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PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMAS IN THE NEUROLOGICAL PRACTICE

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Summary. Primary central nervous system lymphoma is one of the rare tumors of nervous system. Brain lymphoma is a malignancy diseases with peculiar clinical and biologic features, aggressive course, and unsatisfactory outcome. Early diagnostic and adequate treatment can improve the outcome and prognosis of patients.

Key words: primary CNS lymphoma, extranodal lymphoma, blood-brain barrier, immunocompromise and immunocompetent populations, human immunodeficiency virus infection/acquired immunodeficiency syndrome (HIV/AIDS).

Introduction

Primary central nervous system lymphoma (PCNSL) has been called by many other names, including reticulum cell sarcoma, diffuse histiocytic lymphoma, and microglioma.

Many classifications PCNSL have been proposed lately. All of them are based on their cell type, cell markers, location of the cancerous mutation and the way of their growing. The used different systems are the Rappaport System, Kiel System, Working Formulation, Revised European-American Classification of Lymphoid Neoplasms (REAL), and the World Health Organization (WHO) System. The WHO classification was first published in 1893. The Rappaport classification was used until the mid 1970's and divided cells into three categories based on cell differentiation: well differentiated cells, or small lymphocytic lymphoma, poorly differentiated cells, or follicular and small cleaved lymphomas, histiocytic cells, or large cell lymphomas. The Kiel System was popular in Europe and was introduced in 1974. It was based on immunologic tests that identified the proteins which cancer cells formed. In the United States, a similar system, called the Lukes and Collins Classification, was the first to classify based on B-cell and T-cell types. Usually PCNSL is classified as extranodal diffuse histiocytic lymphoma in the Rappaport classification or as large cell or immunoblastic lymphoma in the Working Formulation.

As known the neoplastic cells of PCNSL and Non-Chodgkin lymphoma (NHL) have the same origin. Theories on pathogenesis include migration of lymphocytes to the CNS secondary to infection or inflammation or activation of lymphocytes that have a specific CNS predilection.

On data of different authors [1, 5, 16, 22] Epstein-Barr virus (EBV) may induce B-cell clone transformation. EBV genome has been found in the tumor of up to 100.0 % of immunocompromised patients, in contrast to 16.0 % of PCNSL in immunocompetent individuals, where EBV may not play an important role in pathogenesis. [16]

The diffuse large B-cell lymphomas (DLBCL) of type of PCNSL are composed of immunoblasts or centroblasts that have a predilection for blood vessels. Lymphoid clustering around small cerebral vessels is typically seen. Reactive T-cell infiltrates can also be present in varying degrees. Histologically, the cells are closely packed, infiltrate surrounding brain, and have a characteristic perivascular concentration. Necrosis and hemorrhage are most common in tumors of immunocompromised patients. [16]

Most of lymphomas are large B-cell variants, 5.0 % are T cell in origin. The tumors contain pleomorphic B cells mixed with reactive T cells. Up to 60.0 % of the non-human immunodeficiency virus (HIV) PCNSL are diffuse large cell forms, but about 20.0 % are small to medium size. [16]

PCNSL as a form of extranodal, high-grade non-Hodgkin B-cell neoplasm, usually contains large cell or immunoblastic type. It originates in the brain, leptomeninges, spinal cord, or eyes; typically remains confined to the CNS and rarely spreads outside the nervous system. [22]

PCNSL is being seen with increasing frequency in immunocompetent patients. Most PCNSLs (about 90.0 %) are diffuse large B-cell lymphomas (DLBCLs); the remaining 10.0 % are poorly characterized low-grade lymphomas, Burkitt lymphomas, and T-cell lymphomas. [22]

Primary symptoms tumors may be a result of local mass effect due to raised intracranial pressure, from ocular involvement or focal influence on cranial or spinal nerve roots. PCNSLs are assumed to be diffusely infiltrative at the time of presentation. The areas of disease are not visible on neuroimaging studies because they are behind a relatively intact blood-brain barrier.

PCNSL accounts for less than 2.0 % of all CNS neoplasms and 7.0 % of all malignant lymphomas. The incidence is on the rise, both in the immunocompromised and the immunocompetent populations, more than what can be attributed to improved diagnosis by better imaging. The peak incidence is from the fifth to the seventh decades, with a male to female ratio of 3:2. A peak in the first decade of life is a measure of children with acquired immunodeficiency syndrome (AIDS). [16]

The study by Sugita et al. [21] supported the concept that PCNSLs originate from a later germinal center to an early postgerminal center, and they may be capable of further maturation steps. The study involved 32 PCNSL cases, with expression of proteins found at different stages in lymphocyte development; tumor specimens were immunophenotyped for antigens associated with germinal centers (CD10, Bcl-6) and with nongerminal center stages (SHP-1, CD138). In 30 of 32 cases, tumors were positive for SHP-1 but negative for CD138. However, current evidence argues against the possibility of the fact that malignant lymphocytes perform further maturational steps. [18]

The tumor is likely to arise in an extraneural environment with subsequent localization to the CNS, possibly by virtue of a specific neurotropism. They are not clear risk factors for PCNSL in immunocompetent patients. The disease is more common in men (the male-to-female ratio is 2:1) and in elderly persons.

Risk factors in immunocompromised patients with duration of immune suppression are determining the risk of developing PCNSL. Patients with AIDS who have low CD4+ counts are at the greatest risk for PCNSL. Patients with

AIDS generally have CD4+ counts of fewer than 30 cells/ μ L. Virtually all PCNSLs in patients with AIDS express an Epstein-Barr virus (EBV)-related genome. PCNSL is less frequently associated with EBV in patients without AIDS. Next common risk factor for PCNSL related to human immunodeficiency virus (HIV) infection is intravenous (IV) drug abuse.

Corboy et al. [3] reported that 56.0 % of a group of immunocompetent and immunocompromised patients had human herpes virus 8 (HHV-8) in their tumors. This is the same herpes virus that is associated with Kaposi sarcoma and with primary effusion (i.e., body-cavity-based lymphomas); however, a direct causal relationship of this herpes virus to any PCNSL has not yet been established. [5] (HHV-8 has been detected in PCNSLs by PCR at low copy number, suggesting that HHV-8 is present in a cell compartment other than the malignant one.)

Gomez-Brouchet et al. [9] studied 35 patients (17 with and 18 without AIDS) with PCNSL for the presence of HHV-8 in tumor cells. The antibody LN53, which reacts with the latent nuclear antigen 1 (LNA1) of HHV-8, was used on tissue sections from these patients and in addition, DNA was available for PCR. They found none of the 35 cases contained either DNA sequences or LNA1-positive cells in the tumor cells of PCNSL.

The data of USA, PCNSL incidence has risen steadily since the end of the 20th century. Incidence in immunocompetent patients is approximately 51 cases per 10,000,000 per year.

PCNSL has been reported in 6.0–20.0 % of patients infected with HIV, and the incidence is expected to rise as patients with low CD4+ counts [18]. Similar trends toward rising frequency of diagnosis of PCNSL are reported.

Almost 95.0 % of HIV-infected patients with PCNSL are males [1, 18]. The median age of immunocompetent patients with PCNSL is 55 years. The median age of HIV-infected patients with PCNSL is 35 years. [22]

Clinical manifestations are nonspecific. The most common symptoms which are related to an intracranial mass; an encephalitic-like picture; strokelike presentation, resembling demyelination disease; or cranial nerve palsies. Patients with PCNSL and AIDS tend to have more constitutional signs [1, 16, 17, 22]. Raised intracranial pressure is the main symptom arising from increased pressure within the skull. The pressure can increase because of a blockage in the ventricles, which leads to a build-up of cerebral spinal fluid (CSF). The increased pressure may also be caused by the tumor itself. Raised intracranial pressure

can cause headaches, sickness (vomiting) and problems with vision. Seizures can occur with this type of tumor and the person may change in behavior and personality also. A tumor in the brain may cause a weakness on one side of the body (hemiparesis). If the cerebellum is affected, there may be signs of loss of coordination and balance walk awkward or stumble.

Other manifestations were shown by Levin et al. [14] in their report 100 cases of PCNSL lymphoma over a period of 10 years, of which 5.0 % were primary meningeal lymphoma. These 5 patients presented leptomeningeal involvement as the single manifestation and 4 of them presented with neuronal lymphomatosis affecting cranial and peripheral nerves. These clinical data reflect other neurologic conditions such as pseudotumor cerebri or vasculitis. Meningeal or nerve biopsies were required for exact diagnosis.

Lenarz et al. [13] reported a case of primary CNS lymphoma involving both internal auditory canals that presented with sudden deafness and disequilibrium accompanied by facial and abducens nerve palsy.

Khong et al. [11] reported a rare case of neurolymphomatosis manifesting as acute cauda equina syndrome in a 16-year-old patient. The most typical presentation of PCNSL in an immunocompetent patient is progressive focal symptoms indicative of a mass lesion. Nonspecific mental status changes and seizures may occur. Patients with AIDS are more often to have encephalopathy than other patients with PCNSL. This correlates with the more often multifocal, diffuse enhancement pattern seen on magnetic resonance imaging (MRI) scans [1, 5, 14, 16, 22]. In the process of diagnostic it is necessary to establish if the patient has immune deficiency or not and we also must know about sexual and drug abuse history so as transplant recipient of the patient connected with immune suppression. The diagnosis of PCNSL in immunocompetent and immunocompromised patients is particularly difficult if they get the only syndrome. For example, isolated ocular or meningeal tumor may occur without any focal abnormalities on MRI. The history of such patients gives blurred vision, headache, isolated cranial nerve dysfunction (e.g., diplopia, dizziness, dysphagia, facial numbness, monocular visual loss), or spinal nerve root symptoms (e. g., pain, dysfunction localized to 1 dermatome, bowel or bladder problems). Sometimes in the cases relapsing, remitting lesions may disappear for periods from some months to even a year or more. Use of corticosteroids may cause prolonged remission of clinical

and radiographic signs and symptoms, but remission also occurs from time to time. The patients with AIDS and PCNSL have progressive dementia with get focal signs and enhancement on MRI [1, 5, 16, 22].

Intravascular malignant lymphomatosis (earlier called neoplastic angioendotheliosis) is a series of stroke-like focal events and we can see on the MRI zone of lesion [14, 20]. They may look like multiple large- and small-vessel ischemic strokes and (or) at multiple focal intracerebral hemorrhage. Differential diagnosis contain parasitosis, malignant lymphoma, or metastatic brain tumor [22]. Diagnosis usually requires tissue, CSF, or aqueous humor (by vitreous) examination. Corticosteroids induce a temporary decrease of the lesion in up to 60.0 % of patients [16]. Using the corticosteroid dosage leads to multiple contrast-enhancing lesions that recur rapidly. The incidence of involving leptomeninges meets from 12.0 % to 66.0 %. CSF shows malignant cells in up to 43.0 % of patients. During the diagnostic it is necessary to include neuroophthalmologic examination, contrast MRI of the spine, and lumbar puncture. 20.0 % of patients have ocular lesions. Both infectious and lymphomatous meningitis may coexist. The CSF shows a reactive pleocytosis in infectious meningitis, whereas monoclonal B lymphocytes are seen in lymphomatous meningitis [16]. Disease has the steady progressive clinical course and is often confirmed by brain biopsy and histology and immunochemical staining of the biopsy specimen. Neurolymphomatosis is the only PCNSL syndrome that involves both the central and peripheral nervous systems of patients [20].

Differential diagnosis of a patient with suspected PCNSL depends on the patient's immune status and the zone of the lesions on MRI. For example, the major differential diagnostic for immuno-competent patient with a solitary lesion (besides PCNSL) are high-grade primary brain tumor, such as glioblastoma, and isolated metastasis [5, 16].

Neuroimaging example of PCNSL present on the MRI pictures (A, B, C, D) of the brain [5] shows an expansive mass lesion in the right frontal lobe, which is hypointense in noncontrasted T1 scans (A), isointense with respect to cortex in T2-weighted images (C), with reduced average diffusion coefficient (B), and homogeneous contrast enhancement in contrasted T1 weighted scans (D arrows). Lesion is surrounded by modest edema (A arrows). CT and MRI findings are attributed to the high cell density and scant cytoplasm. Enhancement along the Virchow-Robin spaces, although not constant, is a highly specific feature of PCNSL (figure 1).

Response for treatment of corticosteroids decreases an edema and a cytotoxic effect on lymphoma cells. Up to 10.0 % of lesions disappear, sometimes lasting months after finishing steroids course. [16]. A biopsy taken after corticosteroid therapy may yield falsely negative results. Corticosteroid treatment for a suspected lesion is strongly contraindicated. Response to steroids is not pathognomonic because demyelinating conditions or

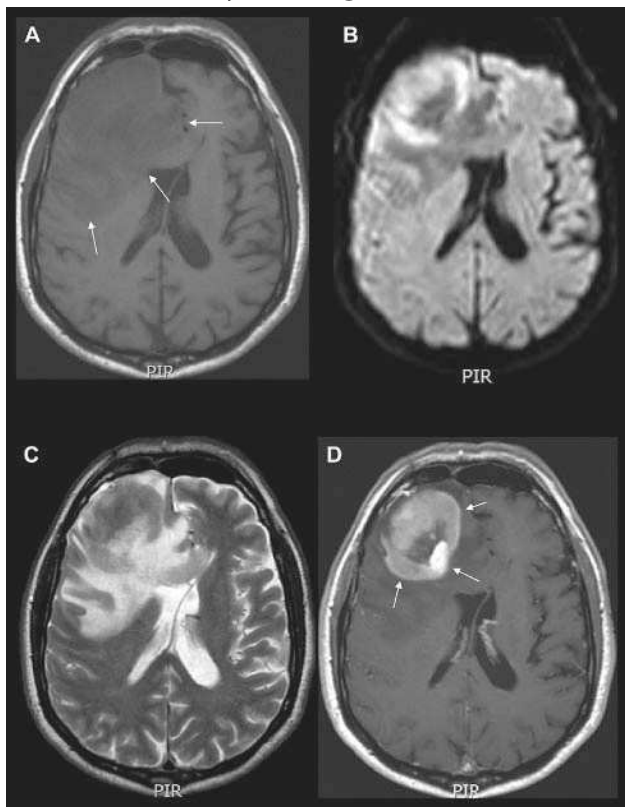


Figure 1. MRI brain neuroimaging (A, B, C, D) of PCNSL.

sarcoidosis may behave similarly [16]. In patients with AIDS, multifocal, ring-enhancing lesions we should exclude toxoplasmosis or another opportunistic infection. More diffuse cognitive and MRI abnormalities suggest a possibility of some infectious encephalitic process, such as herpes zoster, cytomegalovirus encephalitis, cryptococcal meningitis, or AIDS/dementia complex [1, 5, 16].

The list of diagnosis PCNSL include the following: abducens nerve (cranial nerve VI) palsy, acute disseminated encephalomyelitis, multiple sclerosis, aseptic meningitis, herpes simplex and cytomegalovirus encephalitis, other herpes-virus infections, paraneoplastic encephalomyelitis, cauda equina and conus medullaris syndromes, brainstem gliomas, ependymoma, low-grade astrocytoma, glioblastoma multiforme, leptomeningeal carcinomatosis, epilepsy, granulomatous angiitis of the CNS, HIV-encephalopathy

and AIDS dementia complex, HIV-associated meningitis, HIV-associated opportunistic infections: CNS cryptococcosis, progressive multifocal leukoencephalopathy (PML), neurosarcoidosis, neurosyphilis [22].

Diagnosics. The following should be ordered in an immunocompetent patient whose computed tomography (CT)/MRI scan suggests PCNSL. Corticosteroids can't be used, because it may complicate diagnosis.

Chest radiograph help to find the metastatic disease. Complete blood count (CBC), HIV testing, slit-lamp examination for excluding vitreous lymphoma, for cells, glucose, protein, and cytology in the cerebrospinal fluid (CSF) are also used for diagnostic. Polymerase chain reaction (PCR) analysis of gene rearrangement may help determine monoclonality, although up to 16.0 % of both AIDS and non-AIDS PCNSL show biclonal immunoglobulins light chains.

The following should be ordered in an HIV-infected or otherwise immunocompromised patient whose CT/MRI scan suggests PCNSL: avoid corticosteroids, necessary chest radiography, toxoplasma gondii serology, slit-lamp examination for vitreous lymphoma, lumbar puncture for cells, glucose, protein, cytology, syphilis testing, and cryptococcal antigen.

Fischer et al. [7]. presented the report large multicenter study about the first comparison of the diagnostic value cytomorphology of cerebrospinal fluid (CSF) and polymerase chain reaction (PCR) rearranged immunoglobulin heavy-chain (IgH) genes and also MRI-dates together with cell count and protein concentration for detection of meningeal dissemination patients with PCNSL. They found a low rate of meningeal dissemination in primary CNS lymphoma. The rate of discordant PCR and cytomorphologic results was high. CSF pleocytosis had predictive value for meningeal dissemination detection.

Neurolymphomatosis (NL) is a rare clinical fact. The International Primary CNS Lymphoma Collaborative Group retrospectively analyzed 50 patients from 12 centers in 5 countries over a 16-year period. It was found that NL was related to non-Hodgkin lymphoma in 90.0 % and to acute leukemia in 10.0 % [20]. The affected neural structures included peripheral nerves (60.0 %), spinal nerve roots (48.0 %), cranial nerves (46.0 %), and plexus (40.0 %) with multiple site involvement in 58.0 %. MRI imaging gave 77.0 % positive results and the computed positron emission tomography gave 84.0 % positive results. Cerebrospinal fluid cytology was positive in 40.0 %, and nerve biopsy confirmed the diagnosis in 88.0 %. Treatment in 47 patients included systemic chemotherapy (70.0 %), intra-

cerebrospinal fluid chemotherapy (49.0 %), and radiotherapy (34.0 %). Response to treatment was observed in 46.0 %. The median overall survival was 10 months, with 12- and 36-month survival proportions of 46.0 % and 24.0 %, respectively. An aggressive multimodality therapy can prevent neurologic deterioration and is associated with a prolonged survival in a subset of patients [20].

As a known chemotherapy plays a central role in the management of PCNSL. PCNSL is a chemosensitive tumor. The malignant lymphocytes infiltrate the intact brain and drugs must reach all necessary areas. Up to 100.0 % of patients have leptomeningeal disease at autopsy, so chemotherapy addressing these regions is an important component of treatment. Cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) regimen represents the basis for treating extra-CNS DLBCL but exhibits negligible activity in PCNSL; this has been confirmed in a randomized trial with incomplete accrual. In retrospective series, the addition of CHOP to high-dose methotrexate (HD-MTX) resulted in higher toxicity without improved outcome compared with HD-MTX alone [4]. Its effectiveness depend on protect condition of the blood-brain barrier (BBB). Most regimens include drugs able to cross the BBB at usual doses (i.e., steroids, some alkylating agents) and cytostatics with low to moderate ability to cross the BBB that can be safely administered at high doses to improve CNS bioavailability (i.e., methotrexate, cytarabine). And drugs with poor BBB penetration cannot be administered at high doses as they are dose-limiting toxicity (i. e., anthracyclines, vinca-alkaloids) are inefficient in PCNSL [5]. Prophylactic use of antiepileptic drugs (AEDs) should be avoided and their use should be confined to patients who experience seizures. Any of the first-line AEDs (e. g., phenytoin, carbamazepine, valproic acid) would be appropriate for patients with PCNSL, although leukopenia and liver function abnormalities from any of these drugs potentially could be confused with chemotherapy-related toxic effects. New-generation antiepileptic drugs, such as levetiracetam (Keppra), have high efficacy and fewer side effects. Antiemetics are useful in the treatment of nausea associated with chemotherapy and radiation therapy.

Radiotherapy was the exclusive treatment for patients with PCNSL, chemotherapy was added. PCNSL is characterized by high responses to radiation. Patients receive 180 cGy per fraction, for a total of 60 Gy [16]. The median survival is 10 to 18 months; only 3.0 % to 4.0 % live 5 years with this treatment alone. Using

variable chemotherapy regimens and radiation doses, upfront chemoradiotherapy in several trials obtain complete remission rates (CRR) of 30.0 % — 87.0% and 5-year overall survival rates of 30.0 % — 50.0 %. These treatment is often associated with severe neurotoxicity, especially among elderly patients. The strategies of treatment lies in the choice of necessary drugs and their amount to avoid neurotoxicity.

Surgical resection is not the main method of treatment as the tumors are infiltrative and sometimes bilateral. Prognosis of better outcome for patients age less than 60 years better than 70. The goal of surgery is also getting tissue diagnosis.

Newelt et al. (1991) administered methotrexate, cyclophosphamide, and procarbazine, achieving a median survival of 44 months without radiotherapy. The high-dose chemotherapy which influence at bone marrow/stem cell is the accepted treatment for relapsed systemic NHL. The regimen of BCNU (carmustine), etoposide, cytarabine, melphalan is widely used for non-NHL and may be used for PCNSL in the future.

Glass et al. (1994) treated 25 patients with high-dose maintenance intravenous methotrexate alone (more than 3.5 g/m² for one to six cycles). 22.0% had a complete response, and the median survival of 42.5 months for the responding group compared the other scheme using multiple agents, with less toxicity. Philipp Kiewe et al. (2007), Yamanaka R. et al. (2008) also treated with high-dose methotrexate (HDMTX)-based chemotherapy. All patients were alive without disease progression 12–48 months after HDMTX start. No symptoms of late neurotoxicity have occurred so far [12]. Yamanaka R. et al. (2008) indicated that HDMTX is the most effective drug available to treat these lesions, either as a single agent or in combination with other drugs. Treatment regimens were: whole-brain irradiation (WBI) alone, MVP (MTX, vincristine, and prednisone), ProMACE-MOPP hybrid (cyclophosphamide, pirarubicin, etoposide, vincristine, procarbazine, prednisone, and MTX) and R-MTX (rituximab, MTX, pirarubicin, procarbazine, and prednisone) combined-modality therapy.

On datum Julien Cobert et al. (2010) 121 patients received on average 11 cycles of intravenous MTX at a median dose of 8g/m². Median interval between cycles was 10 days. After 3 months of therapy, the overall response rate was 85.0 % (58.0 % complete respond, 27.0 % partial respond). The overall survival (OS) for the cohort was 7 years and progression-free survival (PFS) was 3.14 years. A trend toward a higher PFS was seen in patients who continued

to receive MTX (3.48 years) every three months as compared to patients who ceased MTX after one year (2.86 years). Elderly patients are particularly prone to the neurotoxic effects of irradiation and may get benefit from these chemotherapy-only regimens. They must have a glomerular filtration rate of greater than 100 mL/min, because inadequate renal clearance enhances methotrexate toxicity. Cytosine arabinoside in high doses achieves therapeutic levels as a brain parenchyma as CSF; it has also been used to treat ocular disease.

Excellent results got from a scheme consisting of carmustine, methotrexate, procarbazine, and dexamethasone. Chemotherapy alone, using a combination of drugs, can lead to remission of intraocular lymphoma without radiotherapy and can lead to prolonged survival.

Combination therapy. Several reports suggest that the combination of chemotherapy and radiation improves outcome over radiation alone, but it isn't true in many cases.

DeAngelis and associates (1992) achieved a 41-month median survival with intravenous (1 g/m²) and intrathecal methotrexate, radiotherapy, followed by intravenous cytosine arabinoside. Acute toxicity was minimal. Similar results have been observed with radiotherapy followed by intraventricular methotrexate and CHOP; procarbazine, cyclohexylchloro ethylnitrosourea (CCNU), and vincristine; or vincristine, cyclophosphamide, prednisolone, and doxorubicin.

Prognosis of PCNSL. The median survival for patients treated with combination regimens is 42 months, whereas only irradiation gives 12 to 18 months. 50.0 % of patients had relapse, usually within 2 years of diagnosis and mostly at distant sites. Leptomeningeal or spinal cord recurrence was met in 60.0 %. Extraneural spread is rare but can involve the lymph nodes, heart, gastrointestinal tract, and bone marrow. About one-third of patients treated with chemotherapy and radiation have a syndrome of progressive ataxia, dementia, and urinary incontinence, which appears after a median of 13.2 months from diagnosis. A ventriculoperitoneal shunt may bring benefit. Other patients have cerebrovascular disease, which may be related to treatment or to the disease itself. Leukoencephalopathy is observed in 8 % of patients older than 60 years who survive 1 year.

The prognostic value of serum markers in PCNSL was reported in a prospective study of 45 PCNSLs [16]. Disease status, radiographic appearance, and length of survival correlated with serum levels of YKL-40 and MMP-9. The authors' main objective was to identify disease

severity markers as a treatment guide. YKL-40 is a tissue marker of inflammation related to carcinogenesis, and MMP-9 tissue controls remodeling permeability. YKL-40 and MMP-9 levels were associated with «active disease» particularly if a longitudinal, steady serum level increment was noted. Consistently low serum levels, on the other hand, were found with «absence of tumor»

In another study, overexpression of BCL-6 was associated with improved survival (median, 101 months) over that of patients whose tumors that did not express BCL-6 (median, 14.7 months) [17]. The search is on for additional prognostic markers.

The immunocompromised states associated with PCNSL include renal transplantation, Wiskott-Aldrich syndrome, ataxia telangiectasia, IgA deficiency, rheumatoid arthritis, progressive multifocal leukoencephalopathy, and IgM paraproteinemic neuropathy. [15]

PCNSL patients with AIDS develop in 1.0 % to 3.0 % of all patients. Typically, patients have profound immunosuppression and marked T4 cell depletion (median CD4 counts are less than 50/μL). At autopsy, 75.0 % of patients with AIDS had PCNSL. In immunosuppressed subjects, lymphoma is symptomatic in the third or fourth decades. About 2.0 % of renal transplant patients develop PCNSL, 100 times more than the general population.

About 100.0 % of HIV-related PCNSL are positive for EBV markers, whereas PCNSL in nonimmunocompromised patients are rarely positive for EBV.

Coinfection of the CNS with CMV has been observed, further suggesting a role for infection in AIDS-related PCNSL.

The time from seroconversion to PCNSL is about 2 years. In 10.0 % of patients, the symptoms of PCNSL led to the diagnosis of AIDS. About 56.0 % of patients have focal signs or symptoms compared with 27.0 % of patients with PCNSL without HIV disease. Many patients have concurrent opportunistic infections. The standard of practice for an HIV-positive patient and a cerebral mass is treatment with antitoxoplasmosis medication. If there is no clinical or radiographic response after 2 weeks, tissue diagnosis is considered, via brain biopsy, lumbar puncture, or vitreous examination. CSF can be analyzed for EBV by PCR studies. The tumor may have irregular ringlike contrast enhancement (corresponding to necrosis), and it may be difficult to distinguish the lesion from toxoplasmosis. An irregular type of enhancement is more commonly associated with PCNSL, whereas smooth enhancement is associated with toxoplasmosis.

Prognosis PCNSL patients with AIDS. The median survival after diagnosis is 1 to 2 months with supportive care alone and 2 to 6 months with radiation. Survival correlates closely with Karnofsky performance before treatment, length of time since seroconversion, and the presence of more than one risk factor for HIV. Patients who have radiation therapy commonly die of opportunistic infections, whereas

patients who do not receive radiation usually die of the tumor.

Investigations of PCNSL in immunocompromise and immunocompetent populations show specificity and complexity in diagnostic and treatment for this contingent of patients. And only more early diagnostics and treatment of this disease help increase the duration of life the patients.

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ПЕРВИННА ЛІМФОМА ЦЕНТРАЛЬНОЇ НЕРВОВОЇ СИСТЕМИ В ПРАКТИЦІ КЛІНІЦИСТАВ. І. Пономарьов¹, О. Ю. Меркулова¹,
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Первинна лімфома центральної нервової системи є однією з рідкісних пухлин нервової системи. Мозкова лімфома злоякісне захворювання з особливими клінічними та біологічними рисами, агресивним перебігом і незадовільним результатом. Рання діагностика та адекватне лікування можуть поліпшити результат і прогноз пацієнтів.

Ключові слова: первинна лімфома ЦНС, екстранодальна лімфома, гематоенцефалічний бар'єр, іммунокомпрометоване та іммунокомпетентне населення, вірус іммунодефіциту людини/синдром набутого іммунодефіциту (ВІЛ/СНІД).

ПЕРВИЧНАЯ ЛИМФОМА ЦЕНТРАЛЬНОЙ НЕРВНОЙ СИСТЕМЫ В ПРАКТИКЕ КЛИНИЦИСТАВ. И. Пономарёв¹, О. Ю. Меркулова¹,
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Первичная лимфома центральной нервной системы является одной из редких опухолей нервной системы. Мозговая лимфома — злокачественное заболевание с особыми клиническими и биологическими чертами, агрессивным течением и неудовлетворительным исходом. Ранняя диагностика и адекватное лечение могут улучшить исход и прогноз пациентов.

Ключевые слова: первичная лимфома ЦНС, экстранодальная лимфома, гематоэнцефалический барьер, иммунокомпрометированное и иммунокомпетентное население, вирус иммунодефицита человека/синдром приобретенного иммунодефицита (ВИЧ/СПИД).

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**ЦЕРВИКОГЕННЫЙ ФАКТОР
В ГЕНЕЗЕ ТРИГЕМИНАЛЬНЫХ ВЕГЕТАТИВНЫХ ЦЕФАЛГИЙ**

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Аннотация. Статья посвящена современным представлениям о тригеминальных вегетативных цефалгиях, а также обсуждению роли вертеброгенно-миофасциального шейного фактора в развитии головной боли. Представлено собственное клиническое наблюдение пациента с SUNCT-синдромом. Позитивная динамика болевого синдрома при воздействии на миофасциальную дисфункцию шейной группы мышц у пациентов с тригеминальными вегетативными цефалгиями подтверждает необходимость вертебро-неврологического исследования и лечения миофасциальной дисфункции при ее выявлении у больных с клиническими проявлениями тригеминальных вегетативных цефалгий.

Ключевые слова: тригеминальные вегетативные цефалгии, SUNCT-синдром, миофасциальная дисфункция шейной локализации.

Головная боль на сегодняшний день представляет медико-социальную проблему, учитывая распространенность цефалгий, экономические потери в связи с нетрудоспособностью и влияние головной боли на качество жизни пациентов [1–4]. Согласно Международной классификации головных болей второго пересмотра (International Classification Headaches second edition, ICHD-II) головная боль может являться как синдромом множества неврологических и соматических заболеваний, так и представлять собой нозоло-

гические формы в виде мигрени, головной боли напряжения и тригеминальных вегетативных цефалгий [5].

В группу тригеминально-вегетативных головных болей на сегодняшний день объединяются пароксизмальные головные боли с выраженными вегетативными проявлениями, то есть тригеминальные вегетативные цефалгии (ТВЦ) сочетают в себе как черты головной боли, так и типичные черты краниальных парасимпатических невралгий. Экспериментальные и функциональные нейровизуализационные исследования показали,