doi: 10.53446/actamednicomedia.1198030

Acta Medica Nicomedia

Cilt: 6 Sayı: 3 Ekim 2023 / Vol: 6 Issue: 3 October 2023
https://dergipark.org.tr/tr/pub/actamednicomedia

Case Report | Olgu Sunumu

A RARE CASE OF PARANEOPLASTIC LIMBIC ENCEPHALIT: ANTI-YO ANTIBODY POSITIVE COLON ADENOCARSINOMA

NADİR GÖRÜLEN BİR PARANEOPLASTİK LİMBİK ENSEFALİT OLGUSU: ANTİ-YO ANTİKOR POZİTİF KOLON ADENOKARSİNOMU

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ABSTRACT

Paraneoplastic autoimmune encephalitis (PAE) is a rare clinical condition associated with malignancy, characterized by the development of neuropsychiatric symptoms. In the presence of malignancy, PAE develops without direct neoplastic invasion. Anti-Yo antibody is often associated with ovarian and breast cancers and is more common in women aged 60 and over than in men. We present a rare case of meningoencephalitis who was positive for anti-Yo antibody and had a history of colon cancer. A 77-year-old male patient with a diagnosis of colon adenocarcinoma presented with epileptic seizures and confusion. Biochemical analysis of cerebrospinal fluid was mild increase in protein level. Cranial MR revealed in bilateral cerebral hemispheres, characterized by cortical swelling with a vasogenic edema pattern. Anti-Yo antibody was positive in the serum. He was treated intravenous immunoglobulin at a dose of 0.4 mg/kg for 5 days and improved with no sequelae. Anti-Yo is an autoantibody often causing paraneoplastic cerebellar degeneration (PCD), whereas it is less commonly accompanied by autoimmune encephalitis. Anti-Yo antibody is often associated with ovarian and breast cancers, while its coexistence with colon adenocarcinoma is extremely rare. Accordingly, we found it worth presenting this case.

Keywords: Anti-Yo autoantibody, paraneoplastic cerebellar degeneration, colon adenocarsinoma, autoimmune encephalitis

ÖZ

Paraneoplastik otoimmün ensefalit (POE) nöropsikiyatrik semptomlarla karakterize olan, malignite ile ilişkili nadir görülen bir sendromdur. Malignite varlığında direk neoplastik invazyon olmadan gelişir. Anti-Yo antikoru ile ilişkili paraneoplastik sendromlar genellikle over ve meme kanseri ile ilişkilendirilmiş olup; 60 yaş üstü kadınlarda erkeklerden daha sık gözükmektedir. Biz de literatürde nadir gözüken kolon adenokarsinomuna eşlik eden, anti-Yo pozitif meningoensefalit gelişen erkek bir olgu sunmayı amaçladık. 77 yaşında, kolon adenokarsinom tanısı olan bir erkek hasta epileptik nöbet ve konfüzyon tablosu ile başvurdu. Beyin omurilik sıvısında ılımlı düzeyde protein artışı mevcuttu. Kranial MR'da bilateral serebral hemisferlerde yaygın kortikal vazojenik ödem izlendi. Serumda anti-Yo antikoru pozitif tespit edildi. 5 gün, 0,4 mg/kg dozunda intravenöz immunoglobulin (Ivıg) verilen hastada sekelsiz düzelme izlendi. Anti-Yo antikoru otoimmün ensefalitten ziyade genellikle paraneoplastik serebeller dejenerasyon (PSD) kliniğine sebep olur ve genellikle over ve meme kanseri ile ilişkilendirilmiştir. Literatürde kolon adenokarsinomu birlikteliği oldukça nadir bulunmuştur.

Anahtar Kelimeler: Anti-Yo antikor, paraneoplastik serebeller dejenerasyon, kolon adenokarsinom, otoimmün ensefalit

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Başvuru/Submitted: 01.11.2022 • **Kabul/Accepted:** 17.10.2023 • **Online Yayın/Published Online:** 21.10.2023

Introduction

Paraneoplastic syndromes refer to groups of symptoms occurring in patients with malignant neoplasms, often including endocrine and neurological disorders and seen in less than 10% of such patients. Paraneoplastic neurological syndromes (PNS) result in irreversible immune-mediated effects and thus require early diagnosis and treatment.[1]

Autoimmune encephalitis (AE) is a rare and potentially reversible neurological disease. There are subtypes of AE characterized by antibodies against intracellular and extracellular proteins and cell surface antigens. These antibodies are closely associated with the underlying malignancy and are 'well-characterized' paraneoplastic or onconeuronal antibodies. In some forms of AE, evaluation reveals an underlying malignancy, placing this condition in the category of paraneoplastic autoimmune encephalitis (PAE). PAE is associated with the underlying malignancy and develops without direct neoplastic invasion of the malignancy and often presents as behavioral changes, memory and cognitive impairment, seizures, and movement disorders.[2]

To date, numerous autoantibodies causing PAE have been identified and one of the antibodies against intracellular antigens is known as Purkinje cell cytoplasmic antibody type 1 (PCA-1)-IgG (or anti-Yo antibody). Anti-Yo is an autoantibody responsible for half of the manifestations of paraneoplastic cerebellar degeneration (PCD) except for AE.[3] Moreover, this autoantibody is considered to accompany cytotoxic T cells activated against immunodominant peptides produced from intracellular antigens.[4]

In this report, we present a rare case of meningoencephalitis who was positive for anti-Yo antibody and had a history of colon cancer.

Case Report

A 77-year-old male patient presented to the emergency service with a three-day history of staring into space lasted for seconds and confusion for one day. During emergency service admission, the patient had two generalized tonic-clonic seizures. He had a history of operated colon adenocarcinoma (in 2013), coronary artery disease (for the last four years), hypertension, and diabetes. On neurological examination, the patient was awake, cooperative, oriented, cranial nerve examination was normal, nuchal rigidity was absent, dysarthria was present, there was no paresis, cerebellar examination was normal, plantar reflex was bilaterally flexor, and deep tendon reflexes were normoactive in all extremities. Sensory examination was normal and there was no ataxia. Laboratory parameters showed no metabolic disorder except for hyperglycemia. Biochemical analysis of cerebrospinal fluid (CSF) showed protein 47 mg/dl, glucose 171 mg/dl (simultaneous blood sugar 400), and chlorine 130 mmol/L. Additionally, erythrocyte count was 960 and leukocyte count was 10 cell/mm3. (Lumbar puncture was initiated in another center and acyclovir 750 mg/day 3x1 g and ceftriaxone 2x1 g were administered on the third day of the treatment). No atypical cells or specific inflammation findings were detected in CSF cytology. CSF polyomavirus hominis 1 (BK-virus), herpes simplex virus (HSV) ½ polymerase chain reaction (PCR), John Cunningham (JC) virus, brucella PCR, Epstein-Barr virus (EBV) PCR, varicella zoster virus (VZV) PCR, tuberculosis (TBC) real-time PCR were negative. Cranial magnetic resonance imaging (MRI) revealed in both cerebral hemispheres, particularly in the left frontal cortex, left caudate nucleus, right thalamus, right perisylvian cortex, and right parieto-occipital cortex parenchyma areas characterized by cortical swelling with a vasogenic edema pattern (Figure 1). Pachymeningeal (dural) enhancement was observed in the right cerebral hemisphere, which was suggestive of meningoencephalitis and there was a lesion showing heterogeneous enhancement in the right occipital area (Figure 2).

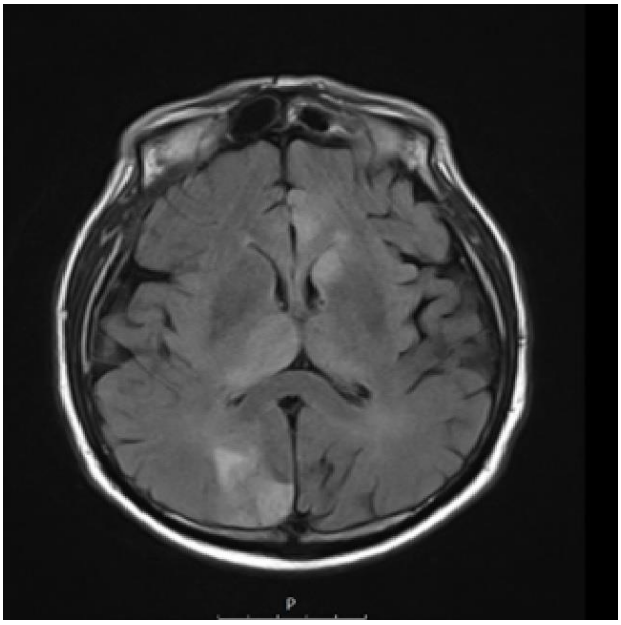

Figure 1. Cranial T2-Flair axial

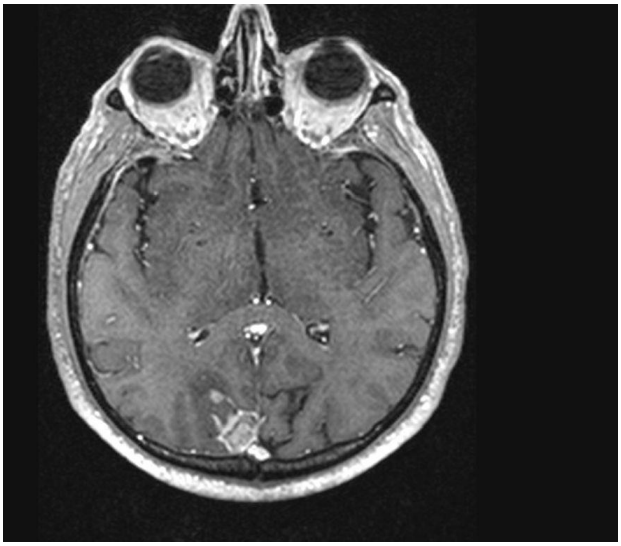

Figure 2. Cranial T1 with contrast

Electroencephalography (EEG) was normal. In contrast-enhanced lower and upper abdominal computed tomography (CT), cecum and the ascending colon were not observed, whereas an appearance indicative of ileocolic anastomosis was observed at the hepatic flexure level. Due to a preliminary diagnosis of paraneoplastic/autoimmune encephalitis, paraneoplastic antibody panel was sent, which showed anti-Yo antibody positivity. Due to the presence of drug-resistant focal motor seizures localized to the right arm and leg, the patient was initiated on valproic acid 3x500 mg and lamotrigine 2x50 mg. Additionally, the patient was given intravenous immunoglobulin (Ivıg) at a dose of 0.4 mg/kg for 5 days. At the end of the treatment, dysarthria improved with no sequelae and the patient was discharged with the recommendation of medical oncology and neurology outpatient clinic control. Approximately three months later, the patient presented to the emergency department with headache complaint and was detected with a new lesion in the left frontal region approximately 6x4 cm in size with irregular borders, showing contrast enhancement and causing vasogenic edema on cranial CT (Figure 3,4) and diffusion MR (Figure 5), thought to be metastasis. This lesion was not observed in previous imaging studies 3 months ago. The patient is still being followed up by neurology since surgical intervention is not recommended by the neurosurgery department.

A written informed consent form was obtained from the patient.

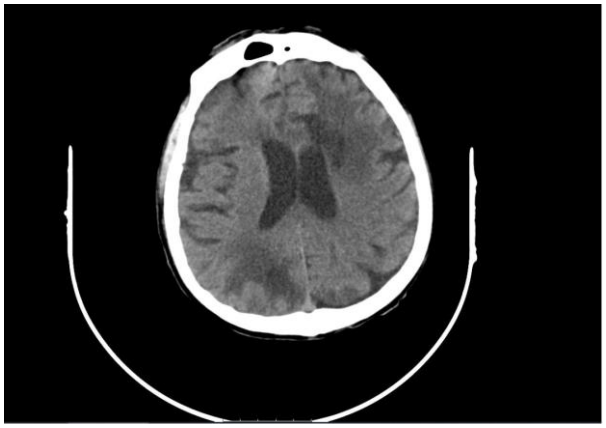

Figure 3. Computerized brain tomography

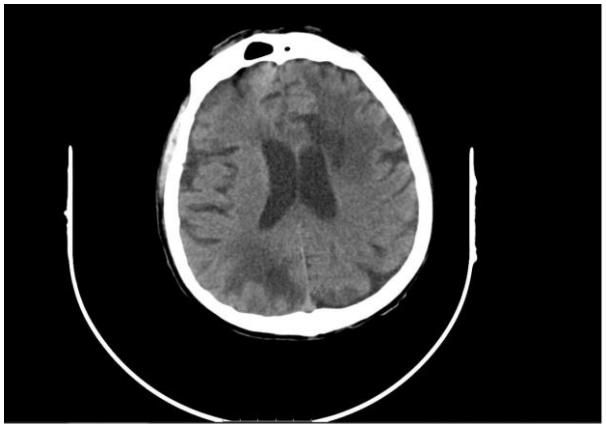

Figure 4. Computerized brain tomography

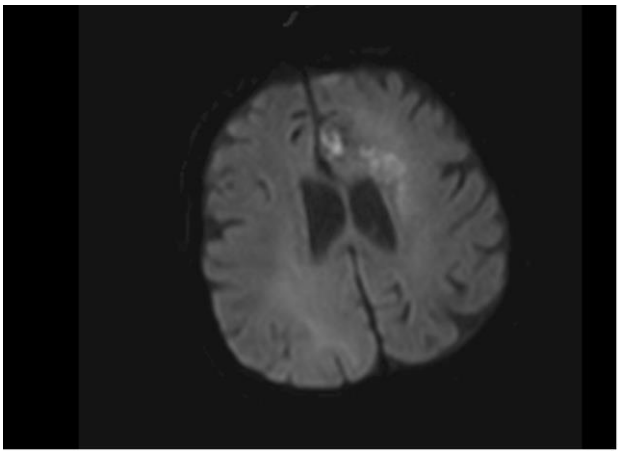

Figure 5. Difussion MRI

Discussion

Paraneoplastic limbic encephalitis is a classic paraneoplastic neurological symptom, commonly accompanied by subacute sensory neuropathy, PCD, paraneoplastic opsoclonus-myoclonus (POM), Lambert-Eaton myasthenic syndrome (LEMS), and paraneoplastic peripheral nerve hyperexcitability.[2]

Anti-Yo is an autoantibody often causing PCD, with its main target being CDR2 protein which is mainly expressed in brain and testicular tissue. Anti-Yo antibody positivity is a potential marker of malignancy.[1]

The symptoms of PCD often occur secondary to brain metastasis, direct invasion of the central nervous system by the tumor, infection, and metabolic disorder. PCD affects the midline of the vermis and cerebellum in the early period and often manifests with more severe findings than cerebellar hemisphere involvement. Moreover, it is often accompanied by acute or subacute truncal or limb ataxia, nystagmus, vertigo, dysarthria, and less commonly by diplopia and oscillopsia. The deficit is always bilateral but may sometimes be asymmetric. PCD usually occurs years before the onset of malignancy. Ovarian and breast cancer is seen in approximately 50% of patients with cerebellar ataxia who have anti-Yo positivity.[5] In the literature, only one female[6] and one male patient[7] who were diagnosed with cholangiocarcinoma and developed anti-Yo-associated paraneoplastic cerebellar degeneration have been reported. Additionally, although there are few publications reporting on lung cancer in male patients with PCD and anti-Yo positivity, most of these patients have been detected with prostate and gastrointestinal adenocarcinomas.[8]

Cerebellar cognitive affective syndrome (CAS), which is characterized by impaired executive functions, visual-spatial memory, mild-to-moderate language disfunctions, and disinhibited or inappropriate behavior, can be observed in approximately 20% of patients with PCD. Moreover, paraneoplastic limbic encephalitis is often accompanied by PCD and CAS. In the literature, only two cases of anti-Yo-associated PCD associated with CAS secondary to breast cancer and ovarian cancer

without paraneoplastic limbic encephalitis have been reported.[5]

In the literature, 90 cases with autoimmune encephalitis associated with intracellular autoantibodies have been reported, and in these patients antibodies including anti-Ma, anti-Hu, anti-Yo, anti-Ri, anti-CV2, and anti-amphiphysin have been detected. Although seizures (69.1%) and cognitive impairment (79.1%) have been frequently reported in such patients, psychotic symptoms have been shown to be less prevalent. In the group of patients who developed autoimmune encephalitis associated with intracellular autoantibodies are mostly diagnosed with tumors. Immunotherapy treatment usually provides good outcomes, 45.6% of these patients have a good clinical course.[5] Similarly, our patient also presented with seizures and he had a poor prognosis and developed brain metastasis during the follow-up period.

In the literature, limbic encephalitis has been rarely associated with colon adenocarcinoma.[9,10] Tsukamoto et al. described an anti-Hu-positive female patient with colon adenocarcinoma who developed PCD and limbic encephalitis.[9] Adam et al. reported on a female patient with anti-Yo-associated colon adenocarcinoma who had no cerebellar degeneration and developed limbic encephalitis.[10] Our patient was a male patient diagnosed with colon adenocarcinoma and he was also positive for anti-Yo antibody and developed meningoencephalitis without cerebellar degeneration. Anti-Yo positivity in serum or CSF is a very strong indicator of PCD, but neurologic symptoms do not develop in 2% of cancer patients. [10] These notions may explain the reason as to why our patient and the other patient in the literature had anti-Yo antibody positivity and had no neurological findings of cerebellar degeneration.

To the best of our knowledge, this case is the first male patient in the literature with a diagnosis of anti-Yo-associated colon adenocarcinoma who manifested with meningoencephalitis before the development of PCD.

The case presented in this report showed that paraneoplastic syndromes can have a diverse course and that it is not always correct to associate known paraneoplastic autoimmune antibodies with a specific syndrome. Paraneoplastic syndromes should be considered in patients with malignancy and unexplained neurological symptoms, and treatment should be planned accordingly.

Compliance with Ethical Standards

Written consent form was obtained from the patient.

Conflict of Interest

The author declares no conflicts of interest.

Author Contribution

MT: Conceived the ideas FEA,MT: Designed the experiments FEA: writing, literature review

Financial Disclosure

No financial support has been received for this article.

References

1. Pelosof LC, Gerber DE. Paraneoplastic syndromes: an approach to diagnosis and treatment. *Mayo Clin Proc*. 2010;85:838-854. doi:10.4065/mcp.2010.0099.
2. Honnorat J. Didelot A, Karantoni E, et al. Autoimmune limbic encephalopathy and anti-Hu antibodies in children without cancer. *Neurology* 2013;80:2226-2232. doi:10.1212/wnl.0b013e318296e9c3.
3. Broadley J, Seneriratne U, Beech P, et al. Prognosticating autoimmune encephalitis: A systematic review. *Journal of Autoimmunity* 2019;96:24-34. doi:10.1016/j.jaut.2018.10.014.
4. Dalmau J, Graus F, Villarejo A, et al. Clinical analysis of anti-Ma2-associated encephalitis,*Brain* 2004;127:1831-1844. doi:10.1093/brain/awh203.
5. De Beukelaar JW, Sillevis Smitt PA. Managing paraneoplastic neurological disorders. *Oncologist* 2006;11:292-305. doi:10.1634/theoncologist.11-3-292.
6. Lou Y, Xu S, Zhang S, Shu Q, Liu X. Anti-Yo antibody-positive paraneoplastic cerebellar degeneration in a patient with possible cholangiocarcinoma: A case report and review of the literature. *World Journal of Clinical Cases*. 2021;9(17);4423-4432. doi:10.12998/wjcc.v9.i17.4423.
7. Hasadsri L, Lee J, Wang BH, Yekkirala L, Wang M. Anti-yo associated paraneoplastic cerebellar degeneration in a man with large cell cancer of the lung. *Case Rep Neurol Med.* 2013;2013:725936. doi:10.1155/2013/725936.
8. Meglic B, Graus F, Grad A. Anti-Yo associated paraneoplastic cerebellar degeneration in a man with gastric adenocarcinoma. *J Neurol Sci* 2001;185:135–138. doi:10.1016/s0022-510x(01)00467-1.
9. Tsukamoto T, Mochizuki R, Mochizuki H, et al. Paraneoplastic cerebellar degeneration and limbic encephalitis in a patient with adenocarcinoma of the colon. *Journal of Neurology, Neurosurgery, and Psychiatry* 1993;56:713-716. doi:10.1136/jnnp.56.6.713.
10. Adam VN, Budinčević H, Mršić V, Stojčić E, Matolić M, Markić A. Paraneoplastic limbic encephalitis in a patient with adenocarcinoma of the colon: a case report. *Journal of Clinical Anesthesia* 2013;25:491-495. doi:10.1016/j.jclinane.2013.03.014.