https://doi.org/10.23934/2223-9022-2020-9-2-292-297

# Clinical Cases of Wernicke Encephalopathy

***G.R. Ramazanov*, E.A. Kovaleva, V.N. Stepanov, H.V. Korigova, E.V. Shevchenko, Y.V. Zabrodskaya, S.S. Petrikov***

**Department of Emergency Neurology and Rehabilitation Treatment**
**N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department**
**3 B. Sukharevskaya Sq., Moscow 129090, Russian Federation**

*** Contacts:** Ganipa R. Ramazanov, Candidate of Medical Sciences, Head of the Scientific Department of Emergency Neurology and Rehabilitation Treatment N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department. Email: ramazanovgr@sklif.mos.ru

**ABSTRACT** This article will discuss the causes of Wernicke encephalopathy, diagnosis, treatment and clinical examples of this disease.
**Keywords:** Wernicke encephalopathy, alcoholism, thiamine deficiency, liver transplantation
**For citation** Ramazanov GR, Kovaleva EA, Stepanov VN, Korigova HV, Shevchenko EV, Zabrodskaya YV, et al. Clinical Cases of Wernicke Encephalopathy. *Russian Sklifosovsky Journal of Emergency Medical Care.* 2020;9(2):292–297. https://doi.org/10.23934/2223-9022-2020-9-2-292-297 (in Russ.)
**Conflict of interest** Authors declare lack of the conflicts of interests
**Acknowledgments, sponsorship** The study had no sponsorship
**Affiliations**

| | |
|---|---|
| Ganipa R. Ramazanov | Cand. Med. Sci., Head of the Scientific Department of Emergency Neurology and Rehabilitation Treatment N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department; https://orcid.org/0000-0001-6824-4114, ramazanovgr@sklif.mos.ru;<br>15%, analysis of clinical data, preparation of illustrations, preparation of manuscript, editing of manuscript, approval of manuscript, answers to questions from reviewers |
| Ella A. Kovaleva | Cand. Med. Sci., Neurologist at the Neurological Department for Patients with Acute Cerebrovascular Event with Intensive Care Unit, N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department; https://orcid.org/0000-0002-8490-1417, elissent@mail.ru;<br>15%: analysis of clinical data, preparation of illustration material, preparation of manuscript, editing of manuscript, approval of manuscript, answers to questions from reviewers |
| Valentin N. Stepanov | Radiologist, Center for Radiosurgery, N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department; https://orcid.org/ 0000-0003-0007-8054, stepanovvn@sklif.mos.ru;<br>15%: preparation of illustrations, preparation of manuscript |
| Khedi V. Korigova | Neurologist, Neurological Department for Patients with Acute Cerebrovascular Event with Intensive Care Unit, N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department; https://orcid.org/0000-0002-9788-592X, khadi.korigova@mail.ru;<br>15%: analysis of clinical data, preparation of illustrations, preparation of manuscript |
| Evgeny V. Shevchenko | Head of the Neurological Department for Patients with Acute Cerebrovascular Event with Intensive Care Unit, N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department; https://orcid.org/0000-0001-9750-3509, shevchenkoev@sklif.mos.ru;<br>15%: clinical data analysis, manuscript preparation |
| Yana V. Zabrodskaya | Head of the Intensive Care Unit for Surgical Patients, N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department; https://orcid.org/0000-0003-2012-9461, zabrodskayayv@sklif.mos.ru;<br>15%: Clinical Data Analysis, Manuscript Preparation |
| Sergey S. Petrikov | Corresponding Member of the Russian Academy of Sciences, Doctor of Medical Sciences, Director of the N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department; https://orcid.org/ 0000-0003-3292-8789; petrikovss@sklif.mos.ru;<br>10%: analysis of clinical data, preparation, editing and approval of the manuscript |

ACVE – acute cerebrovascular event
ADC – measured diffusion coefficient of MRI
BP – blood pressure
CT – computed tomography
DWI – mode of diffusion-weighted imaging of MRI
EMS – emergency medical services
GIT – gastrointestinal tract
GCS – Scale Coma Glasgow
HR – heart rate
MRI – magnetic resonance imaging
T2 FLAIR – MRI mode with hypointense signal
WE – Wernicke encephalopathy

## INTRODUCTION

Wernicke encephalopathy (WE) is a life-threatening disease, caused by acute or chronic deficiency of thiamine, accompanying with edema of brain stem with the development of cerebral and / or focal neurological symptoms. The disease was first described by Carl Wernicke in 1881 under the name of acute upper hemorrhagic polioencephalitis. The triad of clinical symptoms is characteristic: ophthalmoparesis with nystagmus, ataxia, quantitative and / or qualitative changes in consciousness [1–6]. The most frequent cause of the ER is a chronic abuse of alcohol. Besides that, the reason of thiamine insuffiiciency and, as a consequence, the ER, may be malignant neoplasms of gastrointestinal tract (GIT), destructive acute pancreatitis, diseases of the liver, hyperthyroidism, pernicious vomiting, alimentary insufficiency, chronic hemodialysis, annually [11-13]. The ratio of men and women with WE is 1: 1.7, and the average age of disease is from 30 to 50 years [3, 11, 14]. According to *G. Zuccoli et al.* (2009), quantitative and qualitative changes in consciousness were detected in 89%, ophthalmoparesis with nystagmus - in 75%, ataxia - in 54% of patients with WE [15]. At the present time, magnetic resonance imaging (MRI) is considered as the most valuable diagnostic tool for WE. During MRI of the brain in 80% of patients symmetrical increase of MR - signal on images *T2 FLAIR* is revealed in periventricular areas thalamus and third ventricle, in 45% - in the mammillary bodies of hypothalamus, in 59% - in the area of aqueduct, in 7% - periventricularly in the area of the fourth ventricle, in 36% - in area of quadrigeminal plate [6]. In the mode of diffusion-weighted imaging (*DWI)* zones of damage often have a high signal, and the diffusion coefficient (*ADC)* may be normal, increased or decreased [13, 14]. The high signal on the *DWI* images and normal or increased *ADC* indicate on the presence of vasogenic edema, characterized by increased diffusion of molecules into the ode of - for the relative increase of the fluid in the extracellular space, then as a high signal on the *DWI* images to a reduction values *ADC* reflects picture cytotoxic edema brain with limiting the diffusion of water molecules [16–18]. The disease should be differentiated from vein of Galen thrombosis, ischemic stroke with occlusion of the artery Percheron, viral encephalitis, acute disseminated encephalomyelitis, Marchiafava-Bignami disease and metronidazole-induced encephalopathy [11]. The treatment of WE is based on the replacement of thiamine deficiency. For the treatment of WE intravenous administration of thiamine hydrochloride in a daily dose of up to 1000 mg [19-22] is indicated. Studies show, that the neurological manifestations significantly regressed within the first two days of administration of the drug. The use of thiamine hydrochloride for 7 days normalized concentration of thiamine in serum of the blood, and repeated MRI of the brain identified the decreased hyperintense lesions on *T2 FLAIR* images [18, 23-25]. According to the data of the study *M. Victor et al.* (1971), the outcome of the disease was unfavorable in the majority of patients - disability occurred in 84% of patients, and complete recovery if disturbed function was observed only in 16% of the examined [26]. A favorable outcome of WE depends on early diagnosis and timely initiation of therapy. In the absence of treatment WE can lead to gross cognitive disorders, severe disability and death [7, 11, 26].

**The aim of the study:** to raise awareness about the methods of diagnosis and treatment of WE, as late initiation of treatment of the disease may lead to irreversible changes in the brain, severe disability, and death in 20% of cases.

From January 2015 to June 2018, 7 cases of WE were registered at N.V. Sklifosovsky Research Institute for Emergency Medicine, confirmed by MRI results. We report three clinical example most representative from the clinical and diagnostic point of view.

Clinical example 1.

Patient P., 32 year-old, was delivered in the ER of the Center for the treatment of acute poisoning, N.V. Sklifosovsky Research Institute, via the ambulance with suspected poisoning with unknown substances. Relatives informed, that 5 days prior to hospitalization the patient was abusing alcohol. She had been drowsy for 3 days before admission to the hospital. On the day of hospitalization the patient was found by relatives at home unconscious. Upon admission: neurology status - level of wakefulness to sopor, Glasgow Coma Scale (GCS)- 9 points, divergent vertical squint, diffuse decreased tone in the muscles of the limbs. Independent breathing, blood pressure (BP) 110/60 mm Hg, heart rate (HR) 96 beats/ min. Chemical and toxicological examination of blood and urine did not reveal any abnormalities. In the clinical analysis of blood - leukocytosis ($12.8 \times 10^9$/L), in the biochemical analysis of blood - hyperglycemia (14.07 mmol/L), an increase in the level of aspartate aminotransferase (110.27 U / L ), alanine aminotransferase (235.91 U / L ), amylase (324.86 U / L ), total bilirubin (19.69 μmol / L ), creatinine (129.97 μmol / L) and urea (16.06 mmol / L ). Computed tomography (CT) of the head of the brain did not identify areas of abnormal X-ray density. In cerebrospinal fluid - an increase in lactate content up to 8.8 mmol / l with normal cytosis. Given the long-term alcoholism of the patient, as well as neurologic data (depression of level of consciousness and oculomotor disturbances), the preliminary diagnosis was WE. With the aim of verifying the diagnosis MRI was indicated in *DWI* and *T2 FLAIR* modes. Intravenous infusion of thiamin was prescribed in a dose of 1000 mg daily. MRI of the brain revealed a symmetrical high signal on medial parts of the thalamus and quadrigeminal plate in *T2 FLAIR* and weakly hyperintensive signa in *DWI*, that is pathognomic for radiological picture of WE (Fig. 1). On the 3rd day of treatment with thiamine the recovery of the level of wakefulness to the mild obtundation was noted, on the 5th day - clear consciousness, vertical divergent squint, dysphagia.

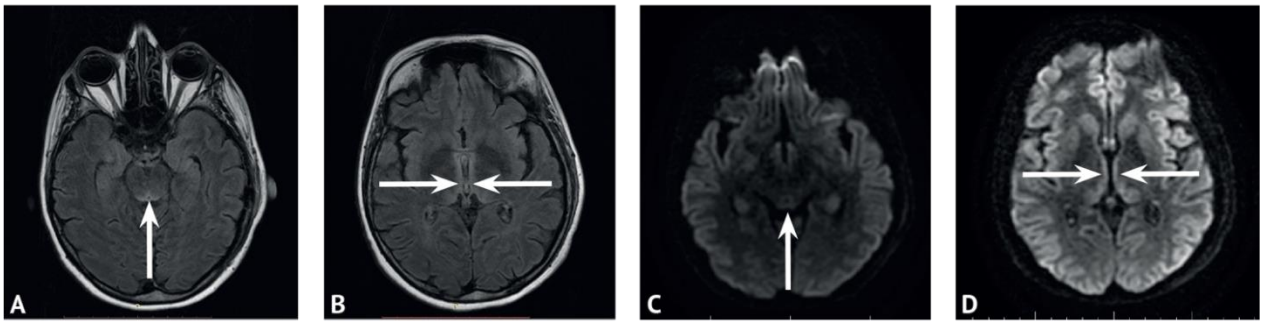


Fig. 1. Magnetic resonance imaging of the brain of patient P. T2 FLAIR-images, axial sections: A — the arrow indicates the high signal area in the region of the quadrigeminal plate; B — symmetric areas of increased signal from the medial parts of the thalamus are specific for Wernicke encephalopathy; DWI-images, axial sections: C — the arrow indicates the area of weakly hyperintensive signal from the quadrigeminal plate, specific for Wernicke encephalopathy; D — arrows indicate the area of weak hyperintensive signal from the medial thalamus

On the background of therapy with thiamine on 6th day positive dynamics was observed in the form of recovery of clear consciousness, regressed oculomotor, coordination disorders and dysphagia. On the 7th day the patient was discharged without neurological deficit.

Clinical example 2.

Patient L., 63 year old, was delivered in ER of the Center for the treatment of acute poisoning, N.V. Sklifosovsky Research Institute with complaints on pain in the abdomen, nausea, vomiting. From the history: chemical burn of the esophagus with the subsequent formation of its stricture in 1979, resection of the stomach, cholecystectomy and the formation of an artificial retrosternal esophagus from the right half of the large intestine in 1982 and 1983. Also, the patient had rheumatoid arthritis, took corticosteroids, couldn't move independently at home. With suspected stenosis of artificial esophagus the patient was hospitalized in the thoracic surgery department. Upon hospitalization: consciousness clear, independent breathing, heart rate 84 bpm, BP 130/80 mm Hg. No abnormalities were found in the clinical analysis of blood. In a biochemical analysis of blood: total protein - 57.72 g / L, total bilirubin - 38.60 mmol / L, direct bilirubin - 14.97 pmol / L, indirect bilirubin - 26.63 pmol / L. The neurological status: sensorimotor aphasia, right gaze deviation, large-swinging horizontal nystagmus. In connection with suspected acute cerebrovascular event (ACVE) the patient underwent CT of the brain – no pathology was revealed. Considering the clinical manifestations in the form of paresis of gaze to the right and large-swinging nystagmus in the absence of signs of stroke on the CT of the brain, WE was suspected. MRI of the brain in *DWI* and *T2 FLAIR* modes was performed to confirm the diagnosis. They symmetrical areas of increased signal on *T2 FLAIR* was revealed in medial parts of both the thalamus, in a region of quadrigeminal plate, and in the mammilary bodies of hypothalamus. In mode *DWI* images had symmetric high signal, which corresponded to low signal on *ADC* maps (Fig. 2), which is characteristic for WE. An intravenous infusion of thiamine solution in a daily dose of 1000 mg was prescribed. Despite the conducted treatment, the condition of the patient progressively deteriorated, and on the 107th day on the background of the respiratory, vascular failure and secondary infectious complications and hemorrhagic syndrome the patient died.

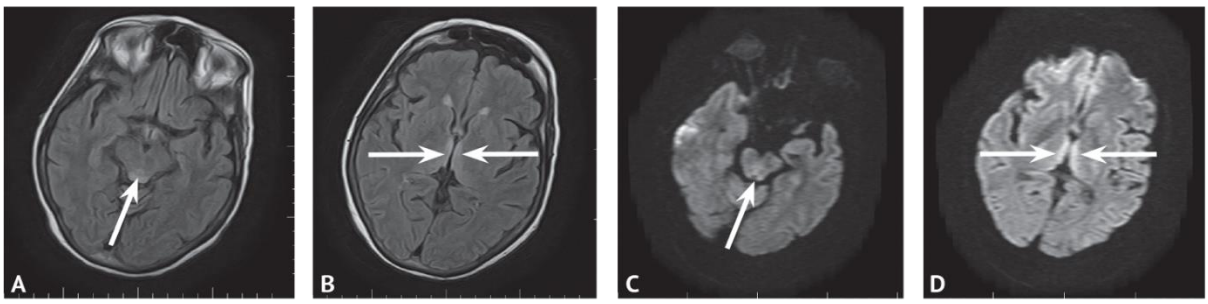


Fig. 2. Magnetic resonance imaging of the brain of patient L. T2 FLAIR-images, axial sections: A — the arrow indicates the high signal area in the region of the quadrigeminal plate, specific for Wernicke encephalopathy; B — symmetric areas of increased signal from the medial parts of the thalamus; DWI-images, axial sections: C — the arrow indicates the area of hyperintensive signal from the quadrigeminal plate; D — arrows indicate the area of hyperintensive signal from the medial thalamus, specific for Wernicke encephalopathy

Clinical example 3.

Patient M., 66 year old, was on treatment in the department of transplantation of N.V. Sklifosofsky Research Institute for Emergency Medicine with a diagnosis "Primary biliary cirrhosis, dysfunction of the hepatic graft." On the 6th day after orthotopic transplantation of the liver and retrograde cholangiopancreatography on the background of high blood pressure to 230/110 mm Hg the patient became disoriented. The neurological status: clear consciousness, GCS - 15 points, disoriented in time, horizontal nystagmus. CT scan of the brain did not reveal any signs of stroke. In the clinical analysis of blood: low hemoglobin (80.0 g / L), low red blood cells ($3.28 \times 10^{12}$ / L) and significantly reduced hematocrit (25.7%). In the biochemical analysis of blood: hypoalbuminemia (27.22 g / L) and a significant increase in the level of gamma - glutamyl transpeptidase (646.66 U / L ). The analysis of the cerebrospinal fluid revealed an increase of the cell composition (11 in L), a high level of lactate (3.6 mmol / L) and glucose (6 mmol / lL). On the 15th day convergent strabismus of the of the left eye and ataxia developed. Taking into account the neurological manifestations, WE was suspected, MRI of the brain was performed, which showed symmetric high signal in *T2 FLAIR* and *DWI* modes in the area of the quadrigeminal plate and aqueduct, which is typical for this disease (Fig. 3).

Intravenous infusion of thiamine in a daily dose of 1000 mg was administered. On the 36 th day positive dynamics was observed - long-term retention of attention and regression of ataxia were reached, but the disorientation in time and in space persisted. On 50th day the patient was transferred to a rehabilitation center for further observation and treatment with persistent oculomotor and cognitive impairment.

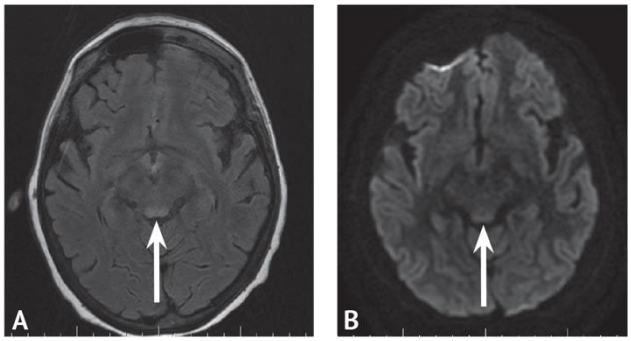


Fig. 3. Magnetic resonance imaging of the brain of patient M. A — T2 FLAIR-images, axial section, the arrow indicates the high signal area in the region of the quadrigeminal plate; B — DWI-images, axial sections, the arrow indicates the area of weakly hyperintensive signal from the quadrigeminal plate, specific for Wernicke encephalopathy

## DISCUSSION

Wernicke encephalopathy is a life-threatening condition. Unfavorable outcomes of WE are often associated with late diagnosis and delayed treatment. Acute cerebral and / or focal neurological symptoms are typical not only for stroke and require careful analysis of anamnestic data, clinical manifestations and radiological picture, which are the key to a correct diagnosis. In our series of observations, we reported WE associated with alcohol abuse, as well as with the diseases of gastrointestinal tract, which were accompanied with thiamine insufficiency. Early diagnosis and preventive appointment of high doses of thiamine is the only correct decision if the disease is suspected. Besides that, the presence of concomitant somatic disorder, determining the development thiamine insufficiency and, as a consequence, WE, even with timely treatment does not guarantee good outcomes. It should be remembered, that mixtures for parenteral nutrition may not include vitamins of group B, in particular, thiamine. This is why the addition to the therapy of vitamins of group B should be considered for patients, undergoing extensive surgical intervention in the gastrointestinal tract and having long parenteral nutrition.

## CONCLUSION

1. In the conditions of a multidisciplinary surgical hospital in patients with risk factors of Wernicke encephalopathy when acute cerebral and / or focal neurological symptoms occur and ACVE is excluded, magnetic resonance imaging in *DWI* and *FLAIR* modes should be urgently performed to confirm the diagnosis.

2. In case magnetic resonance imaging is not available, preventive treatment with high doses of thiamine is indicated. The main clinical signs, which allow Wernicke encephalopathy to be suspected, are ophthalmoparesis with nystagmus, ataxia, and impaired consciousness.

## REFERENCES

1. Alexandrovsky VN, Ostapenko YN, Goldfarb YS, Potskhveriya MM, Kareva MV. Acute Poisoning with Ethyl Alcohol (Alcoholic Coma). *Russian Sklifosovsky Journal Emergency Medical Care*. 2018; 7 (4): 357–365. (In Russ.) Https://doi.org/10.23934/2223-9022-2018-7-4-357-365
2. Krylov VV, Petrikov SS, Ramazanov GR, Solodov AA. *Ney roreanimatologiya.* 2nd ed. Moscow: GEOTAR-Media Publ.; 2016. (In Russ.)
3. Vasan S, Kumar A. Wernicke Encephalopathy: [updated 2018 Nov 14]. StatPearls [Internet]. StatPearls Publishing, Treasure Island, FL2019. PMID: 29261914 Available at: https: //www.ncb i.nlm.nih.gov/books/NBK470344/ [Accessed May 19, 2020].
4. Thorarinsson BL, Olafsson E, Kjartansson O, Blöndal H. Wernicke's encephalopathy in chronic alcoholics. *Laeknabladid.* 2011; 97 (1): 21-29. PMID: 21217196 https://doi.org/10.17992/lbl.2011.01.338
5. Isenberg-Grzeda E, Kutner HE, Nicolson SE. Wernicke-Korsakoff-syndrome: under-recognized and under-treated. *Psychosomatics.* 2012; 53 (6): 507-516. PMID: 23157990 https://doi.org/10.1016/j.psym.2012.04.008
6. Zuccoli G, Santa Cruz D, Bertolini M, Rovira A, Ga llucci M, Carollo C, et al. MR imaging findings in 56 patients with Wernicke encephalopathy: nonalcoholics may differ from alcoholics. *AJNR Am J Neuroradiol.* 2009; 30 (1): 171–176. PMID: 18945789 https://doi.org/10.3174/ajnr.a1280
7. Thomson AD. Mechanisms o f vitamin deficiency in chronic alcohol misusers and the development of the Wernicke – Korsakoff Syndrome. *Alcohol Alcohol Suppl.* 2000; 35 (1): 2-7. PMID: 11304071 https://doi.org/10.1093/alcalc/35.supplement_1.2
8. Schabelman E, Kuo D. Glucose before thiamine for Wernicke encephalopathy: a literature review. *J Emerg Med.* 2012; 42 (4): 488–494. PMID: 22104258 https://doi.org/10.1016/j.jemermed.2011.05.076
9. Arts NJ, Walvoort SJ, Kessels RP. Korsakoff's syndrome: a critical review. *Neuropsychiatr Dis Treat.* 2017; 13: 2875-2890. PMID: 29225466 https://doi.org/10.2147/NDT.S130078
10. Victor M. The Wernicke-Korsakoff syndrome. In: Vinken PJ, Bruyn GW. (eds.) *Handbook of Clinical Neurology.* Amsterdam: North-Holland Publ; 1976; 28 (Pt. II): 243-270.
11. Kim WJ, Kim MM. Wern icke's Encephalopathy Presenting with Bilateral Complete Horizontal and Downward Gaze Palsy in a Malnourished Patient. *Korean J Ophthalmol.* 2017; 31 (4): 372–374. PMID: 28682019 https://doi.org/10.3341/kjo.2017.0014
12. Harper CG, Giles M, Finlay-Jones R. Cl inical signs in the Wernicke-Korsakoff complex: a retrospective analysis of 131 cases diagnosed at necropsy. *J Neurol Neurosurg Psychiatry*. 1986; 49 (4): 341–345. PMID: 3701343 https://doi.org/10.1136/jnnp.49.4.341
13. Lapergue B, Klein I, Olivot JM, Amarenc o P. Diffusion weighted imaging of cerebellar lesions in Wernicke's encephalopathy. *J Neuroradiol.* 2006; 33 (2): 126-128. PMID: 16733427 https://doi.org/10.1016/s0150-9861(06)77243-1
14. Doherty MJ, Watson NF, Uchino K, Hallam DK, Cramer SC. Diffusion abnormalities in patients with Wernicke encephalopathy. *Neurology.* 2002; 58 (4): 655–657. PMID: 11865152 https://doi.org/10.1212/wnl.58.4.655
15. Zuccoli G, Gallucci M, Capellades J, Regnicolo L, Tumiati B, Giadas TC, et al. Wernicke encephalopathy: MR findings at clinical presentation in twenty-six alcoholic and nonalcoholic patients. *AJNR Am J Neuororadio L.* 2007; 28 (7): 1328-1331. PMID: 17698536.https: //doi.org/10.3174/ajnr.a0544
16. Halavaara J, Brander A, Lyytinen J, Setälä K, Kallela M. Wernicke's encephalopath y: is diffusion-weighted MRI useful. *Neuroradiology.* 2003; 2 (2): 141-145. PMID: 12861431 https://doi.org/10.1007/s00234-003-1043-8
17. Latt N, Dore G. Thiamine in the treatment of Wernicke encephalopathy in patients with alcohol use disorders. *J Intern Med.* 2014; 44 (9): 911-915. PMID: 25201422 https://doi.org/10.1111/imj.12522

18. Loh Y, Watson WD, Verma A, Krapiva P. Restricted diffusion of the splenium in acute Wernicke's encephalopathy. *J Neuroimaging.* 2005; 15 (4): 373–375. PMID: 16254404 https://doi.org/10.1 111 / j.1552-6569.2005.tb00339.x
19. Kim JE, Kim TH, Yu I K, Lee BR, Lee SJ, Oh GS. Diffusion-weighted MRI in recurrent Wernicke's encephalopathy: a remarkable cerebellar lesion. *J Clin Neurol.* 2006; 2 (2): 141-145. PMID: 20396499 https://doi.org/10.3988/jcn.20 06.2.2.141
20. Yucebilgin S, Cirpan T, Sanhal CY, Ozan E, Acar T, Ozsener S. Wernicke's encephalopathy: a case report and MRI findings. *JBR-BTR* 2011; 94 (1): 24-25. PMID: 21466059 https://doi.org/10.5334/jbr-btr.480
21. Moritani T, Smoker WR, Sato Y, Numagu chi Y, Westesson PA, Diffusion-weighted imaging of acute excitotoxic brain injury. *AJNR AM J Neuroradiol.* 2005; 26 (2) 216-228. PMID: 15709116 https://doi.org/10.1007/978-3-540-78785-3
22. Thomson AD, Guerrini I, Marshall EJ. Wernicke's Encephalopathy: Role of Thiamine. *Practical Gastroenterol.* 2009; 33 (6): 21-30.
23. Degnan AJ, Levy LM. Neuroimaging of rapidly progressive dementias, part 2: prion, inflammatory, neoplastic, and other etiologies. *AJNR Am J Neuroradiol.* 2014; 35 (3): 424–431. PMID: 23413251 https: //doi.org/10.3174/ajnr.a3455
24. Bae SJ, Lee HK, Lee JH, Choi ChG, Suh DCh. Wernicke's Encephalopathy: Atypical Manifestation at MR Imaging. *Am J Neuroradiol.* 2001; 22 (8): 1480-1482. PMID: 11559494
25. Semple D, Smyth R. *Oxford Handbook of Psychiatry.* 3rd ed. Oxford: Oxford University Press; 2013.
26. Victor M, Adams RD, Collins GH. The Wernicke – Korsakoff syndrome. A clinical and pathological study of 245 patients, 82 with postmortem examinations. *Contemp Neurol Ser.* 1971; 7: 1-206. PMID: 5162155

**Received on 19.09.2019**
**Accepted on 06.02.2020**