Arch Gynecol Obstet (2016) 294:623–629
DOI 10.1007/s00404-016-4050-9

GYNECOLOGIC ONCOLOGY

Treatment principles of ovarian teratoma with anti-*N*-methyl-D-aspartate receptor encephalitis

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Received: 17 September 2015 / Accepted: 11 February 2016 / Published online: 7 April 2016

Abstract
Purpose Anti-*N*-methyl-D-aspartate receptor (NMDAR) encephalitis is a recently discovered paraneoplastic limbic encephalitis. Ovarian teratoma is the only tumor clearly related to anti-NMDAR encephalitis occurrence. This study aimed to assess ovarian teratoma for neurological and mental symptoms highly related with anti-NMDAR encephalitis, treatment principles, and prognosis.
Methods Between June 2011 and October 2014, in Peking Union Medical College Hospital, ten patients with ovarian teratoma associated with anti-NMDAR encephalitis were enrolled. All patients underwent laparoscopic oophorocystectomy followed by immunotherapy.
Results In nine patients, mental and neurological symptoms were significantly relieved 13.7 ± 5.5 days after surgery; however, symptoms persisted in one patient, who was still hospitalized when writing this paper. During the postoperative follow-up period, seven patients showed no mental symptoms or tumor recurrence; one subject had symptom recurrence 28 days after surgery, while another patient showed suspected tumor recurrence 273 days after operation.
Conclusions Ovarian teratoma associated with anti-NMDAR encephalitis is usually associated with neurological and mental symptoms at onset. Its manifestations are complex, and nursing care is difficult. Laparoscopic oophorocystectomy followed by immunotherapy led to symptom resolution in most patients.

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Keywords Anti-NMDAR encephalitis · Epileptic nursing care · Immunization therapy · Laparoscopic perioperative care · Ovarian teratoma

Introduction

Encephalitis is defined as an inflammation of the brain parenchyma. This life threatening condition requires prompt diagnosis and treatment. Etiologies include a wide range of inflammatory conditions of paraneoplastic, autoimmune, and infectious origins [1, 2]. Encephalitis symptoms vary depending on disease etiology or the specific brain regions being affected; common symptoms include headache, confusion, altered level of consciousness, memory disturbance, seizure, and hallucination.

Recently, an unknown autoimmune cause for encephalitis has been identified. Encephalitis signs are primarily psychiatric in nature, and the disease may be mistaken for a primary psychiatric disorder, delaying definitive diagnosis and treatment. Psychiatrists should be aware of medical or neurologic disorders that cause psychiatric symptoms to rule out organic etiologies such as anti-*N*-methyl-D-aspartate receptor (anti-NMDAR) encephalitis [3].

Anti-NMDAR encephalitis caused by specific antibodies against NMDAR is a paraneoplastic limbic encephalitis (PLE). It was first described in 2007, when Dalmau et al. [4] identified female patients with mental and behavior disorders alongside ovarian teratoma. In 2010, Xu et al. [5] reported the first anti-NMDAR encephalitis case in China; since then, the disease is being increasingly diagnosed.

Multiple studies described the clinical presentation, diagnosis, and pathophysiology of anti-NMDAR encephalitis. Although it primarily affects adult women and

is frequently associated with tumors, anti-NMDA receptor encephalitis is increasingly identified in males and children, without tumors. Despite the wealth of knowledge regarding anti-NMDAR encephalitis, the basis for effective treatment is limited. The available information concerning management focuses primarily on tumor management and immunotherapy to control the antibody response. Indeed, the management of psychiatric symptoms in critically ill patients remains a challenge, due to the limited information available on the disease [6].

This study assessed ten cases, evaluating ovarian teratoma for neurological and mental symptoms highly related with anti-NMDAR encephalitis, treatment principles, and prognosis. For optimal treatment, the ovarian teratoma should be removed and immunotherapy applied as soon as possible. Finally, a good prognosis was obtained.

Methods

Patients

Between June 2011 and October 2014, at the Chinese Academy of Medical Sciences, Peking Union Medical College Hospital, ten patients with ovarian teratoma associated with anti-NMDAR encephalitis were enrolled. After tumor resection and combined immunotherapy, mental and neurological symptoms were significantly relieved in these patients. The study was approved by the Ethics Committee of Peking Union Medical College Hospital. Because of the risks on patient fertility, informed surgical consent was obtained from all patients.

Treatment and care

Laparoscopic perioperative care

Surgical treatment is the only therapeutic method for ovarian teratoma.

Preoperative care

Preoperative routine examination was carried out, including electrocardiography (ECG), chest X-ray, blood urine and stool test, blood grouping, coagulation function, and pelvic B-mode ultrasound. Skin preparation was performed 1 day before operation, covering the abdominal and perineal regions; the umbilical skin was cleaned and disinfected or the patient was bathed according to her condition, paying attention to personal hygiene. For vaginal preparation, 1:40 iodine complex solution was used in the morning and evening the day before operation. Preparation of the gastrointestinal tract was carried by fasting the patients for 12 h before operation. Polyethylene glycol-electrolyte powder or 25 % magnesium sulfate was prescribed for bowel preparation. Finally, patient history of drug allergy was recorded, and drug allergy test was carried out before operation.

Postoperative care

After patient return to the ward, nurses assessed the patient condition in detail. Each one was asked to lie flat with the head turned to one side, without pillow for 6 h. Patients were provided low flow of oxygen; the respiratory tract and trachea were kept smooth for tracheal intubation and tracheostomy. Blood pressure, pulse, respiration, and blood oxygen were closely monitored. Abdominal wounds were observed for capillary hemorrhage or vaginal bleeding; the dressing was changed for three patients with capillary hemorrhage. To prevent infection, body temperature was measured three times a day, and antibiotic treatment was administered. To keep the perineal region clean, 1:40 iodine complex solution was used to wash the vulva twice daily for 3 days after operation. The ureter and drainage tube were kept smooth, observing drainage number, nature, and color. Three patients used drainage tubes after operation, for 1 day. Among complications, shoulder pain is a normal phenomenon, which results from carbon dioxide stimulating the diaphragm; it normally happens 1 or 2 days after operation and is relieved within a few days. Subcutaneous emphysema is a specific laparoscopic complication: owing to increased intra-abdominal pressure, gas can diffuse from the stomach to skin or directly penetrate into the skin (in the case of pneumoperitoneum); normally, it is self-resolved, with no need for further treatment. Pharyngeal pain occurs due to tracheal cannula damage; it can be relieved by atomization inhalation.

Immunotherapy

For, immunotherapy, intravenous immunoglobulin (IVIG) was administered at 20–25 g QD for 4–5 days and 2–4 cycles. The incidence of adverse reactions to immunoglobulin is 1 % [7]. For a patient who developed erythema, IVIG treatment was discontinued and methylprednisolone pulse therapy (1, 0.5, 0.25 g/day for 5 days, respectively) was applied. During immunoglobulin infusion, flow rate was controlled, and allergy symptoms and thrombus were monitored, as well as blood glucose, and liver and kidney functions.

Glucocorticoid therapy

Hormone impact therapy was administered with prednisone at 1 g for 5 days, gradually reduced to 60–80 mg/day. In case of peptic ulceration or bleeding, hormone

administration to an empty stomach was avoided, and a gastric mucosal protective agent was used. Long-term treatment with large hormone doses causes metabolic imbalance of water, salt, sugar, protein, and fat in the human body, resulting in Cushing's syndrome, whose main manifestations are centripetal obesity (commonly known as moon face or buffalo hump), acne, hirsutism, atony, low blood potassium, edema, hypertension, and diabetes mellitus [8]. To avoid osteoporosis, vitamin D and calcium IV supplements were provided. Surgery was carried out in sterile conditions, and nursing staff used masks to control infection.

Plasma replacement

Four patients received plasma replacement, among whom two individuals were administered plasma replacement in another hospital.

Rituximab treatment

Two patients received rituximab treatment at 375 mg/m^2, once a week, four times per course. During rituximab infusion, continuous ECG monitoring and blood pressure measurements were performed to prevent hypotension.

Intrathecal injection of dexamethasone and methotrexate

Patient was laid on the side, with head and neck bent to the chest, with double knee flexion to the abdomen, and the back kept vertical. Facial color and expression, respiration, and pulse were observed. After operation, patients were laid flat with head turned to one side, without pillow for 6 h, and state of consciousness and pupil reflex were assessed, keeping wound dressing clean and dry.

Epilepsy may occur at any disease stage; its frequency and intensity are reduced with increasing recovery [9]. In case of epileptic seizures, emergency control measures were implemented, strictly limiting patient behavior and guaranteeing safety.

Nursing

Prevention of suffocation

The respiratory tract was kept smooth, oxygen inhalation provided, and the patient laid flat with head turned to one side, to facilitate the discharge of respiratory secretions and vomiting.

Prevention of tongue bite

First, the tongue was protected before attack, putting a tongue depressor wrapped with gauze between the patient's upper and lower molars, to avoid tongue bite. If a tongue depressor was not placed before attack, it should be placed after the patient opens the mouth in the tonic phase. It should not be placed forcibly in the clonic phase, avoiding injury.

Prevention of fracture and dislocation

Limb joints with appropriate force (e.g. shoulder, elbow, hip, and knee) were pressed; twitch amplitude was limited, avoiding excessive force and forcible press, which prevents joint damage and fracture.

Safe nursing

To fight falls and bruises, security measures were enforced; bed rails were provided, while hard objects and sharp instruments in the attack stage were quickly removed. Attack time and duration (including unconsciousness and seizure durations), and seizure location were recorded: unconsciousness, upward staring eyes, and urinary and fecal incontinence were observed.

Sedative drugs

Midazolam injection, midazolam, morphine, and propofol were used.

Management of tracheotomy

Dressing for tracheal incision was changed once a day; proper elasticity of the catheter with fixed length was guaranteed, ensuring that a finger was held. After connection of the catheter and ventilator pipe, appropriate pipe support was provided; pushing gravity for catheter was avoided, preventing tracheal compression and necrosis. In order to prevent long-term compression of the tracheal tampon on organs or the mucous membrane, air was discharged for 3–5 min every 3–4 h. Before air discharge, oropharyngeal suction was applied.

Artificial airway management

Airway temperature and humidity

Airway inlet gas temperature was maintained at 32–35 °C using a heater, with distilled water in the humidifier changed every day.

Correct sputum suction

Strict sterile operation was performed with care; suction of the trachea was first carried out, followed by that of the

mouth, preventing airway infection. Suction pressure was 40–53 kPa.

Monitoring of mechanical ventilation

24-h ECG for blood pressure monitoring was performed; changes in physical signs were observed, and oxygen saturation index was provided.

Other auxiliary treatments

Psychological nursing

When the patient awakes in a strange environment with impaired verbal communication and cannot live or study normally, she is prone to anxiety, loneliness, and fear [10]. For a young patient in critical condition, the family usually is in great mental pressure; therefore, nursing staff communicated well with them, providing psychological counseling and discussing significance of surgical treatment and immunotherapy, which alleviated mental stress, and increased trust and understanding, for a smooth treatment.

Environment

In critical condition, the room window was open for good ventilation twice a day; indoor air was refreshed, and appropriate temperature and humidity were maintained. These measures prevented infection, and the respirator was kept in a well-ventilated place.

Skin care

Bed time is long, with the patient having no self-care ability. To avoid local long-term compression, patient's back was gently turned every 2 h; drag and pull were avoided, preventing skin injury. Various pipes kept smooth were set up. Protuberances were taken care of daily, to promote blood circulation and prevent pressure ulcer. Skin irritation caused by contamination and moisture was avoided.

Nursing care of various cannulations

Patients may have multiple cannulations simultaneously. Indwelling needles were replaced every 3 days, and dressing was changed weekly for the deep venous pathway; in the case of tracheal catheter, ventilator tube disinfection was applied, the tube was replaced monthly, and gastric tubes were replaced every 45 days; urine bags were changed every week, ureter catheters were replaced every 30 days, and the perineum was scrubbed once a day.

Propaganda and education

Serum anti-NMDAR antibody and tumor markers were assessed regularly; patients were instructed to take drugs on time after leaving the hospital; in particular, they were advised to never miss, reduce, or stop taking hormone drugs, use potassium and calcium supplements, take rest, avoid tiredness, enhance body resistance, enforce rehabilitation training, do well in safety protection, and prevent fortuitous event. For female patients above 12 with clinical symptoms, pelvic MRI was scheduled every 6 months for 4 continuous years [11].

Mouth case

When a patient cannot take food by mouth, increased oral and respiratory secretions are obtained, the frequent sputum suction was used to dry oral mucosa and fungal infection.

Results

Clinical information

The ten female patients ranged from 10 to 31 years in age; average age at onset was 24.3 years.

Clinical symptoms

Precursory symptoms

Seven patients had precursory symptoms of upper respiratory tract infection before attack; main manifestations were headache, fever, runny nose, and sore throat. Time interval of precursory and initial mental symptoms averaged 9 days.

Mental symptoms

All ten patients had typical mental symptoms. Initial symptoms included mental and behavior disorder ($n = 9$, 90 %), cognitive abnormalities ($n = 4$, 40 %), memory disorder ($n = 1$, 10 %), language barrier ($n = 1$, 10 %), dyskinesia ($n = 1$, 10 %), and seizure with disturbance of consciousness ($n = 1$, 10 %). Throughout the disease course, all patients suffered from epileptic seizures; nine (90 %) patients had mouth chewing-like or limb involuntary movements. Meanwhile, five (50 %) patients suffered from autonomic- and central ventilation dysfunction; two (20 %) had increased heart rate, and two (20 %) suffered from increased oral secretion.

Laboratory data

Nine (90 %) patients showed positive signals in serum and cerebrospinal fluid samples for NMDAR; only one (10 %) patient's cerebrospinal fluid was negative after probe by anti-NMDAR antibody.

Cerebrospinal fluid cytological and biochemical examination

Cytological and biochemical changes in cerebrospinal fluid samples from anti-NMDAR encephalitis patients were similar to those obtained with viral encephalitis. Cerebrospinal fluid pressure increased, as well as the white blood cell number and percentage of multinucleated or mononuclear cells. Biochemical examination revealed that protein levels were normal or slightly high, while sugar and chloride amounts were mostly normal.

Video EEG

All ten patients underwent EEG examination. Four of them had local or diffused slow waves, including three and one patients with frontal and/or temporal slow waves and epileptic waves, respectively. One patient had δ and θ waves; the remaining individuals had no specific changes.

Head MRI

Nine patients received head MRI examination after disease onset. Of these, four had no overtly abnormal condition. Five patients showed abnormalities, including four (80 %) with *T*2 and/or FLAIR high signal intensity at the posterior horn of lateral ventricle, frontal lobe, temporal lobe; only one (20 %) patient had leptomeningeal enhancement.

Serum tumor markers

CA125 and/or CA19-9 were slightly increased in six patients before operation. Treatment was combined tumor resection and immunotherapy.

Ovarian tumor

All ten patients were submitted to pelvic CT or transvaginal ultrasound for tumor screening pre-operation. All patients underwent laparoscopic oophorocystectomy. Laparoscopic ovarian cyst resection and postoperative pathology confirmed the presence of ovarian teratoma: one (10 %) and nine (90 %) patients had bilateral and unilateral ovarian teratoma, respectively. In the latter group, five and four cases, respectively, left and right organs were affected. Ovarian teratoma diameter averaged 4 cm and was <2 cm for patients treated after August 2012; only one case was immature teratoma I, the rest being all mature teratomas. Mature brain tissue was found in pathological sections from four patients; one case had multinucleated giant cell reaction. The time interval from initial symptom to tumor resection averaged 89.3 days.

Immunotherapy

All ten patients received first-line immunotherapy with intravenous immunoglobulin (IVIG) therapy; glucocorticoid therapy was administered in seven cases and four cases underwent plasma replacement. One patient received second-line immunotherapy, i.e. rituximab treatment. In addition, one patient received IVIG, glucocorticoid therapy, tumor resection operation, rituximab treatment, and intrathecal injection of dexamethasone and methotrexate, but the symptoms were not significantly relieved; this patient was still hospitalized at the time of submitting this paper.

Prognosis

Except for one patient, mean follow-up time of the remaining nine patients was 14.2 months. In nine patients, mental and neurological symptoms were significantly relieved 13.7 ± 5.5 days after surgery. There was no death. Seven patients had no mental symptoms or tumor recurrence during postoperative follow-up. One patient had recurrent mental symptoms 15 days after the initial discharge, which were not accompanied with tumor recurrence; improvement was obtained after immunotherapy. Another patient had suspected tumor recurrence 9 months after operation; ultrasound showed a 3.9×3.5 cm mixed echoic mass in the left adnexa. The patient underwent tumor resection in a local hospital, and pathological results are unknown; there was no recurrence of mental symptoms.

Epileptic nursing care

All ten patients had epileptic seizures.

Mechanical ventilation

Five autonomic dysfunction patients suffered from coma and respiratory failure. Among them, four patients received tracheal intubation, including one carried out in another hospital; one patient underwent tracheotomy, and sputum was timely cleared every 2 h.

Treatment of fever

Aspirin-DL-lysine for injection was prescribed in three cases; ice blanket for physical cooling was provided for one case when aspirin treatment was ineffective.

Mouth case

Saline cotton ball was used for mouth care twice a day, timely clearing the sputum.

Nutritional support treatment

Seven patients had difficulty eating; therefore, we used gastric intubation to administer the nutrient solution. Alternatively, intravenous nutritional support was provided.

Discussion

Until as recently as 5 years ago, limbic encephalitis was primarily considered a paraneoplastic phenomenon, frequently encountered with lung or testis cancers, with associated antibodies to intracellular neuronal antigens [12]. This concept includes two conditions in which antibodies to cell membrane antigens in hippocampal and cerebellar neuropils are present. These encephalitides are associated with antibodies to voltage-gated potassium channels, NMDA receptors [13–17], AMPA receptors [18], and other yet to be characterized neuronal surface antigens. Abnormal appearance of neurons can be observed in NMDAR encephalitis [19]. Clinically, anti-NMDA receptor encephalitis varies, showing a myriad of neurological and psychiatric symptoms, similar to other neurological disorders, including posterior reversible encephalopathy syndrome (PRES), which is usually found during pregnancy and after delivery [20]. Clinical presentations markedly differ between the affected adults and youths. Neoplasm is less frequently encountered in children and adolescents, and autonomic disruption, particularly hypoventilation, is less severe in this group [21]. While most reported adult cases initially present to psychiatric care providers with symptoms suggestive of mood, anxiety, and/or psychotic disorders, children more often exhibit subtle behavioral and neurological changes.

Psychiatrists may find patients with anti-NMDA receptor encephalitis in different settings, including emergency departments, inpatient units, consultation liaison services, and outpatient offices. Thus, basic understanding of clinical characteristics, differential diagnosis, currently available treatment interventions, and unique management dilemmas of this condition should be described.

The exact incidence of anti-NMDAR encephalitis is unknown. After a first report in 2007, many other cases have been identified around the world, well over 600 cases [22]. According to ICU [23], pediatrics [21], and neurology medical records, attack rate of anti-NMDAR encephalitis is higher than that of any other known paraneoplastic encephalitis [9, 24]. Anti-NMDAR encephalitis is often found in children and adolescents, with about 81 % of patients being females. Dalmau et al. assessed 501 cases and found that 38 % of patients suffer from tumor, with 94 % and 2 % having ovarian teratoma and extraovarian teratoma, respectively [25].

In the present study, after laparoscopic ovarian cyst resection and immunotherapy, mental symptoms were significantly relieved in all ten patients. Interestingly, symptomatic relief showed a reverse order to disease incidence: patients first recovered consciousness, a few days after operation; this was followed by restored autonomic function, reduced frequency of epileptic seizures and abnormal motion, decreased amplitude, and finally, recovered social ability. This usually takes several months. According to the life assessment scale, ten patients had 0–3 points at admission, and 40–75 points at discharge. In addition, symptomatic and supportive treatment, including anti-epileptic care, sedation, mechanical ventilation, and nutritional support should be strengthened; narcotic sedatives should be used with caution, since some of them target NMDAR, and may induce or aggravate mental symptoms, autonomic dysfunction, and central hypoventilation in such patients.

The findings described here corroborate previously published data by Dalmau et al. [25]. In the latter study, 207 cases of ovarian teratoma associated with anti-NMDAR encephalitis were assessed, and all had nervous tissue damage and showed NMDAR expression. Ovarian teratoma is the only tumor closely related to anti-NMDAR encephalitis at present [11]; it is uncertain how ovarian teratoma leads to increased anti-NMDAR antibody levels. Adults mostly have abnormal behavior at the onset, while children mostly suffer from epileptic seizures and dyskinesia. Dalmau et al. evaluated 501 anti-NMDAR encephalitis patients, and after tumor resection and first-line immunotherapy, 53 % of them showed improved condition 4 weeks after disease onset; 97 % had a favorable outcome after follow-up for 2 years [25]. Among the patients without obvious improved condition after first-line immunotherapy, 57 % obtained a favorable prognosis after second-line immunotherapy; after 2 year-follow-up, about 80 % of patients had a good prognosis. Therefore, timely tumor resection plays an important role in the prognosis of ovarian teratoma associated with anti-NMDAR encephalitis [24].

Conclusion

Anti-NMDAR encephalitis should be suspected in patients with ovarian teratoma with neurological and mental symptoms and based on positive examination results of

cerebrospinal fluid and serum anti-NMDAR antibody. Treatment should be carried out by removing the ovarian teratoma and applying immunotherapy as soon as possible. In addition, correct understanding of the disease and accurate diagnosis should help improve prognosis. The manifestations of ovarian teratoma associated with anti-NMDAR encephalitis are complex, rendering nursing care difficult.

Limitations

This was a single-center study, which is subject to selection bias. In addition, the sample size was relatively small. Therefore, further large sample size studies in multiple centers are needed to further understanding of ovarian teratoma associated with anti-NMDAR encephalitis, which would improve the diagnostic and treatment of this disease.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Source of funding None.

Ethical standards This study was approved by the Ethics Committee of Peking Union Medical College Hospital and performed in accordance with the 1964 Declaration of Helsinki and later amendments. Informed surgical consent was obtained from all subjects prior to surgery.

References

1. Tunkel AR, Glaser CA, Bloch KC et al (2008) The management of encephalitis: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis 47(3):303–327. doi:10.1086/589747
2. Vincent A, Bien CG, Irani SR, Waters P (2011) Autoantibodies associated with diseases of the CNS: new developments and future challenges. Lancet Neurol 10(8):759–772. doi:10.1016/S1474-4422(11)70096-5
3. Kruse JL, Jeffrey JK, Davis MC, Dearlove J, IsHak WW, Brooks JO 3rd (2014) Anti-*N*-methyl-D-aspartate receptor encephalitis: a targeted review of clinical presentation, diagnosis, and approaches to psychopharmacologic management. Ann Clin Psychiatry 26(2):111–119
4. Dalmau J, Tuzun E, Wu HY et al (2007) Paraneoplastic anti-*N*-methyl-D-aspartate receptor encephalitis associated with ovarian teratoma. Ann Neurol 61(1):25–36. doi:10.1002/ana.21050
5. Xu CL, Zhao WQ, Li JM, Wang JW, Wang SW, Wang DX, Liu MY, Qiao SS (2010) One case of anti-NMDAR encephalitis. Chin J Neurol 43(11):781–783
6. Chapman MR, Vause HE (2011) Anti-NMDA receptor encephalitis: diagnosis, psychiatric presentation, and treatment. Am J Psychiatry 168(3):245–251. doi:10.1176/appi.ajp.2010.10020181
7. Schwartz SA (1990) Intravenous immunoglobulin (IVIG) for the therapy of autoimmune disorders. J Clin Immunol 10(2):81–89
8. Sathasivam S (2008) Steroids and immunosuppressant drugs in myasthenia gravis. Nat Clin Pract Neurol 4(6):317–327. doi:10.1038/ncpneuro0810
9. Dalmau J, Lancaster E, Martinez-Hernandez E, Rosenfeld MR, Balice-Gordon R (2011) Clinical experience and laboratory investigations in patients with anti-NMDAR encephalitis. Lancet Neurol 10(1):63–74. doi:10.1016/S1474-4422(10)70253-2
10. Pelander T, Leino-Kilpi H (2010) Children's best and worst experiences during hospitalisation. Scand J Caring Sci 24(4):726–733. doi:10.1111/j.1471-6712.2010.00770.x
11. Titulaer MJ, Soffietti R, Dalmau J et al (2011) Screening for tumours in paraneoplastic syndromes: report of an EFNS task force. Eur J Neurol 18(1):19–e13. doi:10.1111/j.1468-1331.2010.03220.x
12. Graus F, Saiz A (2008) Limbic encephalitis: an expanding concept. Neurology 70(7):500–501. doi:10.1212/01.wnl.0000299189.43164.96
13. Chan LW, Nilsson C, Schepel J, Lynch C (2015) A rare case of anti-*N*-methyl-D-aspartate receptor encephalitis during pregnancy. N Z Med J 128(1411):89–91
14. Acien P, Acien M, Ruiz-Macia E, Martin-Estefania C (2014) Ovarian teratoma-associated anti-NMDAR encephalitis: a systematic review of reported cases. Orphanet J Rare Dis 9:157. doi:10.1186/s13023-014-0157-x
15. Zandi MS, Paterson RW, Ellul MA et al (2015) Clinical relevance of serum antibodies to extracellular *N*-methyl-D-aspartate receptor epitopes. J Neurol Neurosurg Psychiatry 86(7):708–713. doi:10.1136/jnnp-2014-308736
16. Cleverly K, Gambadauro P, Navaratnarajah R (2014) Paraneoplastic anti-*N*-methyl-D-aspartate receptor encephalitis: have you checked the ovaries? Acta Obstet Gynecol Scand 93(7):712–715. doi:10.1111/aogs.12386
17. Tachibana N, Ikeda S (2012) Localization of NMDAR-related epitopes in ovarian teratoma: comparison between patients and controls. Rinsho Shinkeigaku 52(11):982–984
18. Hoftberger R, van Sonderen A, Leypoldt F et al (2015) Encephalitis and AMPA receptor antibodies: novel findings in a case series of 22 patients. Neurology 84(24):2403–2412. doi:10.1212/WNL.0000000000001682
19. Day GS, Laiq S, Tang-Wai DF, Munoz DG (2014) Abnormal neurons in teratomas in NMDAR encephalitis. JAMA Neurol 71(6):717–724. doi:10.1001/jamaneurol.2014.488
20. Cozzolino M, Bianchi C, Mariani G, Marchi L, Fambrini M, Mecacci F (2015) Therapy and differential diagnosis of posterior reversible encephalopathy syndrome (PRES) during pregnancy and postpartum. Arch Gynecol Obstet 292(6):1217–1223. doi:10.1007/s00404-015-3800-4
21. Florance NR, Davis RL, Lam C et al (2009) Anti-*N*-methyl-D-aspartate receptor (NMDAR) encephalitis in children and adolescents. Ann Neurol 66(1):11–18. doi:10.1002/ana.21756
22. Irani SR, Vincent A (2011) NMDA receptor antibody encephalitis. Curr Neurol Neurosci Rep 11(3):298–304. doi:10.1007/s11910-011-0186-y
23. Varvat J, Lafond P, Page Y, Coudrot M, Reynaud-Salard M, Tardy B (2010) Acute psychiatric syndrome leading young patients to ICU: consider anti-NMDA-receptor antibodies. Anaesth Intensive Care 38(4):748–750
24. Dalmau J, Gleichman AJ, Hughes EG, Rossi JE, Peng X, Lai M, Dessain SK, Rosenfeld MR, Balice-Gordon R, Lynch DR (2008) Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. Lancet Neurol 7(12):1091–1098. doi:10.1016/S1474-4422(08)70224-2
25. Titulaer MJ, McCracken L, Gabilondo I et al (2013) Treatment and prognostic factors for long-term outcome in patients with anti-NMDA receptor encephalitis: an observational cohort study. Lancet Neurol 12(2):157–165. doi:10.1016/S1474-4422(12)70310-1