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## WERNICKE ENCEPHALOPATHY: A CASE OF AMYOTROPHIC LATERAL SCLEROSIS COMPLICATION

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### Case Report

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### Abstract

Hypovitaminosis secondary to undernutrition is presented with clinical diseases coursing with broad spectrum symptoms. Thiamine (vitamin B1) deficiency is frequently associated with malnutrition and causes serious neurological disorders as Wernicke's encephalopathy (WE), and beriberi disease. Even though clinical trials have predicted the incidence of WE as 0,04-0,13%, post-mortem studies have demonstrated a higher incidence as 0,8-2,8% which means that most of the cases go undiagnosed. Treatment with thiamine supplementation protects the patient from all these diseases.

In this article, a case who was diagnosed as amyotrophic lateral sclerosis who displayed Wernicke-Korsakoff syndrome pattern was discussed. This manuscript was prepared to attract attention to this potentially fatal easily overlooked Wernicke-Korsakoff syndrome pattern developing in especially undernourished amyotrophic lateral sclerosis patients with percutaneous gastrostomy (PEG) which may be mostly reversed with treatment at an early stage.

**Key Words:** Wernicke Encephalopathy, Wernicke-Korsakoff Syndrome, Amyotrophic Lateral Sclerosis, Myroides.

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## Özet

Yetersiz beslenmeye bağlı hipovitaminozis geniş spektrumlu semptomlarla seyreden klinik hastalıklarla karşımıza çıkmaktadır. Tiamin (vitamin B1) eksikliği yetersiz beslenmeyle ilişkilidir ve Wernicke Ensefalopatisi (WE) ve Beriberi gibi ciddi nörolojik hastalıklara sebep olmaktadır. Klinik araştırmalar WE insidansını %0,04-0,13 olarak öngörmüş olsa da postmortem çalışmalar %0,8- 2,8 gibi daha yüksek bir insidansı göstermiştir ki bu da çoğu vakanın teşhis edilmediği anlamına gelmektedir. Tiamin takviyesi ile tedavi hastayı tüm bu hastalıklardan korur.

Bu yazıda Wernicke-Korsakoff sendromu paterni gösteren amiyotrofik lateral skleroz tanılı bir olgu tartışıldı. Bu makale özellikle perkütan gastrostomili yetersiz beslenmiş amiyotrofik lateral skleroz hastalarında gelişen, potansiyel olarak ölümcül, kolayca gözden kaçabilen, erken dönem tedavi ile geri döndürülebilen Wernicke-Korsakoff paternine dikkat çekmek için hazırlanmıştır.

**Anahtar Kelimeler:** Wernicke Ensefalopatisi, Wernicke-Korsakoff sendromu, amiyotrofik lateral skleroz, myroides

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## 1. Introduction

Wernicke encephalitis (WE) is a neurological disorder caused by thiamine (vitamin B1) deficiency. WE is the most important cause of encephalitis associated with only one vitamin deficiency. WE is characterized by a classical triad of ocular symptoms, cerebellar dysfunction (ataxic gait), and confusion (encephalopathy) (Donnino et al., 2007; Sechi & Serra, 2007).

In case of long-term alcohol abuse or malnutrition, the presence of acute confusion, delirium, ataxia, ophthalmoplegia, memory disorders, hypothermia coursing with hypotension, and delirium tremens should be suggestive of WE. Since WE and Korsakoff psychosis are seen in association, these two disease states are frequently termed as Wernicke-Korsakoff Syndrome (WKS) (Antunez et al., 1998; Gordan, 2013).

In great majority of the patients who survived WE, WKS which is characterized by retrograde amnesia (difficulty in recalling information), anterograde amnesia (inability to comprehend new information), various degrees of cognitive disorders, decreased spontaneity, and initiatives, and confabulation.

Alcohol abuse, AIDS, malignancy, hyperemesis gravidarum, prolonged total parenteral nutrition, overloading glucose in patients with thiamine deficiency, and other disorders associated with the impaired nutritional state have been found to be related to WKS.

Amyotrophic lateral sclerosis (ALS) is a prototype of a neurodegenerative disease coursing with degeneration of anterior horn of the spinal cord, motor nuclei of cranial nerves, pyramidal cells of motor cortex leading finally to progressive paresis of skeletal muscles. Typically, amyotrophy onsets as a focal disease, and gradually affects predominantly neighboring muscles. During the disease, paresis of the diaphragm, and intercostal muscles leads to global respiratory failure. Twenty-five percent of ALS patients present with paresis-related dysphagia with resultant weight loss, malnutrition, and cachexia (Jesse et al., 2015).

In this paper, a case that remained in a state of prolonged malnutrition due to dysphagia developed during ALS and suffered from WE secondary to thiamine deficiency which emerged as a potential complication after percutaneous endoscopic gastrostomy (PEG) was discussed.

## **2. Case report**

44-year-old female patient presented to our outpatient clinic with dysarthria, dysphagia, and involuntary weight loss being more apparent within the last months. She was previously diagnosed as ALS at an external center, and she was receiving riluzole treatment. At her first admission, her neurological examination revealed the presence of generalized spontaneous fasciculations, distal atrophy, increased tendon reflexes, and bilateral extensor plantar reflexes. She couldn't tolerate oral intake, so a PEG was opened. Cerebral, and spinal MRI performed at her first admission did not display any pathology. On cerebral MRI performed 2 months after her hospitalization global cortical atrophy, and enlargement of lateral ventricles were observed, but restricted diffusion or any hyperintense lesion was not encountered. Analysis of cerebrospinal fluid performed at the following days of her hospitalization did not disclose the presence of an abnormal cell, and CSF protein was detected. The patient worsened during her monitorization, so she was connected to a mechanical ventilator. On neurological examination during her monitorization in intensive care unit bilateral upbeat vertical nystagmus was detected. Since IV thiamin preparation for the treatment of her WE were not available, high doses of thiamine was started to be delivered through PEG. However, the patient did not respond to thiamine therapy, and her clinical symptoms were not relieved markedly, however her nystagmus improved a little bit. On her urine culture obtained on the following days of her monitorization in the anesthesia

intensive care unit growth of Myoids spp. was observed. Her conscious state increasingly worsened. The patient was hospitalized in the intensive care unit for more one year and connected to mechanical ventilator under our surveillance. She was responding to painful stimuli, and only partially to verbal stimuli. After one year she lost her life due to severe multi organ failure and fatal cardiac arrhythmia.

### **3. Discussion**

In the diagnosis of Wernicke encephalopathy clinical signs, and symptoms in addition to the group under risk should be identified. The Classical triad of the disease is characterized by encephalopathy, truncal ataxia, and ophthalmoparesis. However rarely these three symptoms are found in combination. (17%), sometimes none of these three symptoms may be detected (11%). Confusion and other alterations in consciousness are the most frequently seen symptoms (82%), followed by ataxia (23%), oculomotor disorders (29%), and polyneuropathy (11%). If the diagnosis is delayed probably three symptoms may become manifest. In our case, also encephalopathy, and ocular symptoms were seen since the patient was bedridden, and uncooperated ataxia could not be evaluated fully.

Encephalopathy is characterized by global confusional state, apathy, indifference, or agitation. The most frequent presenting symptoms of WE are alterations in mental state. Stupor and coma are rarely seen symptoms. Coma is the rarely seen sole symptom of WE. In our case, as an alteration in mental state, confusion, and afterwards rarely seen symptoms of stupor, and coma developed.

Ocular abnormalities are main findings of WE. Oculomotor symptoms include nystagmus, bilateral lateral rectus paralysis, and conjugate gaze paralysis which reflects cranial nerve involvement of oculomotor, abducens, and vestibular nuclei. Less frequently observed symptoms include hyporeactive pupils, ptosis, scotoma, and anisocoria. Most frequently seen ocular abnormality is nystagmus, rather than abducens (6. cranial nerve) ophthalmoplegia (Donnino et al., 2007).

In our case as an ocular symptom, upbeat vertical nystagmus, and bilateral conjugate gaze paralysis were seen, and in the upcoming days rarely seen symptom of anisocoria was added to the picture. Ophthalmoplegia and ocular disorders are rarely reported symptoms in ALS (Kobayashi et al., 1999). Therefore, ocular symptoms seen in our patient raised suspicion for WE.

As available evidence suggests, treatment with thiamine provides a rapid recovery from ataxia, and ophthalmoplegia, and ensures a gradual, but prominent decrease in the severity of nystagmus. The global confusional state tends to improve rapidly within hours. Memory and learning disorders respond thiamine treatment more slowly, and incompletely which suggests the presence of a different mechanism of action. (Day et al., 2013). In our case, an intravenous formulation of thiamine as recommended in the literature was not available, so after administration of thiamine supplementation through PEG nystagmus of the patient markedly improved, however improvement in her consciousness, and mental state was not observed.

Cerebral computed tomography with an indicated sensitivity of 13%, does not appear to be a useful screening tool for WE (Antunez et al., 1998). On cerebral computed tomogram of our patient a major abnormality other than marked atrophy on frontal, and parietal regions could not be detected. Sensitivity, specificity, and positive predictive value of MRI are 53, 93, and 89%, respectively. In other words, MRI is a better modality for confirmation of the diagnosis of WE, rather than ruling it out (Galvin et al., 2010). MRI is a useful imaging modality in establishing the definitive final antemortem diagnosis. Imaging modalities performed in chronic WE, and WKS, and especially MRI may be normal or demonstrate symmetrical low-density abnormalities in the periventricular area, diencephalon, and mesencephalon or mamillary body, cerebellar, and cerebral atrophy. These asymmetrical lesions are rarely seen in cerebral encephalopathies, and they are warning signs for WKS. Indeed, thiamine is the cofactor of many enzymes involving in glucose metabolism and use of cerebral energy. Thiamine deficiency induces signal alterations, and neuronal damage in mamillary bodies, periventricular thalamus, and periaqueductal gray matter observed as hyperintensities in MRI T2-weighted images and Flair sequences (Galvin et al., 2010).

Wernicke encephalopathy is a medical emergency. If untreated it results in death in 20% of the patients. Following acute phase, if WE is not treated appropriately with thiamine after the emergence of edema and resolution of the inflammation of the affected brain tissue, in 85 % of the survived patients Korsakoff Syndrome whose main symptomatic characteristic feature is global amnesia may develop.

Neuropathology detected on MRI has different neuroradiologic feature apart from that seen during the acute phase. Tissue shrinkage or atrophy of certain cerebellar formations as a mamillary body, and thalamus, and probably ventricular enlargement secondary to atrophy of the periphery of gray matter nuclei may be observed. Since intravenous formulation is not available

in our country, vitamin B1 delivered through PEG became inadequate for treatment which may lead to the development of KS. In compliance with the literature on cerebral MRI, global cortical atrophy, and ventricular enlargement that may be seen in patients with KS were detected.

The growth of *Myroides* spp. was detected in urine culture of the patient. *Myroides* spp. are frequently found in environmental sources like water and soil. They are rarely seen opportunistic pathogens and tend to affect immunocompromised patients (Beharrysingh, 2017).

The immune system of our case may be suppressed because of malnutrition secondary to ALS, and she might be infected with *Myroides* spp. which is a rarely seen cause of infection in human beings. As an infectious agent in human beings *Myroides* spp. is mostly resistant to antibiotics. Since mechanism of antimicrobial resistance of *Myroides* spp. has not been understood so far, taking the risk of nosocomial infection, and pandemic, complete genome sequencing, and advanced bioinformatic analyses targeting these species should be realized. These analyses will also aid in the development of appropriate treatment strategies. Moreover, complete genome sequencing method may be a routinely used potential diagnostic tool soon (Beharrysingh, 2017).

#### **4. Conclusion**

The Wernicke-Korsakoff syndrome is not only seen in alcoholic patients, but this condition can be seen in some diseases as ALS which progresses with dysphagia and causes long-term malnutrition. Raising awareness on this issue, treatment at an early stage may intervene WE before its conversion, and progression to KS.

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None.

#### **Conflicts of interest**

The authors declare that there are no potential conflicts of interest relevant to this article.

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