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■ Case report ■

A case of paraneoplastic limbic encephalitis due to ovarian mature teratoma

Seong Heon Kim, M.D., Hye Young Kim, M.D., Young Tak Im, M.D.
Sang Ook Nam, M.D. and Young Mi Kim, M.D.

Department of Pediatrics, Pusan National University Hospital
Pusan National University College of Medicine, Busan, Korea

= Abstract =

Paraneoplastic limbic encephalitis, a remote effect of cancer without nervous system metastasis, is rare, especially in childhood. Here, we report a case of paraneoplastic limbic encephalitis associated with an ovarian mature teratoma in an adolescent girl. The 15-year-old girl developed neuropsychiatric symptoms, memory loss, seizures, and unconsciousness. Cerebrospinal fluid analysis and brain magnetic resonance imaging (MRI) findings were normal, while single photon emission computed tomography imaging showed hypoperfusion in both temporal lobes. Ultrasound and MRI of the abdomen revealed a left ovarian cystic mass. The patient experienced a significant recovery of cognitive function after surgical resection of the tumor, which was pathologically identified as a mature ovarian teratoma, and treatment with intravenous immunoglobulin. (Korean J Pediatr 2010;53:603-606)

Key Words : Paraneoplastic limbic encephalitis, Teratoma, Adolescent

Introduction

Paraneoplastic limbic encephalitis is a rare disorder characterized by personality change, memory loss, neuropsychiatric abnormalities in behavior, speech and mood, and seizures. Paraneoplastic limbic encephalitis can develop as a remote effect of cancer; areas of the nervous system other than the limbic system are also often involved, in particular the cerebellum and brainstem[1]. This clinical neurological syndrome may precede the diagnosis of systemic neoplasm by months or years, with the symptoms developing after the diagnosis of malignancy only very rarely. This suggests that it is important to recognize the neuropsychiatric symptoms of paraneoplastic limbic encephalitis as a first expression of cancer[2].

Paraneoplastic limbic encephalitis is most commonly associated with small cell lung cancer, although it has also been associated with Hodgkin's lymphoma, gynecologic neoplasms, thymoma, and testicular cancer[1]. Paraneoplastic limbic encephalitis is rare in pediatric-aged patients. Here, we report the first case of reversible paraneoplastic limbic encephalitis associated with a mature ovarian teratoma in an adolescent girl in Korea.

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Address for correspondence : Young Mi Kim, M.D.
Department of Pediatrics, College of Medicine, Pusan National University Hospital, 10, 1-Ga, Ami-dong, Suh-gu, Busan 602-739, Korea
Tel : +82.51-240-7298, Fax : +82.51-248-6205
E-mail : pink2129@naver.com

Case report

A 15-year-old girl was referred to our hospital because of an acute onset of confusion and decreased mentality, prior to which she has been introversive and in good health. The patient first complained to her parents of headache and insomnia, and had no history of head injury or substance abuse.

Five days later, her family noticed abnormal behavior, inappropriate mood, and personality change. The patient seemed to be confused, and was speaking irrationally and experiencing auditory hallucinations. Upon admission to a local hospital, she was diagnosed by a psychiatrist, as being in an acute confusional state of schizophrenia. This diagnosis was consistent with the clinical signs, the patient's age, and the normal findings obtained using MRI of brain, electroencephalography, and cerebrospinal fluid analysis. Thereafter, an antipsychotic drug was prescribed. However,

the patient's mental state deteriorated further rather than improvement. Physical examination on admission was normal; there was no evidence of external injury, though there was generalized rigidity. Neurological examination revealed the patient to be stuporous, but having normal corneal reflexes in both eyes, and a normal deep tendon reflex. Additionally, mild neck stiffness, rigid muscle tone, and tonic seizures with upward deviation of both eyeballs were noted.

The patient was within normal limits for complete blood count and other laboratory tests, which included toxicology screening, antinuclear antibodies, rheumatoid factor, thyroid function tests, and several tumor markers, including α-fetoprotein, β-human chorionic gonadotropin, carcinoembryonic antigen, carbohydrate antigen 19-9, and cancer antigen 125. Erythrocyte sedimentation rate and C-reactive protein levels were elevated at 74 (5-15) mm/h and 5.73 (0-0.5) mg/dL respectively. There was no remarkable elevation of anti-viral antibody titers from serum samples, including those for mumps, rubella, varicella-zoster, Epstein-Barr, and herpes simplex virus. Tests for measles Ig M and herpes simplex virus Ig M in the cerebrospinal fluid were negative, and the test for Mycobacterium tuberculosis in gastric juice was negative with acid-fast bacteria staining, culturing, and polymerase chain reaction. The test for Japanese encephalitis was also negative, in both serum and cerebrospinal fluid samples. The cerebrospinal fluid did not show pleocytosis or other biochemical abnormalities, and tested negative for the cultures of bacteria and virus. Non-specific diffuse slow waves were seen in the EEG, and the brain MRI scan was normal. The patient was empirically treated for acute encephalitis with an intravenous antiviral agent, antibiotics, and mannitol, and for tonic seizures with phenytoin. On the 7th day in hospital, antiviral and antibiotic treatments were stopped because there was no evidence of bacterial or viral infection. A repeat MRI was performed on the 8th day; however, no significant abnormalities were observed.

On the 10th day in hospital, a pelvic ultrasonography revealed a left cystic mass (size, 50-60 mm) (Fig. 1). The mass was observed at low signal intensity in T1-weighted images, and at high signal intensity in T2-weighted images obtained with a pelvic MRI scan, which also revealed the mass as containing calcifications (Fig. 2). These findings

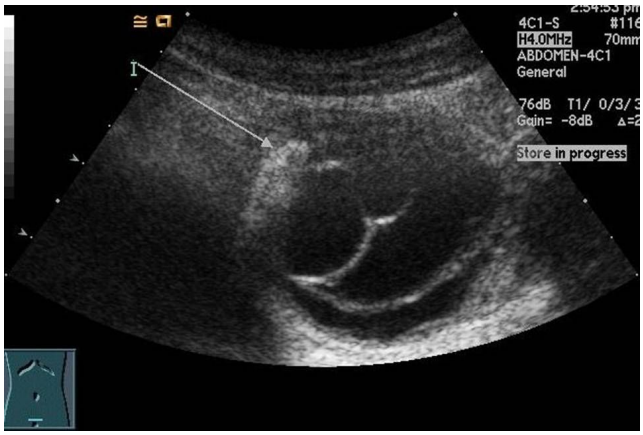

Fig. 1. The echogenic focus (arrow) and speckled debris within the cyst of the left ovary on ultrasonography are characteristic of a benign cystic teratoma.

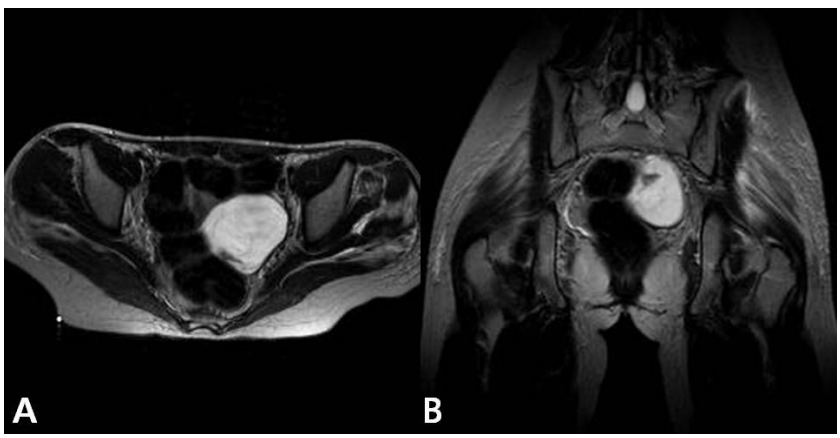

Fig. 2. Axial T1 weighted MRI (A) and coronal T2-weighted MRI (B): a multilocular mass is present superior to the uterus, inseparable from the left ovary. The mass has a dominant lobulated portion that contains a heterogeneous internal component.

were suggestive of a cystic teratoma with calcifications in the left ovary.

Because of the finding of a conincidental tumor with no evidence of an infective agent, a presumptive diagnosis of paraneoplastic limbic encephalitis was made. Serum tests for anti-Hu and anti-Yo antibodies were negative.

On the 13th day in hospital, the tumor was removed by performing an ovarian cystectomy, and was confirmed as a mature cystic teratoma by histological analysis. Postoperatively, the patient appeared to be in a confused state, and exhibited fluctuating drowsiness. A few days later, the patient's confused state resolved, and she was able to recognize people and speak simple words and sentences. Her muscular rigidity also improved. However, the patient was unable to concentrate on conversations lasting more than some minutes. She also exhibited volatile emotional reactions, such as crying, and was easily angered, often cursing. Intravenous immunoglobulin therapy was again undertaken for 5 days from the 23rd day in hospital.

Between the 35th and 40th days in hospital, the patient began to walk, eat well, and talk to others; she could now concentrate on conversations. Her general condition was good, and her intellectual abilities were within the normal range. She had returned to her premorbid level of functioning. There were continuous follow-up examinations, with a SPECT scan, at 6 weeks after the surgical resection of the tumor, showing reduced perfusion in both temporal lobes.

Discussion

Paraneoplastic neurological syndromes are relatively rare, and one of the most unusual and intriguing being paraneoplastic limbic encephalitis. This syndrome was first characterized and named in 1968[3]. The most commonly associated neoplasm is small cell carcinoma of the lung, though others that include ovarian, breast, gastric, esophageal, testicular, endometrial, and colonic cancers, and Hodgkin's lymphoma have been reported[1, 2]. Rarely, the causative neoplasm might not be detected[4]. Accurate and rapid detection of the syndrome can be difficult, because the condition often precedes the clinical diagnosis of a tumor by months or years, and is closely mimicked by infectious, metabolic, psychiatric, and autoimmune disorders[5]. Previous studies suggest that paraneoplastic limbic encephalitis is an immune-mediated disorder, caused by an autoimmune reaction that can be induced by several types of tumor[1, 2, 5, 6]. Histopathological observations include an inflammatory infiltrate with perivascular cuffing, gliosis, and microglial proliferation[5, 6]. Gultekin et al. proposed a set of clinical criteria for paraneoplastic limbic encephalitis including (a) a compatible clinical features; (b) an interval of <4 years between the development of neurological symptoms and tumor diagnosis; (c) exclusion of other neuro-oncological complications; and (d) at least one of the following: cerebrospinal fluid with inflammatory changes but negative cytology; MRI demonstrating temporal lobe abnormalities; EEG showing epileptic activity in the temporal lobes[7]. The patient we report here met 3 of these criteria and her single photon emission computed tomography scan showed reduced perfusion in both temporal lobes.

A number of anti-neuronal autoantibodies have been described, including anti-N-methyl-D-aspartate receptor to glutamate (NMDA-R) antibodies. The presence of anti-NMDA-R antibodies in the serum of patients with limbic encephalitis is strongly associated with an ovarian teratoma[8]. But anti-NMDA-R antibodies of the patient in present case were not checked.

Resection of the causative tumor is the best important treatment of paraneoplastic limbic encephalitis. The time interval of the clinical improvement after surgery has been reported diversely from 2 weeks to 6 months[5, 9]. Our patient had started to improve from 3 weeks after surgery.

Paraneoplastic limbic encephalitis is generally a disease of adults. We could find only one report of paraneoplastic limbic encephalitis associated with a mature ovarian teratoma, in adolescence[10].

In conclusion, the present report is the first case of a paraneoplastic limbic encephalitis associated with a mature ovarian teratoma in Korea. Patients with paraneoplastic limbic encephalitis typically present initially to a psychiatrist or neurologist, and it is important to recognize the syndrome as the first manifestation of an underlying malignancy.

한 글 요 약

성숙 난소기형종에 동반된 부신생물 변연계뇌염 1례

부산대학교 의학전문대학원 소아과학교실

김성헌 · 김혜영 · 임영탁 · 남상욱 · 김영미

부신생물 변연계뇌염(paraneoplastic limbic encephalitis)은 신경계의 전이가 없이 종양의 원격 작용에 의해 발생하는 질환으

로 소아에서는 드물게 보고되고 있다. 저자들은 사춘기 여아에서 발생한 성숙 난소기형종에 동반된 부신생물 변연뇌염을 경험하고 보고하고자 한다. 15세 여자 환자가 신경정신증상, 기억력 저하, 경련, 의식 저하를 주소로 내원하였다. 뇌척수액 검사, 뇌 MRI는 정상이었으나, 뇌 SPECT 검사에서 양측 측두엽의 저관류가 관찰되었다. 복부 초음파와 MRI에서 좌측 난소의 낭성 종양이 발견되었다. 종양의 수술적 제거 후 성숙 난소기형종으로 확인되었으며, 종양 제거 및 면역글로불린 정맥 투여로 완전한 인지 기능의 회복을 보였다.

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