Acta Clin Croat 2023; 62:355-361
doi: 10.20471/acc.2023.62.02.14

Review

PRIMARY ANGIITIS OF THE CENTRAL NERVOUS SYSTEM – A DIAGNOSTIC CHALLENGE

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SUMMARY – Primary angiitis of the central nervous system (PACNS) is a rare and severe disease confined to the central nervous system, i.e., the brain and spinal cord. The etiology, pathogenesis and immune mechanism of PACNS have not yet been completely elucidated. The diagnosis is challenging; it is based upon constellation of clinical picture, cerebrospinal fluid analysis, imaging methods or tissue biopsy as the gold standard. In differential diagnosis of PACNS, it is necessary to rule out infectious, malignant or systemic inflammatory diseases, as well as reversible cerebral vasoconstriction syndrome. Immunosuppressants are cornerstone therapy for PACNS, although evidence-based strategies for the management are lacking so far. PACNS is an entity with considerable morbidity and mortality. Awareness of this rare and heterogeneous disease is crucial for establishing early diagnosis and treatment initiation.

Key words: *Vasculitis; Central nervous system; Immunosuppressive therapy*

Introduction

Primary angiitis of the central nervous system (PACNS) is a rare and severe disease confined to the central nervous system, i.e., the brain and spinal cord. It was first described by Harbitz in 1922 as an unknown form of angiitis in the central nervous system (CNS)[1], and then, in recent history, in the mid-1950s, Cravioto and Feigin described several cases of a "non-infectious granulomatous angiitis" with a predilection for the nervous system[2]. By 1986, only 46 cases were reported in the English-language medical literature[3] and by 2007, the number of described cases increased over 500 patients. The mean annual incidence of PACNS is 2.4 cases *per* 1 million person-years. The disease mainly affects male patients with a median occurrence at around 50 years of age[4].

The etiology of PACNS has not yet been conclusively elucidated, but it is believed that due to the interaction between several endogenous and environmental factors, activation of the immune system and inflammatory infiltration of blood vessel walls occurs. As a result, vascular damage causes ischemia and infarction or intracranial hemorrhage[5]. Infectious agents, viruses and bacteria, such as varicella-zoster virus (VZV), cytomegalovirus (CMV), West Nile virus, and *Mycoplasma gallisepticum* have been proposed as the etiologic factors in PACNS[6,7,8], as well as amyloid deposits in

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Received December 13, 2022, accepted May 8, 2023

vessel walls, which can act as a potential trigger in the immune system[5]. Memory T-cells have been suggested to be involved in the immune mechanisms, with a predominance of activated T lymphocytes (CD45R0+) in and around blood vessels[9]. Most often, PACNS affects blood vessels in the cerebral cortex and leptomeninges.

Headache is a predominant clinical symptom in central angiitis, reported by about 60% of patients. Headache is usually chronic, progressive, and insidious in its onset. About 50% of patients report cognitive impairment while focal neurological deficits such as hemiparesis, ataxia, aphasia, dysarthria, or visual disturbances are reported less commonly. Strokes, if present, are usually multiple and bilateral. Furthermore, encephalopathy, seizures, or rarely signs and symptoms of spinal cord affection (5% of patients) are reported. According to clinical presentation, it can be indirectly concluded whether large or small blood vessels are affected. In the case of involvement of large blood vessels, symptoms similar to a stroke with focal neurological deficits predominate, while in the case of involvement of smaller blood vessels, symptoms related to the loss of cognitive functions, encephalopathy, and epileptic seizures are more common[10,11].

Methods

Preparing this review article, the authors performed a comprehensive search through Scopus, Web of Science, and PubMed/MEDLINE databases using the following keywords: vasculitis, central nervous system, immunosuppression therapy, chosen from the MeSH terms. The filter was used to select papers published within the last 15 years; however, older publications were also taken into account if scientifically fundamental. The literature review included both original articles and case reports.

Diagnostics

The diagnosis of PACNS is challenging, so multidisciplinary approach based upon constellation of clinical picture, analysis of cerebrospinal fluid (CSF) and imaging methods (magnetic resonance imaging (MRI), magnetic resonance angiography) (MRA) or conventional angiography) is often necessary. If clinical picture together with imaging findings is inconclusive, it is obligatory to perform brain biopsy with its typical histopathologic findings. Laboratory testing, including acute phase reactants and immunologic serologic assays, is usually normal. The purpose of these tests is to exclude an eventually underlying systemic disease, e.g., collagenosis, systemic vasculitis, etc. Lumbar punction is a crucial procedure in evaluating patients with suspected PACNS. CSF finding is abnormal in 80%-90% of patients[4]. Typical CSF finding is modest lymphocytic pleocytosis and/or elevated protein level (proteinorachia). If CSF analysis is normal (number of cells <5/mcL or proteins <45 mg/dL), one should consider another possible diagnosis[12]. Some authors find CSF analysis as a useful method for treatment evaluation and monitoring[5]. In all patients with suspected PACNS, brain MRI should be performed. MRI shows nonspecific abnormalities in more than 90% of patients with PACNS, so it should be interpreted in the context of clinical picture and other diagnostic tests[4]. Typical MRI findings (Figs. 1, 2 and 3) in PACNS are multifocal bilateral lesions in T2 or FLAIR sequence in the cortical and subcortical region, but also in deep white and grey matter (basal ganglia)[13]. Enhanced contrast imbibition in leptomeninges suggests the possible involvement of small blood vessels. It should be emphasized that the probability of a PACNS diagnosis with a negative CSF finding is very low. In the case of

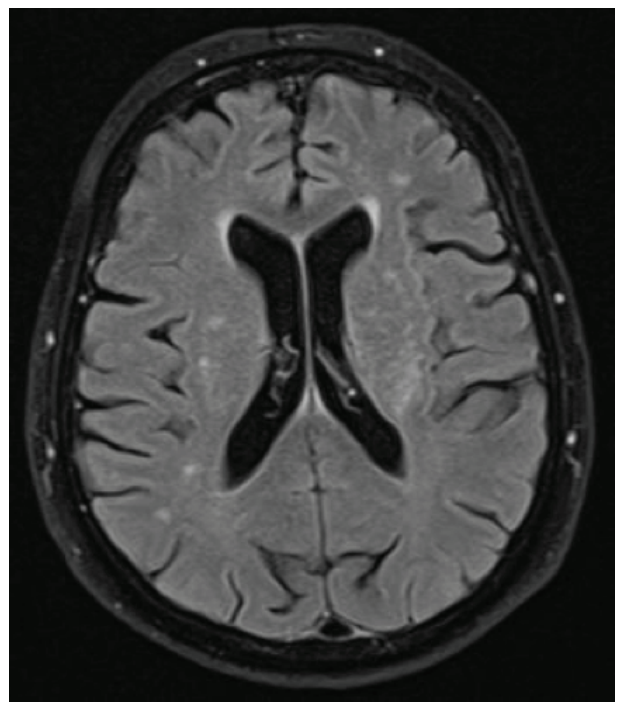

Fig. 1. Magnetic resonance imaging, T2 sequence: supratentorial region, hyperintense punctiform lesions.

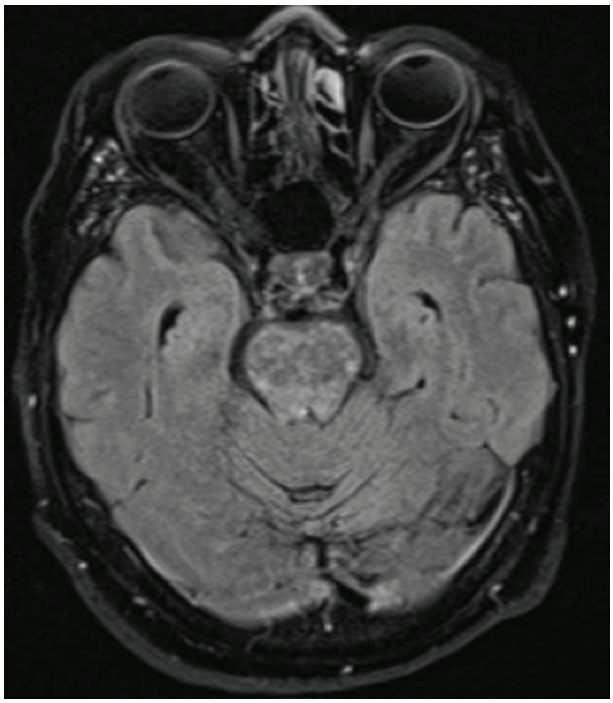

Fig. 2. Magnetic resonance imaging, T2 sequence: cerebellum, hyperintense punctiform lesions.

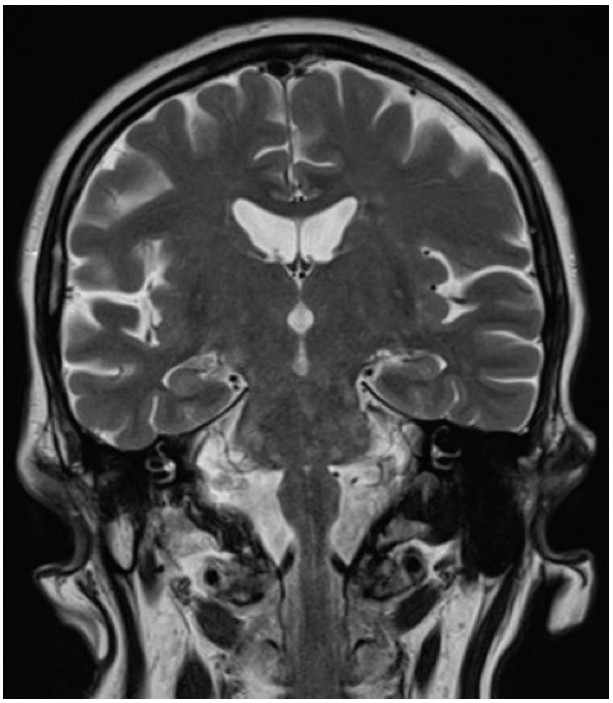

Fig. 3. Magnetic resonance imaging, T2 sequence: coronary section, hyperintense punctiform lesions.

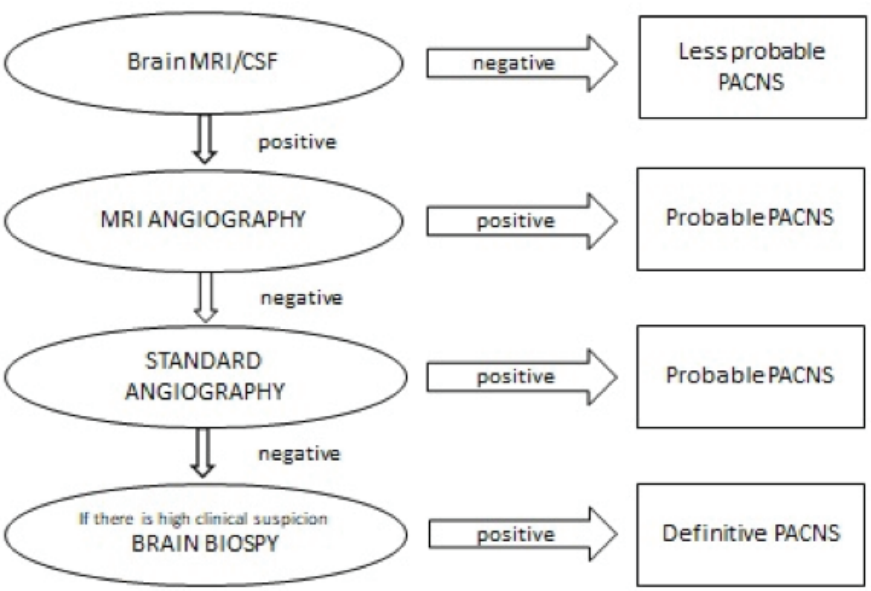

Fig. 4. Diagnostic algorithm in suspected primary angiitis of the central nervous system.

PACNS = primary angiitis of the central nervous system; MRI = magnetic resonance imaging; CNS = central nervous system

suspicious changes on MRI, which are in correlation with the clinical picture or with the CSF analysis, it is necessary to consider further diagnostic work up. The rational approach is to start with less invasive methods, i.e., with MRA. This imaging modality detects changes mainly in larger blood vessels in the form of wall thickening and intramural post-contrast imbibition as a sign of active vasculitis. High-resolution MRA can distinguish intracranial atherosclerotic plaques (eccentric) and inflammatory (concentric) changes in the blood vessel wall[14]. MRA is limited in detecting both lesions localized in the posterior circulation and in distal (small) arteries[15]. In these cases, conventional angiography represents a method that is more sensitive. Its sensitivity ranges between 40% and 90%, while the specificity of this technique is around 30%[12]. Standard angiography often appears normal in vasculitis affecting small blood vessels beyond angiographic resolution (arteries <500 μm in diameter)[16]. In patients with normal angiography findings but with reasonable suspicion of PACNS based on the clinical picture, MRI of the brain and CSF analysis, it is mandatory to perform brain biopsy. Most authors believe that brain biopsy is the only way to establish a reliable diagnosis of PACNS, while patients who have positive angiographic finding without performed biopsy are considered to have a probable diagnosis of PACNS (Fig. 4). The gold standard for diagnosis of PACNS is biopsy of the brain and meninges. The procedure itself is safe, and the risk of neurological impairment in experienced centers is estimated to be only 1%. An optimal biopsy sample should include part of the dura, leptomeningeal tissue, cortex, and white matter. A positive biopsy confirms vasculitis and excludes PACNS mimicking and other diseases. The characteristic histopathologic finding is transmural inflammation with secondary injury of the vessel wall of the small- or medium-sized arteries of the leptomeninges or brain parenchyma. The sensitivity of biopsy for PACNS is 53%-63%. It is reduced because of the presence of skipping lesions due to focal and segmental distribution of the disease. In order to increase diagnostic yield, it is advisable to perform biopsy of the areas of imaging abnormality, i.e., pia mater. There are 3 main histopathologic patterns in the brains affected by PACNS[17,18]. The most common pattern is granulomatous vasculitis (58% of cases) with a characteristic feature of mononuclear inflammatory infiltrate and granulomas. Biopsy samples of this vasculitis group can show extensive beta-A4 amyloid deposition in tunica media and tunica adventitia of the small leptomeningeal and cortical arteries. The second most prevalent pattern of PACNS is lymphocytic vasculitis (28% of cases) characterized by lymphocytic infiltration of vessel walls with consequent deformities and possible destruction of blood vessels. Necrotizing vasculitis is found in 14% of patients. Its feature

Table 1. Diagnostic criteria proposed by Calabrese and Mallek in 1988. A diagnosis of primary central nervous system vasculitis is made if all the criteria below are satisfied

1) A history or clinical findings of an acquired neurological deficit, which remained unexplained after a thorough initial basic evaluation
2) Either classic angiographic or histopathologic features of vasculitis within the central nervous system
3) No evidence of systemic vasculitis or of any other condition to which the angiographic or pathologic features could be secondary

Table 2. Diagnostic criteria proposed by Birnbaum and Hellmann in 2009

Definitive diagnosis • Confirmation of vasculitis on analysis of a tissue biopsy specimen
Probable diagnosis • In the absence of tissue confirmation, high probability of finding of vasculitis on an angiogram, with abnormal findings on MRI, and CSF profile consistent with PCNSV

MRI = magnetic resonance imaging; CSF = cerebrospinal fluid; PCNSV = primary central nervous system vasculitis

is transmural fibrinoid necrosis, which possibly leads to vascular rupture with concomitant hemorrhage[19]. Based upon data from the literature and their own experiences, Calabrese and Mallek proposed diagnostic criteria for PACNS in 1988. The diagnosis can be made if 3 major criteria are met (Table 1)[3]. In 2009, Birnbaum and Hellmann proposed modified diagnostic criteria according to which a diagnosis can only be made in those patients in whom the disease is proven by histopathologic findings (Table 2)[20].

Differential Diagnosis

The possible differential diagnosis is of great importance and represents a challenge for the clinician. It is necessary to rule out infection, systemic vasculitis, other systemic rheumatic diseases, as well as demyelinating, lymphoproliferative and many other diseases[5].

The major infectious agents of concern are the following:

- bacteria and mycobacteria: *Treponema pallidum*, *Borrelia burgdorferi*, *Mycobacterium tuberculosis*, *Bartonella* species, *Bartonella henselae*, *Rickettsia* species;
- viruses: herpesviruses (varicella zoster, cytomegalovirus), hepatitis B and C viruses, human immunodeficiency virus; and
- fungi and parasites: *Aspergillus*, *Coccidioides*, *Histoplasma* species, *Candida* species, *Cysticercosis*

Systemic vasculitides that most often involve brain are Behçet syndrome, polyarteritis nodosa, granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis, giant cell arteritis, Takayasu's arteritis, and cryoglobulinemic vasculitis.

Systemic rheumatic diseases also should be taken into account as differential diagnosis, e.g., systemic lupus erythematosus, mixed connective tissue disease, dermatomyositis, rheumatoid arthritis, Sjögren's syndrome, and antiphospholipid syndrome.

A number of other diseases could be included in differential diagnosis of PACNS, such as primary demyelinating diseases of the CNS, nonvasculitic autoimmune inflammatory meningoencephalitis, atherosclerosis, multiple cerebral emboli, bacterial thrombotic endocarditis, intravascular lymphoma, neurosarcoidosis, paraneoplastic and autoimmune encephalitis, Susac's syndrome, Sneddon's syndrome, mitochondrial encephalopathy, cerebroretinal vasculopathy, moyamoya disease, Creutzfeldt-Jacob disease, drug induced vasculitis (cocaine, amphetamine, ephedrine, phenylpropanolamine)[5,13].

Most authors primarily emphasize the importance of recognizing reversible cerebral vasoconstriction syndrome (RCVS) in the differential diagnosis. It is characterized by recurrent thunderclap headache with or without neurological symptoms in addition to reversible multifocal vasoconstriction of cerebral arteries. The clinical course is mostly benign, although major cerebral infarctions and permanent damage or death are possible. RCVS occurs predominantly in young female patients due to predisposing conditions acting as provoking factors, including pregnancy, migraine, use of vasoconstrictive medications or drugs (selective serotonin reuptake inhibitors, cocaine), hypercalcemia, neurosurgical procedures, etc. In RCVS, CSF analysis is mostly normal, unlike PACNS. Angiographic findings are often difficult to distinguish between these two diseases, but significant in differential diagnosis is complete resolution of angiographic findings after 3 months in patients with RCVS[21,22].

Treatment

In most patients diagnosed with PACNS, it is necessary to start induction therapy with methylprednisolone pulses (1000 mg daily for 3-5 days), while others, with either slowly progressive disease, or those without cerebral infarcts and other major vascular damages, can be treated with oral prednisone at a dose of 1 mg/kg *per* day[23,24].

In more severe cases, it is required to add an additional immunosuppressive drug in remission induction strategy along with high-dose intravenous glucocorticoids. Cyclophosphamide is usually the immunosuppressant of choice, administered either as an oral dose (2 mg/kg daily for 3-6 months) or as intravenous pulse (0.75 g/m^2 monthly for 6 months). As a second line, rituximab can be administered at a regimen of 375 mg/m^2 weekly for 4 weeks. Individual cases of treatment with tumor necrosis factor inhibitors (mostly infliximab and etanercept) are described in the literature[23,25-27].

Induction therapy is effective in a large number of patients, but despite a good therapeutic response, disease relapses are common, thus continuation of treatment with maintenance therapy reduces the possibility of disease relapse. In maintenance therapy, a low dose of prednisone is most often used in combination with azathioprine (1-2 mg/kg daily), mycophenolate mofetil (1-2 g daily) or methotrexate (20-25 mg/week).

According to data from the literature, most patients were treated for a period of at least 24 months, but there are no distinct recommendations on the duration of therapy; it should be individualized to each patient based upon clinical picture[22].

In conclusion, PACNS is a rare and severe disease of the CNS, which represents a diagnostic challenge for the clinician and requires a multidisciplinary approach to the patient (neurologist, clinical immunologist/rheumatologist, and neuroradiologist). We would like to emphasize that it is very important to eliminate differential diagnostic dilemmas, primarily infectious and malignant diseases, due to different therapeutic approach to these entities.

Early diagnosis of PACNS and aggressive treatment with immunosuppressive therapy prevents severe neurological complications and reduces the rate of disability and mortality.

The existence of a diagnostic algorithm and guidelines for the treatment of this disease would certainly improve both the recognition and treatment of this rare and life-threatening disease. Advances in neuroimaging, as well as in molecular diagnostic methods, such as genome sequencing, open up new possibilities in the diagnosis and follow up of these patients.

References

1. Harbitz F. Unknown forms of arteritis, with special reference to their relation to syphilitic arteritis and periarteritis nodosa. Am J Med Sci.1922;163: 250-71.
2. Cravioto H, Feigin I. Noninfectious granulomatous angiitis with a predilection for the nervous system. Neurology. 1959 Sep;9:599-609. doi: 10.1212/wnl.9.9.599. PMID: 13812692.
3. Calabrese LH, Mallek JA. Primary angiitis of the central nervous system. Report of 8 new cases, review of the literature, and proposal for diagnostic criteria. Medicine (Baltimore). 1988 Jan;67(1):20-39. doi: 10.1097/00005792-198801000-00002. PMID: 3275856.
4. Salvarani C, Brown RD Jr, Calamia KT, Christianson TJ, Weigand SD, Miller DV, Giannini C, Meschia JF, Huston J 3rd, Hunder GG. Primary central nervous system vasculitis: analysis of 101 patients. Ann Neurol. 2007 Nov;62(5):442-51. doi: 10.1002/ana.21226. PMID: 17924545.
5. Beuker C, Schmidt A, Strunk D, Sporns PB, Wiendl H, Meuth SG, Minnerup J. Primary angiitis of the central nervous system: diagnosis and treatment. Ther Adv Neurol Disord. 2018 Jul 9;11:1756286418785071. doi: 10.1177/1756286418785071. PMID: 30034536; PMCID: PMC6048610.
6. Nagel MA, Cohrs RJ, Mahalingam R, Wellish MC, Forghani B, Schiller A, Safdieh JE, Kamenkovich E, Ostrow LW, Levy M, Greenberg B, Russman AN, Katzan I, Gardner CJ, Häusler M, Nau R, Saraya T, Wada H, Goto H, de Martino M, Ueno M, Brown WD, Terborg C, Gilden DH. The varicella zoster virus vasculopathies: clinical, CSF, imaging, and virologic features. Neurology. 2008 Mar 11;70(11):853-60. doi: 10.1212/01.wnl.0000304747.38502.e8. PMID: 18332343; PMCID: PMC2938740.
7. Thomas L, Davidson M, McCluskey RT. Studies of PPLO infection. I. The production of cerebral polyarteritis by *Mycoplasma gallisepticum* in turkeys; the neurotoxic property of the Mycoplasma. J Exp Med. 1966 May 1;123(5):897-912. doi: 10.1084/jem.123.5.897. PMID: 5938817; PMCID: PMC2138161.
8. Arthur G, Margolis G. Mycoplasma-like structures in granulomatous angiitis of the central nervous system. Case reports with light and electron microscopic studies. Arch Pathol Lab Med. 1977 Jul;101(7):382-7. PMID: 577394.
9. Iwase T, Ojika K, Mitake S, Katada E, Katano H, Mase M, Yoshida S, Ueda R. Involvement of CD45RO+ T lymphocyte infiltration in a patient with primary angiitis of the central nervous system restricted to small vessels. Eur Neurol. 2001;45(3):184-5. doi: 10.1159/000052120. PMID: 11306864.
10. Berlit P, Kraemer M. Cerebral vasculitis in adults: what are the steps in order to establish the diagnosis? Red flags and pitfalls. Clin Exp Immunol. 2014 Mar;175(3):419-24. doi: 10.1111/cei.12221. PMID: 24117125; PMCID: PMC3927902.
11. Salvarani C, Brown RD Jr, Calamia KT, Christianson TJ, Huston J 3rd, Meschia JF, Giannini C, Miller DV, Hunder GG. Primary CNS vasculitis with spinal cord involvement. Neurology. 2008 Jun 10;70(24 Pt 2):2394-400. doi: 10.1212/01.wnl.0000314687.69681.24. PMID: 18541872.
12. Salvarani C, Brown RD Jr, Hunder GG. Adult primary central nervous system vasculitis. Lancet. 2012 Aug 25;380(9843):767-77. doi: 10.1016/S0140-6736(12)60069-5. Epub 2012 May 9. PMID: 22575778.
13. Hajj-Ali RA, Singhal AB, Benseler S, Molloy E, Calabrese LH. Primary angiitis of the CNS. Lancet Neurol. 2011 Jun;10(6):561-72. doi: 10.1016/S1474-4422(11)70081-3. PMID: 21601163.
14. Swartz RH, Bhuta SS, Farb RI, Agid R, Willinsky RA, Terbrugge KG, Butany J, Wasserman BA, Johnstone DM, Silver FL, Mikulis DJ. Intracranial arterial wall imaging using high-resolution 3-tesla contrast-enhanced MRI. Neurology. 2009 Feb 17;72(7):627-34. doi: 10.1212/01.wnl.0000342470.69739.b3. PMID: 19221296.
15. Eleftheriou D, Cox T, Saunders D, Klein NJ, Brogan PA, Ganesan V. Investigation of childhood central nervous system vasculitis: magnetic resonance angiography *versus* catheter cerebral angiography. Dev Med Child Neurol. 2010 Sep;52(9):863-7. doi: 10.1111/j.1469-8749.2009.03591.x. Epub 2010 Jan 28. PMID: 20132140.
16. Kadkhodayan Y, Alreshaid A, Moran CJ, Cross DT 3rd, Powers WJ, Derdeyn CP. Primary angiitis of the central nervous system at conventional angiography. Radiology. 2004 Dec;233(3):878-82. doi: 10.1148/radiol.2333031621. Epub 2004 Oct 21. PMID: 15498898.
17. Giannini C, Salvarani C, Hunder G, Brown RD. Primary central nervous system vasculitis: pathology and mechanisms. Acta Neuropathol. 2012 Jun;123(6):759-72. doi: 10.1007/s00401-012-0973-9. Epub 2012 Mar 16. PMID: 22421812.

18. Miller DV, Salvarani C, Hunder GG, Brown RD, Parisi JE, Christianson TJ, Giannini C. Biopsy findings in primary angiitis of the central nervous system. Am J Surg Pathol. 2009 Jan;33(1):35-43. doi: 10.1097/PAS.0b013e318181e097. PMID: 18941399.
19. Salvarani C, Brown RD Jr, Hunder GG. Adult primary central nervous system vasculitis. Isr Med Assoc J. 2017 Jul;19(7):448-53. PMID: 28786262.
20. Birnbaum J, Hellmann DB. Primary angiitis of the central nervous system. Arch Neurol. 2009 Jun;66(6):704-9. doi: 10.1001/archneurol.2009.76. PMID: 19506130.
21. Ducros A. Reversible cerebral vasoconstriction syndrome. Lancet Neurol. 2012 Oct;11(10):906-17. doi: 10.1016/S1474-4422(12)70135-7. PMID: 22995694.
22. Ivanković M, Bogoje-Raspopović A, Drobac M, Mamić-Martinović D, Vodopić M. Benign angiopathy of the central nervous system or reversible cerebral vasoconstriction syndrome. Acta Clin Croat. 2011 Jun;50(2):253-5. PMID: 22263392.
23. Salvarani C, Brown RD Jr, Christianson T, Miller DV, Giannini C, Huston J 3rd, Hunder GG. An update of the Mayo Clinic cohort of patients with adult primary central nervous system vasculitis: description of 163 patients. Medicine (Baltimore). 2015 May;94(21):e738. doi: 10.1097/MD.0000000000000738. PMID: 26020379; PMCID: PMC4616419.
24. de Boysson H, Zuber M, Naggara O, Neau JP, Gray F, Bousser MG, Crassard I, Touzé E, Couraud PO, Kerschen P, Oppenheim C, Detante O, Faivre A, Gaillard N, Arquizan C, Bienvenu B, Néel A, Guillevin L, Pagnoux C; French Vasculitis Study Group and the French NeuroVascular Society. Primary angiitis of the central nervous system: description of the first fifty-two adults enrolled in the French cohort of patients with primary vasculitis of the central nervous system. Arthritis Rheumatol. 2014 May;66(5):1315-26. doi: 10.1002/art.38340. PMID: 24782189.
25. Salvarani C, Brown RD Jr, Calamia KT, Huston J 3rd, Meschia JF, Giannini C, Miller DV, Hunder GG. Efficacy of tumor necrosis factor alpha blockade in primary central nervous system vasculitis resistant to immunosuppressive treatment. Arthritis Rheum. 2008 Feb 15;59(2):291-6. doi: 10.1002/art.23337. PMID: 18240197.
26. De Boysson H, Arquizan C, Guillevin L, Pagnoux C. Rituximab for primary angiitis of the central nervous system: report of 2 patients from the French COVAC cohort and review of the literature. J Rheumatol. 2013 Dec;40(12):2102-3. doi: 10.3899/jrheum.130529. PMID: 24293623.
27. Salvarani C, Brown RD Jr, Huston J 3rd, Morris JM, Hunder GG. Treatment of primary CNS vasculitis with rituximab: case report. Neurology. 2014 Apr 8;82(14):1287-8. doi: 10.1212/WNL.0000000000000293. Epub 2014 Mar 5. PMID: 24598711.

Sažetak

PRIMARNI VASKULITIS SREDIŠNJEGA ŽIVČANOG SUSTAVA – DIJAGNOSTIČKI IZAZOV

J. Mitrović, M. Golob i *I. Lazibat*

Primarni vaskulitis središnjega živčanog sustava (PVSŽS) je rijetka i teška bolest ograničena na središnji živčani sustav, tj. mozak i leđnu moždinu. Etiologija, patogeneza i imuni mehanizam PVSŽS-a još nisu u potpunosti razjašnjeni. Dijagnoza je zahtjevna i postavlja se na temelju kliničke slike, nalaza lumbalne punkcije, slikovnih metoda ili biopsije tkiva kao zlatnog standarda. U diferencijalnoj dijagnozi PVSŽS-a potrebno je isključiti infektivne, maligne ili sistemske upalne bolesti, kao i reverzibilni vazokonstrikcijski sindrom. Imunosupresivi su temelj terapije, iako zasad nema jasnih smjernica i preporuka za liječenje ove bolesti. PVSŽS je entitet sa značajnim pobolom i smrtnošću. Svijest o ovoj rijetkoj bolesti složene kliničke prezentacije ključna je za postavljanje rane dijagnoze i početak liječenja.

Ključne riječi: *Vaskulitis; Središnji živčani sustav; Imunosupresivna terapija*