULTATION

Considering that previous neurological symptoms had improved significantly, surgical excision was decided by gynecologists and pediatricians. A laparoscopic exploration was performed carefully under general anesthesia (day 18), and the left ovarian tumor was removed completely with minimal bleeding.

FINAL DIAGNOSIS

Anti-NMDAR encephalitis secondary to teratoma.

TREATMENT

Considering that previous neurological symptoms had improved significantly, surgical excision was decided by gynecologists and pediatricians. A laparoscopic exploration was performed carefully under general anesthesia (day 18), and the left ovarian tumor was removed completely with minimal bleeding (Figure 1). The operative time was 62 min.

The operation and anesthesia went very well. The patient could breathe spontaneously without snoring or apnoea after extubation. Her vital signs were stable, and in the immediate postoperative period, the girl was transferred to the PICU and went to the pediatric neurology ward that night based on a stable condition. Postoperative pathological results confirmed that the tumor was a mature cystic teratoma and that the teratoma contained a component of mature neuroglial tissue. Immunotherapy, including intravenous administration of methylprednisolone and oral prednisone acetate, was initiated on day 23. During hospitalization, the body temperature of the patient increased intermittently until day 25, reaching a maximum of 38.5 °C on day 10. After this date, the patient's temperature was normal.

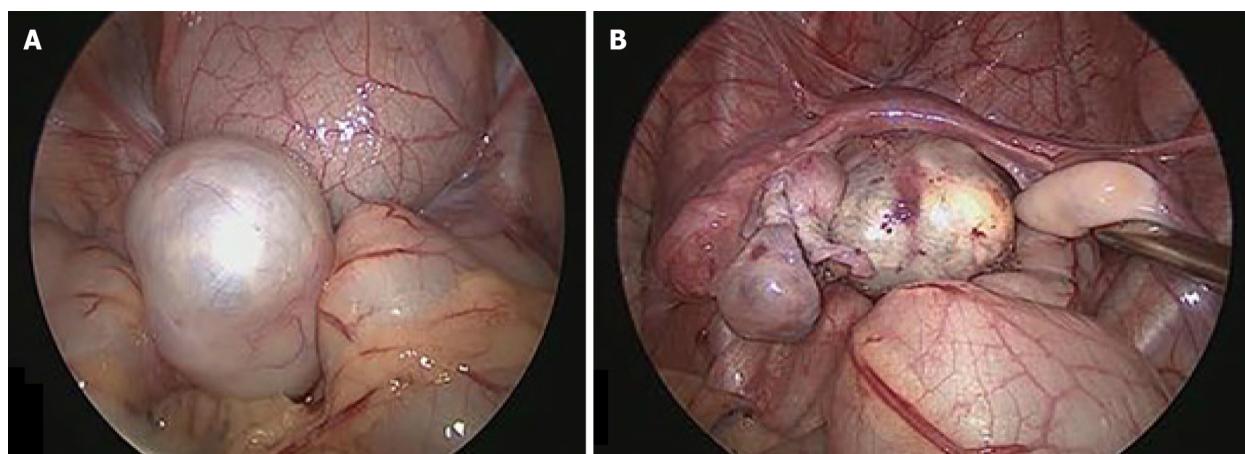


Figure 1 Laparoscopy. A: Initial laparoscopic image; B: Laparoscopic image after the tumor was removed completely.

OUTCOME AND FOLLOW-UP

After treatment, the patient's previous symptoms gradually disappeared. She was discharged on the 20th postoperative day with prednisone acetate and levetiracetam. The total duration of hospitalization was 37 d. The pediatrician followed up with the patient, and her symptoms have completely improved without relapse or sequelae to date. EEG with normal results was performed 15 wk after discharge. The antiepileptic drug and glucocorticoid had been stopped with a total course of 6 mo. Colony-stimulating factor (CSF) and serum anti-NMDAR antibodies were tested again 6 mo after discharge, and the results were all negative. EEG was also performed again at the same time, and the result was normal. The girl is vigorous to date with no signs of encephalitis and no recurrence of the ovarian tumor.

DISCUSSION

In 2007, Dalmau *et al*[9] formally proposed the concept of anti-NMDAR encephalitis [9], which has since been observed in patients of all ages but most often in young adults and children with or without teratomas[7]. The age distribution of anti-NMDAR encephalitis reported in the literature is very wide, ranging from 8 mo to 85 years[5]. The younger the patient is, the less likely a tumor will be present[5]. In a study conducted by Florance *et al*[3], the frequency of ovarian teratoma in patients with anti-NMDAR encephalitis was 56% in women aged > 18 years, 31% in girls < 18 years, and 9% in girls aged < 14 years. To the best of our knowledge, this detailed case report describes the youngest patient to date with anti-NMDAR encephalitis who underwent laparoscopic ovarian cystectomy. Since the disease was first proposed in 2007, clinicians' understanding of anti-NMDAR encephalitis has gradually increased. However, given that the disease is relatively rare and the clinical manifestations are complex, it is difficult to make accurate and timely diagnoses. It is important to note that although brain MRI may be within normal limits in 67% of patients, 90% of these patients commonly exhibit EEG abnormalities. The final diagnosis is made with the detection of anti-NMDAR antibodies in the blood or CSF[7]. However, early treatment is associated with better outcomes. At present, the production of anti-NMDA receptor antibodies has been unanimously recognized as the ectopic expression of NMDA receptors in ovarian tumor tissues, which stimulates the production of antibodies in the body and causes disease when acting on NMDA receptors in the nervous system under appropriate conditions. However, the mechanism of antibody production in patients with nonovarian tumors remains unclear. Brain NMDA receptors determine the existence of higher mental functions, playing a fundamental role in the mechanisms of consciousness, memory, learning, emotions, and even in some motor functions. In the process of anti-NMDAR encephalitis, antibodies are generated in response to the neural elements within the teratoma. The newly formed autoantibodies react with the NMDA receptor 1 subunit of the ligand-gated cation channel NMDA receptor, which is primarily expressed in the hippocampus and forebrain and is implicated in memory and learning[7,10]. This reaction results in specific and recognizable syndromes that develop in five stages of illness and recovery as first

reported by Sansing *et al*[11], including prodromal, psychotic, unresponsive, hyperkinetic, and gradual recovery phases. However, there are no strict boundaries for each stage. In this case report, we present a typical case of anti-NMDAR encephalitis with rapid improvement after laparoscopic ovarian cystectomy and immunotherapy without sequelae. The initial prodromal phase was a nonspecific viral-like symptom disease with fever and headache, which later progressed into two stages of neuropsychiatric abnormalities. With IVIg and symptomatic treatment, her condition was controlled. After the tumor was surgically removed, glucocorticoid treatment was performed, and her condition improved significantly. An observational cohort study revealed two independent predictors of good outcome: Lower severity of symptoms, which is assessed as no need for admission to an intensive care unit, and prompt initiation of immunotherapy and tumor removal[5]. On the second day after the girl was admitted to our hospital, IVIg was implemented by a pediatrician. The diagnosis of anti-NMDAR encephalitis was confirmed 1 wk after hospitalization, and surgery was performed 18 d after admission. Glucocorticoids were applied 23 d after admission. The total duration of hospitalization was 37 d with 8 d of PICU admission. The patient has a good prognosis given our timely diagnosis and treatment with laparoscopic tumor resection and immunotherapy.

CONCLUSION

The younger the patient is, the less likely a tumor will be detected[5]. This case report intends to emphasize that all patients with suspected or confirmed anti-NMDAR encephalitis should be screened for ovarian tumors if possible. Prompt initiation of immunotherapy and tumor removal are crucial for good outcomes.

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