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CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Mature ovarian teratoma-associated encephalitis

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SUMMARY

Introduction Autoimmune encephalitis associated with ovarian teratoma is a serious and potentially fatal pathology. While this clinical entity is known to neurologists, the available literature rarely mentions the role of a gynecologist in diagnostic imagining and treatment. Although several months have passed from the onset of symptoms to surgical treatment, this case shows that even then a complete recovery is possible.

Case presentation The patient was a 28-year-old female, brought to the hospital because a sudden onset of unusual behavior – an acute psychosis with suicidal thoughts and auditory hallucinations. Soon after the admission she became delirious, uncooperative and agitated. Blood check, neurological assessment and cranial computed tomography yielded normal results. Therefore, a psychiatric disorder was suspected. Electroencephalogram revealed a diffuse encephalitic insufficiency. As cerebrospinal fluid was negative for infections, the autoimmune etiology of the disease was suspected. Abdominal computer tomography showed a complex right ovarian mass measuring 50 × 40 × 30 mm, confirmed by vaginal ultrasound. Laparoscopy with right adnexectomy was performed. The pathohistological finding showed a mature teratoma. In the meantime, the result of the cerebrospinal fluid test came positive for Anti-N-Methyl-D-Aspartate antibodies. Six months after surgery, the patient was in a good mental and neurological status without symptoms.

Conclusion Gynecologists should be aware of the presence of ovarian tumors in encephalitis cases. A timely diagnosis of the underlying gynecological cause of a neurological condition, allows for prompt treatment and can remarkably improve clinical conditions and, thus, be lifesaving.

Keywords: autoimmune encephalitis; teratoma; tumor; young women

INTRODUCTION

Anti-N-Methyl-D-Aspartate (NMDA) receptor encephalitis has been recognized as the second most common cause of autoimmune encephalitis, after acute demyelinating encephalomyelitis [1]. Anti-NMDAR encephalitis in young women is usually associated with the presence of ovarian masses. [1, 2]. Due to the prevalence of psychiatric symptoms, 77% of patients are initially hospitalized by a psychiatrist [3, 4, 5]. The above symptoms are followed by a memory deficit, autonomic instability, seizures, muscle rigidity, movement disorder and hypoventilation [6]. It is not uncommon for such patients to require ventilation support and intensive care to stay alive [7]. In this patient, withdrawal symptoms and recovery occurred immediately after surgical treatment, although literature data show that recovery can take up to 24 months [1, 2, 7]. However, some patients still have problems with cognition (understanding, memory, attention and expression) and motor function (walking, taking care of yourself, swallowing) [1]. Anti-NMDAR encephalitis is well known to neurologist. Still, this is less well known to gynecologists, who may have a decisive role in etiological management. Raising awareness about this disease among gynecologists can be of great importance for earlier diagnosis and thus faster healing [8].

We present a rare case of Anti-NMDAR encephalitis induced by ovarian teratoma. Although five months passed from the appearance of the first symptoms to removal of the tumor, our patient completely recovered without consequences. The purpose of the study was to present our first experience, as gynecologists, with such a rare pathology and to point out the challenge in diagnosis and treatment patient with NMDAR encephalitis.

CASE REPORT

A 28-year-old woman was hospitalized at the Clinic for Psychiatry, Clinical Center of Vojvodina, complaining of symptoms of an acute episode of psychotic behavior. According to hetero-anamnestic data, the patient had a sudden onset of unusual behavior, an acute psychosis with suicidal thoughts, auditory hallucinations and decreased food intake. Soon after admission, she became delirious, uncooperative and agitated. She had no past medical history and there was no history of substance abuse. Fear, loss of appetite, decreased oral intake and insomnia were the dominant symptoms. The

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neurological assessment and basic blood evaluation yielded negative results; cranial computed tomography (CT) was unremarkable. The patient exhibited severe psychomotor agitation, which led to self-inflicted harm. In the further course of hospitalization, she destroyed her lower lip and caused a fracture of the alveolar extension of the lower jaw. An extensive array of microbiological and serological tests were done, and all were negative. The autoimmune antibodies and tumor marker examination results were also negative. The brain magnetic resonance imaging (MRI) and angiography (MRA) were unremarkable. Electroencephalogram (EEG) revealed a diffuse encephalitic insufficiency. The sample of cerebrospinal fluid was negative for infections and was placed for further testing of anti-NMDAR antibodies. The patient was started on intravenous (IV) steroids, IV immunoglobulin (IVIG) and plasma exchange. There was a slight improvement after the applied therapy.

Finally, since autoimmune encephalitis (anti-NMDAR) is usually caused by the presence of a dermoid cyst in young women [1], a gynecologist was consulted. The CT showed the presence of a complex right ovarian mass measuring 50 × 40 × 20 mm, confirmed by vaginal ultrasound (Figures 1 and 2). Laparoscopy with right adnexectomy was performed. The ovarian mass contained cystic components as well as skin, hair, brain tissue and cartilage. The final pathology result was mature teratoma. In the meantime, the result of the cerebrospinal fluid test was positive for anti-NMDAR antibodies. After four months, the patient had problems with short-term memory. Six months after the surgery, the patient was in a good mental and neurological status, without any symptoms.

Written consent to write and publish this case report was obtained from the patient. The review was approved by the Ethics Committee of the Clinical Center of Vojvodina.

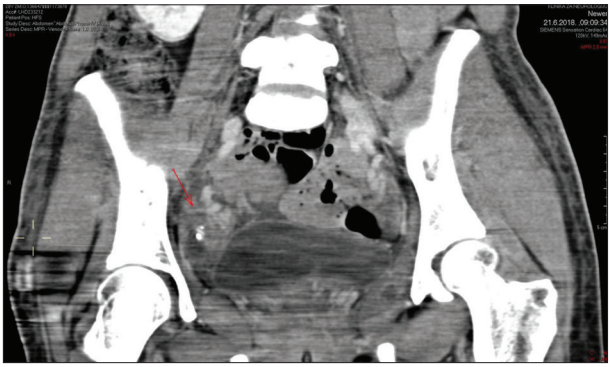

Figure 1. Computed tomography scan of the patient's pelvis

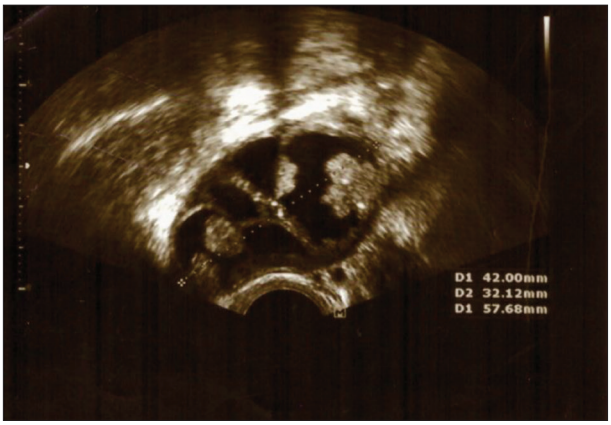

Figure 2. Transvaginal ultrasound of the ovarian teratoma in our patient

DISCUSSION

Teratoma-associated encephalitis (Anti-NMDAR encephalitis) was first noted in 1997 [1, 2, 9, 10]. Dalmau et al. [11] was the first to describe the progressive and potentially fatal course of this phenomenon. NMDA receptors are involved in cognitive processes: behavior, memory and learning [3]. Delay in diagnosis adversely affects the outcome which ranges from complete recovery, recovery followed by psycho–neurological sequelae, to death. An accurate and rapid diagnosis, followed by an early removal of the tumor in combination with immunotherapy, leads to a favorable outcome. This disease affects mostly young women and is associated with ovarian teratomas, which can contain nervous tissue expressing NMDA receptors [1, 2, 12]. However, cases have been reported in patients aged from eight months to 85 years [1]. Although there is a possibility of extra -ovarian teratomas (2%) and other tumors (4%, for instance lung, breast, thymus), ovarian teratomas are most often associated with this type of encephalitis [13]. Anti-NMDA receptor encephalitis often (70%) begins with prodromal flu-like symptoms (fever, headache and fatigue) [2]. After this uncharacteristic clinical picture, psychological symptoms develop with a predominance of the following: agitation, hallucinations, changes in behavior and anxiety [14]. There is a significant overlap of neurological and psychiatric symptoms associated with autoimmune encephalitis. Therefore, cases like this can manifest as a whole spectrum of neurological or psychiatric diseases (schizophrenia, paranoia, hallucinations, agitation, depression, anxiety, or substance abuse) [15]. The diagnosis of autoimmune encephalitis is challenging because the differential diagnosis involves the exclusion of the entire spectrum of the diseases (herpes simplex virus encephalitis, cytomegalovirus encephalitis, Hashimoto's encephalopathy, systemic lupus erythematosus encephalopathy, antiphospholipid antibody syndrome, Sjögren's syndrome, and primary central nervous angiitis). However, inadequate response to psychiatric therapy and neurological status should lead clinicians to consider encephalitis. MRI has been reported to be negative in up to 50–70% of cases, and in our case as well [15]. EEG abnormalities are present in most cases (90%) [1]. The final diagnosis is based on the presence of anti-NMDA autoantibodies in cerebrospinal fluid [2]. After anti-NMDA encephalitis has been confirmed, imaging studies are performed, such as vaginal ultrasound examination, MRI, CT and positron emission tomography [16, 17]. It is important to note that if autoimmune etiology is suspected it is necessary to intensively search for tumor changes in the ovaries [18]. Transvaginal ultrasound should be the first step in the

diagnosis of ovarian masses [2]. Therefore, gynecologists must be aware of the connection between ovarian tumors and autoimmune encephalitis and look in detail for even minimal ovarian changes. Sometimes this syndrome has been associated with patients without detectable underlying neoplasms. It is theorized that the syndrome may be triggered by microscopic germ cell tumors undetectable by imaging diagnostic methods [4]. Moreover, it has been reported that ovarian teratomas were discovered years after the onset of symptoms of anti-NMDAR encephalitis [4]. Surgical intervention is imperative, since a study by Titulaer MJ et al. [1] showed that five out of six patients with a confirmed NMDA encephalitis and an ovarian teratoma who did not undergo surgery died. The removal of the tumor will lead to an improvement in the patient's neurological performance within a few days or weeks [15]. The data from previous research indicate that a surgical procedure with immunotherapy have the best results in the treatment of this potentially fatal condition [2, 11]. Any delay in treatment can result in worsening of the patient's condition and even death [1]. It has been found that the outcome is more favorable if the operation is conducted after less than four months from the onset of symptoms [11]. In the case of this patient, the surgical treatment was performed 5.5 months after the appearance of the first symptoms. Women of the reproductive age are most often affected with this disease so the biggest challenge for gynecologists is how to completely remove the tumor while preserving fertility in the patient. Because a laparoscopic examination for determining ovarian teratoma is less-invasive than laparotomy, trial laparoscopy is acceptable if an ovarian tumor cannot be detected by various imaging tests [8]. Additionally, there have been cases where, despite the fact that the imaging procedures did not determine the existence of ovarian tumors, an ovariectomy was performed in order to stop the production of antibodies [3, 19, 20]. Postoperative histological examination in these cases confirmed the existence of occult teratoma consisting of skin, hair, cartilage and nervous tissue. Types of surgical treatment range from selective removal of lesions by ultrasound-guided laparoscopy, cystectomy, uni/bilateral ovariectomy and uni/bilateral adnexectomy [21]. Although some studies emphasize that cystectomy and adnexectomy have similar outcomes, we decided to perform a unilateral adnexectomy [22, 23]. As a possible limitation of the type of treatment in this case, we can mention the extent of the surgical procedure, which is not in accordance with the previous statements about preserving the fertility of young women. Pathohistological examination confirmed the existence of a mature teratoma with components of nervous tissue. This is consistent with literature reports showing that dermoid cysts, containing nervous tissue, are the most common pathohistological finding in patients with anti-NMDAR encephalitis [12].

As a limitation of the study, we state the period of postoperative monitoring. We followed the patients for six months postoperatively and it is not known whether the patient will develop new symptoms in the subsequent period. However, this case report may help identify this rare disease and therefore it is an important educational article.

In conclusion, it should be highlighted that it is extremely important to discover the cause of the disease as soon as possible, in order to give the patient the best chance of complete recovery. Since gynecologists play an important role in the treatment of these patients, they should be aware of the presence of tumors in patients with encephalitis. Determining the gynecological etiology of this condition, with the earliest possible surgical treatment, can lead to a favorable outcome and thus save the lives of young women.

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Conflict of interest: None declared.

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Зрели тератом јајника повезан са енцефалитисом

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САЖЕТАК

Увод Аутоимуни енцефалитис повезан са тератомом јајника је озбиљна и потенцијално фатална болест. Иако је ово познат клинички ентитет неуролозима, желели бисмо да скренемо пажњу гинеколозима, јер имају посебну улогу у дијагностици и оперативном лечењу болесница оболелих од аутоимуног енцефалитиса.

Приказан је случај болеснице чији је исход лечења успешан, иако је од појаве првих симптома па до постављања дијагнозе и операције прошло више месеци.

Приказ болесника Болесница стара 28 година хоспитализована је због изненадног развоја психозе са звучним халуцинацијама и суицидним мислима. Убрзо након пријема болесница постаје изразито узнемирена и агресивна. Лабораторијске анализе, неуролошки статус и компјутеризована томографија ендокранијума били су уредни. Електроенцефалограм је показао дифузни енцефалитис. Прегледом ликвора искључен је инфективни узрочник. Постављена је сумња на аутоимуну етиологију обољења. Компјутеризованом томографијом абдомена и вагиналним ултразвучним прегледом уочена је комплексна туморска промена десног јајника димензија 50 × 40 × 30 *mm*. Урађена је десна аднексектомија лапароскопски. Патохистолошка анализа је показала да се ради о зрелом тератому. Накнадно је пристигао позитиван узорак ликвора на анти-НМДА антитела. Шест месеци након операције болесница је уредног психичког и неуролошког статуса без тегоба.

Закључак Гинеколози треба да буду свесни постојања везе између енцефалитиса и тумора јајника младих жена. Брзо постављање дијагнозе, утврђивање гинеколошког узрока неуролошког обољења и адекватан терапијски поступак воде излечењу овог озбиљног, а понекад и смртоносног обољења.

Кључне речи: аутоимуни енцефалитис; тератом; тумор; младе жене