Case Report

Timely Laparoscopic Intervention for Ovarian Tumor-related Autoimmune Encephalitis: A Challenging Pathology at Tu Du Hospital in Vietnam and Literature Review

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Abstract

A previously fit and healthy 39-year-old woman was admitted to our tertiary referral hospital with coexisting autoimmune encephalopathy and ovarian tumor. Due to the presence of anti-N-methyl-d-aspartate receptor (anti-NMDAR) in the cerebrospinal fluid, a diagnosis of anti-NMDAR encephalitis was first suggested after ruling out other etiologies. Thus, a laparoscopy was promptly performed to remove the ovarian tumor. The histological endpoint revealed an ovarian teratoma. Consequently, the patient recovered completely in good health condition after 2 months in a coma status. Herein, we report an uncommon case of anti-NMDAR encephalitis associated with ovarian teratoma at our hospital, thus raising awareness of physicians.

Keywords: Anti-N-methyl-d-aspartate receptor encephalitis, autoimmune disease, laparoscopy, mortality, ovarian teratoma

Introduction

Ovarian teratoma, particularly, the mature teratoma is the most frequent histologic type of germ cell tumor.[1-3] Anti-N-methyl-d-aspartate receptor (anti-NMDAR) encephalitis refers to a rare autoimmune encephalitis, one of the subcategory of encephalitis caused by the N-methyl-D-aspartate (NMDA) receptor antibody which is commonly related to ovarian teratoma. Rarely, ovarian dermoid cysts associated with other autoimmune diseases such as hemolytic anemia have also been described in the medical literature.[4]

In this catastrophic event, clinical features are widely variable and progressive symptoms gradually become severe in most patients, leading to potentially life-threatening conditions.[5] An adequate treatment remains controversial. However, the surgical excision of the ovarian tumor may be potentially selective. A multidisciplinary approach is the cornerstone of the management of this fatal condition.[2] Herein, we reported the case of a Vietnamese woman of reproductive age related to this complex issue at our center. Through this clinical presentation, we purpose to add to the literature, a difficult case of immune-mediated encephalopathy, and to increase the essential recognition of gynecologists.

Case Report

A 39-year-old female patient was transferred to our hospital from the tropical hospital due to autoimmune encephalitis suspected of ovarian tumor, after exclusion from other pathologies. Her medical history revealed diabetes type II,

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hypertension, and appendicectomy. Her obstetric record included two cesarean sections, one abortion, and the use of an intrauterine device for contraception. Familial history was irrelevant. Fifteen days before hospitalization, the patient presented with acute onset of psychotic symptoms, behavioral changes, fever, anorexia, orofacial dyskinesia, abnormal movements, and seizures. Her consciousness seriously deteriorated, resulting in a coma and required mechanical ventilation. Immediately, the patient was hospitalized and received the treatment of intravenous ampicillin 2 g per 6 h, methylprednisolone 1 g per 24 h, and phenobarbital 300 mg every 8 h. In addition, the patient was investigated with imaging modalities, laboratory tests, and lumbar puncture. The extensive findings revealed a urine infection positive for *Ecoli Faecalis*, anti-NMDA receptor encephalitis, and an abnormal structure consistent with ovarian teratoma. Therefore, a rapid diagnosis of autoimmune encephalitis associated with an ovarian tumor was strongly suspected.

On admission, her vital signs were remarkable as follows: pulse rate of 92 bpm, blood pressure of 150/100 mmHg, respiratory frequency of 22 times/min, and body temperature of 36.8°C. The patient's body mass index was measured at 20.8 kg/m^2. The abdominal tenderness was soft. On gynecological examination, no vaginal bleeding was observed. The uterus was small in size. The right adnexal structure was larger than normal, a 5 cm × 6 cm ovarian tumor was palpable. The left ovary was not identifiable. Laboratory tests showed white blood cells of 22.000/mm^3, hemoglobin level of 11 g/dl, and platelet count of 429.000/mm^3. The pregnancy test was negative. The ovarian tumor markers revealed the following: cancer antigen 125 of 34.5 IU/ml, human epididymis protein-4 of 60.6 pmol/l, risk of ovarian malignancy algorithm value of 11.81%, and alpha-fetoprotein within the normal reference range. The glycemia was measured at 12.79 mmol/l. The electrolyte disturbance was absent. The hepatic and renal function tests were within the normal limits. Other serum tests were unremarkable.

After multidisciplinary counseling, the patient underwent an emergency laparoscopy for ovarian resection. Intraoperatively, abdominal cavity was normal, a multilobular tumor was observed in the right ovary without abnormal vascularity. Macroscopically, the smooth mass appeared likely benign, measured at 5 cm × 6 cm in size, and a small amount of transparent liquid was found in the tumor. In general, a surgical procedure was uneventful. At operating room, her intrauterine device was also withdrawn. Postoperatively, the patient was sent back to tropical hospital for further intensive care. The female patient was discharged from the hospital after 2 months with well-being health and without neurological sequelae on follow-up. The histopathological result confirmed an ovarian teratoma [Figure 1]. She felt grateful to the multidisciplinary team for saving her life.

Discussion

Similar to all autoimmune encephalitis, clinical manifestations of anti-NMDAR encephalitis range from mild to severe in 80% of cases, close to paraneoplastic neurological syndromes.[1,6] Risk factors have been poorly demonstrated; however, almost all cases are noted in young women along with the existence of ovarian tumors.[7] Accordingly, a diagnosis of autoimmune encephalitis owing to an ovarian tumor remains strongly a challenge for the physician. The mechanism is unknown-well and lacking data. Up to 50% of young females have an underlying ovarian teratoma that contains nervous tissue and NMDAR, which probably trigger the immune response. Nevertheless, 14% of female patients do not have detectable antibodies in serum.[6]

The literature has coincidentally reported a relationship between unexplained encephalitis and benign ovarian tumor in several clinical circumstances. The first description was presented by Dalmau *et al*. in 2007.[8] Until today, this disorder has still been described by case report and case series over the past decade.[7,9,10] Recently, Cho *et al*. reported a young female with anti-NMDAR encephalitis associated with ovarian mucinous cystadenoma.[11] Following elimination of other etiologies such as viral and bacterial encephalitis, suspicion of this pathology was based on the predominant presence of the positive NMDA receptor antibodies in serum and cerebrospinal fluid (CBF), even when the ovarian tumor was small.[1,12] Thus, a careful exploration should be considered during exploratory surgery.[2] In our case, the histopathological examination revealed the presence of hair, teeth, cartilage, bone, and sebaceous material. Thus, an ovarian mature cystic teratoma was accurately identified. In addition, NMDA receptor antibodies were present in the CBF sample confirmed teratoma-induced anti-NMDAR encephalitis.

Regarding management, the practical guideline is still poor. Laparoscopic procedures can be indicated not only in common ovarian tumor but also in autoimmune ovarian tumors [Table 1].[4,13] Using laparoscopy in the large size teratomectomy could be considered in some circumstances when applicable.[3,13,14] In most individuals, the surgical intervention aims to remove the tumor, thus decreasing the immune factors related to the underlying tumor.[2,11] On the contrary, unnecessary intervention can damage the general condition of a coma patient. Cirkel *et al*. mentioned a tiny mature teratoma of 6 mm in size on the ovary with a normal appearance. However, following the hidden cyst removal, the clinical improvement was not significantly responsive.[12]

Table 1: Characteristics of anti-N-methyl-d-aspartate receptor encephalitis and ovarian tumor in the past 5 years

Author (year)	Patient's age (years old)	Mental status	Features of ovarian tumor	Intervention	Outcomes
Leel *et al*. (2018)[5]	7	Coma	The right mature cystic teratoma with neural tissue	Laparoscopy for excision of the lesion, methylprednisolone and plasmapheresis	Complete recovery after 2 years
Mitra and Afify (2018)[20]	22	Encephalopathy	The right 4 cm×8 cm mature ovarian teratoma with neural tissue	Surgical excision of the teratoma and immunomodulating therapies	Recovery
Cho *et al*. (2019)[11]	23	Hypoventilation, focal tonic seizures, and immobilization	The right-5 cm ovarian mucinous cystadenoma	Laparoscopic salpingooophorectomy + immunotherapy	Recovery completely after 2 months
El Hanna *et al*. (2021)[15]	19	Deterioration of psychiatric disorders	The right-4 cm ovarian teratoma	Laparoscopy and immunotherapy	Recovery after 7 months
Schiavi *et al*. (2021)[17]	30	Epileptic seizure accompanied by other neurological disorders	The right ovarian teratoma approximately 2 cm in size	Laparoscopic resection and first-line immunotherapy	Recovery after 3 months
Hwang and Kim (2022)[18]	27	Rigidity and dyskinesia, then, in coma status	The left-2.8 cm mature cystic teratoma	Immunotherapy+laparoscopic oophorectomy	Recovery on the 154th day

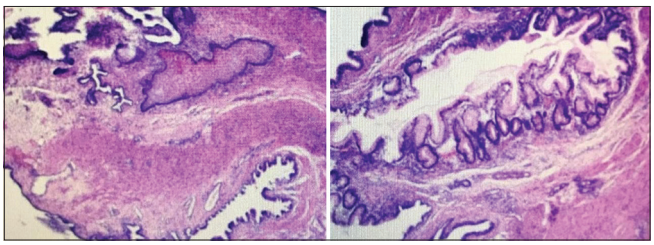

Figure 1: Histopathological result showed mature cystic ovarian teratoma (dermoid cyst) on the microscopic image with hematoxylin and eosin stain (H and E: ×10, ×40, respectively)

Besides surgery, an intervention with immunotherapy as second-line treatment may be effective in some clinical contexts.[1,15,16] Occasionally, immunotherapy was administered as the first line, but no recovery was demonstrated.[17,18] Importantly, the prognosis depends on the timing of appropriate intervention, resources of health-care settings, and the medical status of the patient.[2] Between 80% and 90% of patients respond to treatment which includes immunotherapy and removal of the tumor when applicable.[6] The recurrent possibility should be noted. Rarely, ovarian torsion occurring shortly after ipsilateral dermoid cystectomy has been reported.[19]

Conclusion

Anti-NMDAR encephalitis usually causes severe neurological syndromes. Clinicians need a high index of suspicion for this disorder among women of childbearing age with ovarian tumors. Early cystectomy should be taken into consideration for proper management after excluding of other etiologies. Surgical intervention before immunotherapy appears to optimize the favorable outcome but requires careful evaluation and further practical guideline.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her 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.Thanh Hai Pham and Phuc Nhon Nguyen contributed equally to this work and share the first authorship.

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