REVIEW ARTICLE

Neurologia i Neurochirurgia Polska
Polish Journal of Neurology and Neurosurgery
2022, Volume 56, no. 2, pages: 141–147
DOI: 10.5603/PJNNS.a2021.0082

ISSN: 0028-3843, e-ISSN: 1897-4260

Susac's syndrome diagnostic difficulties — the neurological point of view

Paulina Fonderska[1], Joanna Tomalka-Kochanowska[1], Jan Kochanowski[1, 2], Izabela Domitrz[1, 2]

[1]Department of Neurology, Bielański Hospital, Warsaw, Poland
[2]Department of Neurology, Faculty of Medical Science, Medical University of Warsaw, Poland

ABSTRACT

Susac's syndrome is a rare microangiopathy affecting small vessels of the retina, inner ear and brain. It is characterised by a triad of symptoms: encephalopathy, visual defects, and sensorineural hearing loss. The disease is probably caused by an autoimmune process. Diagnosis is based on the typical symptoms, brain MRI, and, most importantly, fluorescein angiography. It is important to distinguish between Susac's syndrome and multiple sclerosis or migraine with aura, because misdiagnosis leads to the wrong treatment. To date, no detailed guidelines for the treatment of Susac's syndrome have been developed. Immunosuppression seems to be effective. It must be remembered that early and aggressive treatment is crucial, and that delays in diagnosis, and as a result in treatment implementation, worsen the prognosis.

Key words: Susac's syndrome, microangiopathy, MS, headache, encephalopathy, BRAO

(*Neurol Neurochir Pol 2022; 56 (2): 141–147*)

Introduction

Susac's syndrome (SuS) is a rare microangiopathy characterised by a triad of symptoms: encephalopathy of varying severity, visual disturbances due to branch retinal artery occlusion, and sensorineural hearing loss. It was 1979 when the disease entity was first described by Susac [1], and in 1986, it was named after him. To date, almost 500 cases of this disease among patients of both sexes aged between 2.5 [2] and 72 [3] years have been described worldwide, although it most frequently affects young women. The majority of patients are aged between 21 and 41 years, and the female-to-male ratio is 3:1 [4]. No differences in incidence among different races have been observed [5]. Suggestions of more frequent occurrences during spring and summer have appeared in the literature [6, 7].

The full triad of symptoms appears from the beginning of the disease in less than 15% of patients [7], which creates huge diagnostic challenges. The time elapsed from the first symptoms until the appearance of the fully developed syndrome can reach six months or more [8].

Etiopathogenesis

So far, the causes of this disease have not been fully understood, but most authors incline to the hypothesis that it is based on an autoimmune process which results in damage to the endothelial cells in precapillary arterioles of the brain, retina and inner ear. It was believed that anti-endothelial cell antibodies (AECA) played an important role. A study using Western blots, indirect immunofluorescence and flow cytometry has detected AECA in sera of SuS patients [9]. Recently, researchers demonstrated oligoclonal expansion of terminally differentiated activated cytotoxic CD8+ T cells (CTLs). Their study has identified CD8+ T-cell-mediated endotheliopathy to be a key disease mechanism in SuS, and this highlights therapeutic opportunities [10].

Changes occur in vessels < 100 um in size and include: necrosis of endothelial cells, thickening of the basement membrane, infiltration of inflammatory cells, and accumulation of complement deposits in the arterial wall (C4d and C3d). All these changes lead to the occlusion of the affected vessel and, as a consequence, the formation of microischaemia in the

Address for correspondence: Paulina Fonderska, Department of Neurology, Bielański Hospital, 80 Cegłowska St, 01-809 Warsaw, Poland; e-mail: p.fonderska@wp.pl

Received: 28.06.2021 Accepted: 24.08.2021 Early publication date: 5.11.2021

affected organs, which leads to clinical manifestations in the form of the aforementioned triad of symptoms [11].

A study has tested the hypothesis of a genetic basis to SuS. In the light of current research, it is impossible to identify a gene responsible for this syndrome. The theory of a common background with known monogenic small vessel diseases has also been ruled out [12].

Diagnostic criteria

In 2016, Kleffner et al. [13] presented proposed diagnostic criteria for Susac's syndrome based on data collected from case reports published from 1990-2016: 1) Brain involvement:— symptoms: cognitive impairment and/or behavioural change and/or focal symptoms and/or new nature of headache;— typical changes in brain MRI — hyperintense, small, diffuse, circular lesions; at least one in corpus callosum on T2 images (or FLAIR);2) Retinal involvement:— BRAO or AWH in retinal fluorescein angiography or characteristic symptoms of retinal branch ischaemia in fundoscopy/SD-OCT examination; 3) Vestibulocochlear involvement:— symptoms: new onset or change in tinnitus and/or hearing loss and/or peripheral vertigo;— hearing loss confirmed by audiogram; vestibular vertigo supported by specific diagnosis.

On this basis, two categories of diagnostic accuracy have been distinguished: The first is a d efinite diagnosis of Susac's syndrome — this requires the fulfillment of all three criteria along with subcriteria; The second is a probable diagnosis of Susac's syndrome — this requires two out of the three diagnostic criteria to be met [13].

The limitation of these presented criteria, as indicated by the authors [13], is the fact that the full triad of symptoms only rarely manifests at the beginning of the disease. Nevertheless, these criteria can be very helpful in deciding when to implement aggressive treatment, or when to perform watchful waiting.

Encephalopathy

Headache is the most common first symptom of Susac's syndrome, and it may appear six months before other symptoms. The headaches are migraine-like (and mimic migraine attacks) or oppressive in nature, and are likely to result from the affection of leptomeningeal vessels [14]. However, headache, although the most common symptom of SuS, is also present in many other diseases, often of a far more mundane nature. Hence, a very extensive differential diagnosis is necessary.

In the next stages, encephalopathy develops, which may include: cognitive impairment, memory impairment, confusion, and mood disturbances. Neuropsychiatric symptoms are also quite characteristic, which can dominate in nearly 75% of patients [15]. There is no one cognitive-behavioural picture typical for SuS [16]. Cognitive-behavioural global impairment usually depends on brain damage location and its volume [16]. In the available literature, there are only a few report cases to have included a neuropsychological assessment. At first, patients and also their environment most often observe psycho-motor slowness, fatigue, attention deficits, and memory disturbances of varying severity. In order to achieve a detailed assessment of the nature of the deficits, selected neuropsychological tests seem to be very useful e.g.: the Wechlsler Adult Intelligence Scale-revised (WAIS-R) for evaluation of intellectual functioning; the Addenbrooke's Cognitive examination-III (ACE-III); the Rivermead Behavioural Memory Test (RBMT-III); the Behavioural Assessment of Dysexecutive Syndome (BADS); the Dysexecutive Questionnaire (DEX); and the Hospital Anxiety and Depression Scale (HADS).

The major limitation of these tests is the lack of standardisation in many languages. The tests reveal a limitation of visual-spatial abilities and executive functions (impaired planning, set shifting and new problem-solving ability), and reduced efficiency of logical reasoning [16, 17]. Additionally, behavioural disorders in the form of inadequate reactions and emotional lability are noteworthy. There have also been episodes of depression, hypomania, anxiety disorders, and panic attacks [17, 18]. Symptoms partially resolve with treatment, but very often recovery is incomplete and difficult to predict.

In the course of Susac's syndrome, focal symptoms such as paresis, paraesthesia, speech disorders, and cerebellar symptoms may be involved in the pathological process. Seizures have also been observed.

Brain MRI is the test of choice in the diagnosis of Susac's syndrome. This allows the visualisation of the typical, small, snowball-like lesions in the corpus callosum, visible in T2 images. They mimic demyelinating lesions and can lead to a misdiagnosis of multiple sclerosis (MS). They can be located throughout the whole corpus callosum, but usually they occupy its centre, and less so its peripheral parts. Over time, the described lesions change and begin to resemble holes, best visible in T1 images mainly within the splenium of the corpus callosum [19].

Additionally, typical, small, multifocal lesions in white matter are visible and they are located subcortical, periventricular, in the centrum semiovale and also in the internal capsule. In the acute phase, they enhance in 70% of cases. Grey matter, basal ganglia and thalamus affections have been observed in 70% of cases, cerebellum in 52%, and brainstem in 33% [14, 20]. Leptomeningeal enhancement is present in one in three patients [21]. In the MRI test, affection of the cranial nerves has not been observed [4]. After acute onset of the disease, atrophy of the whole brain, cerebellum and corpus callosum develops [20]. The number and size of lesions detectable in conventional brain MRI does not correlate with the severity of the encephalopathy symptoms or clinical status, which has led researchers to look for different ways to present tissue damage.

Diffusion Tensor Imaging is a non-invasive and sensitive technique that allows structural impairment of the fibre

integrity to be revealed on the basis of the normal values for fractional anisotrophy (FA). Using this test, Kleffner et al. demonstrated a reduction of FA, particularly in the prefrontal white matter and in the genu of the corpus callosum [22, 23]. Damage in the genu of the corpus callosum seems to be specific for Susac's syndrome [14].

Computed tomography usually shows no significant abnormalities at the beginning of the disease. However, as it progresses, it can reveal atrophy of the cerebral cortex [24].

The result of cerebral arteriography is almost always normal, because the affected precapillary arterioles (< 100 um) are out of scope of arteriography [7].

For every patient with suspected Susac's syndrome, a cerebrospinal fluid (CSF) examination should also be performed in order to exclude other diseases. In most patients, a mild pleocytosis with usually not more than 20 cells/uL and increased protein level to 2g/L is observed [25]. Oligoclonal bands can be detected in about 15% of patients, and this can produce a mistaken diagnosis of MS rather than Susac's syndrome. Their presence does not exclude the diagnosis of Susac's syndrome [26]. However, their absence can be helpful in differentiating Susac's syndrome from multiple sclerosis [14].

EEG testing, while contributing little to the diagnosis of Susac's syndrome, is often performed at the very beginning of a neurological evaluation. EEG findings usually show generalised slowing and frontal intermittent rhythmic delta activity (FRIDA) [27], which is typical for encephalopathy, but not characteristic (especially in younger people).

Visual disturbance

Visual disturbances mostly result from branch retinal artery occlusion (BRAO). The type of presented symptoms depends on the location and the extent of diseased vessels within the retina [11]. Occupation of peripheral arteries may be asymptomatic without any irregularities in fundoscopic exam [28]. With more intense lesions, patients most often report reduced visual acuity, scintillating scotomas, photopsia and visual field defects [29], and even complete blindness. These visual symptoms can be wrongly interpreted as visual aura of migraine with aura.

Fundoscopic findings show narrowing or complete occlusion of the branch retinal artery and small punctuate yellow-white arterial wall plaques (Gass plaques, named after J. Don Glass, who was the first to describe them in idiopathic BRAO). Gass plaques are present not only in Susac's syndrome, they can also be found in toxoplasmosis, primary vitreoretinal lymphoma, arterial macroaneurysms, and acute retinal necrosis [30].

The most helpful, and very often confirmatory, test in diagnosing Susac's syndrome is fluorescein angiography. Abnormalities seen in the examination are pathognomonic for Susac's syndrome and include segmental arterial wall hyperfluorescence (AWH) with dye leakage [7, 29]. Changes

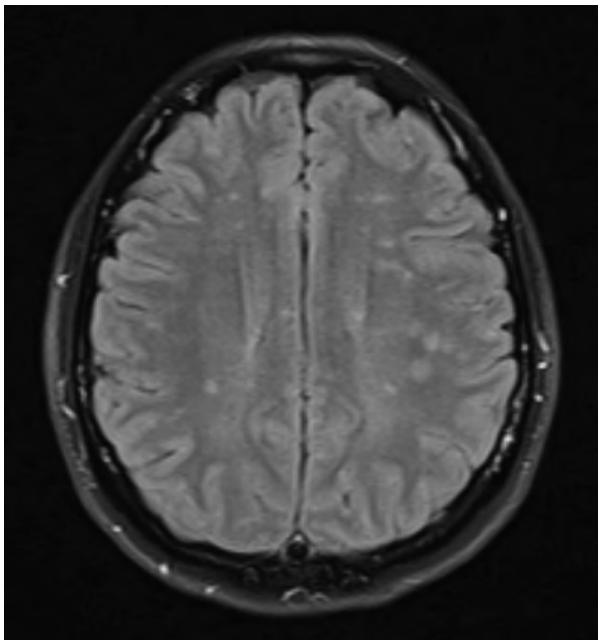

Figure 1. T2-weighted MRI: multifocal lesions in white matter

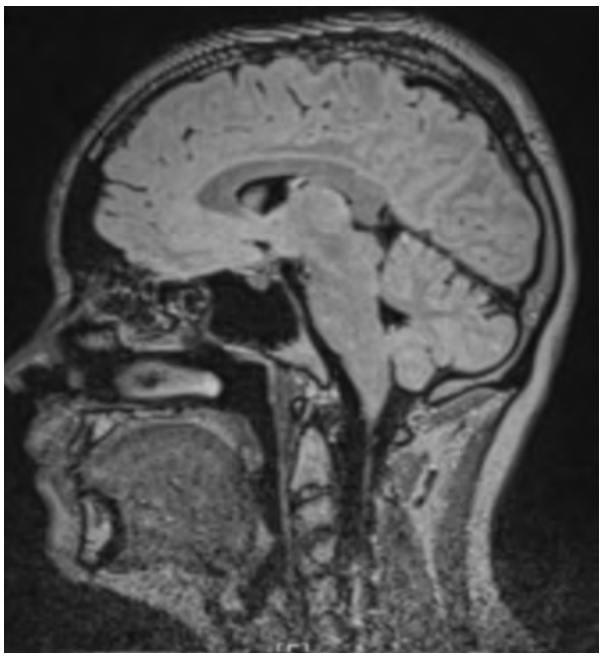

Figure 2. Midline sagittal T2-weighted MRI: typical lesions in corpus callosum

are located unilaterally or bilaterally and may completely disappear over time [14].

A recent addition as a valuable diagnostic tool is optical coherence tomography (OCT). This method allows the illustration of the posterior part of the eyeball — retina and optic nerve. In the study performed by Ringelstein et al., which included 17 patients with SuS, significantly reduced average retinal nerve fibre layer thickness (RNFLT) was revealed in

68% of patients. Additionally, a pattern of scattered changes is very characteristic within the inner retina. In OCT, areas with severe thinning are adjacent to normal areas.

The described phenomenon allows for a clear differentiation between Susac's syndrome and the relapsing-remitting form of multiple sclerosis [31, 32].

Depending on the stage of the disease, both fluorescein angiography and optical coherence tomography provide specific, complementary information.

Hearing loss

Hearing loss often has a very abrupt onset and rapidly progressing course. It can appear one day in one ear, and take over the other ear within as little as a couple of days. Losses in the range of low and medium frequencies are typical, although disturbances in receiving high tones may also appear. Sensorineural hearing loss coexists with preserved acoustic reflexes [33]. Tinnitus and vertigo are frequent accompanying symptoms, which may also precede hearing impairment.

Hearing loss results from the occlusion of the cochlear and semicircular canals precapillary arterioles [3]. Although changes seen in an audiometric examination are very typical, they are not characteristic for Susac's syndrome, and can be observed in different disease entities.

It is worth mentioning the fact that hearing loss, unlike other symptoms, is very often irreversible, and cochlear implantation may be necessary [6].

Other symptoms

Some authors have shown that other organs such as muscle and skin can also be affected by the disease process. In some cases, additional symptoms such as muscle aching or skin rash have appeared. Muscle biopsies performed on patients reporting such symptoms have shown swollen endothelial cells that occluded some small arterioles [34] and foci complement deposits within their walls [35].

Turc et al. [36] reported the case of a young man with skin involvement in the course of Susac's syndrome in the form of livedo racemosa of the flanks and feet. Biopsy showed occlusion in several dermal arterioles due to the presence of thrombus in their lumen, endothelial cells swelling, and mild perivascular lymphocytic infiltrate [36]. The obtained results are identical to the changes observed in the brain or muscles, and this may be confirmation that Susac's syndrome is an autoimmune disease involving small arteries [14].

In 2013, Allmendinger et al. [37] presented a single case of a middle-aged man with the syndrome of cauda equine in the course of Susac's syndrome. A performed spinal MRI showed diffuse lumbosacral nerve root enhancement [37]. In the available literature, there are no other case reports confirming the coexistence of this type of symptoms with Susac's syndrome.

Differential diagnosis

In a differential diagnosis, first of all multiple sclerosis and acute disseminating encephalomyelitis (ADEM) should be considered. The presence of lesions in the centre of the corpus callosum speaks for a diagnosis of Susac's syndrome, as do the typical round shape of lesions, grey matter involvement, or leptomeningeal enhancement. In MS, the lesions are ovoid and are sometimes called Dawson's fingers [14], and in cerebrospinal fluid most commonly oligoclonal bands are present.

A proper distinction between multiple sclerosis and Susac's syndrome is crucial because treatment with interferon beta (commonly used in treating MS) can exacerbate SuS [38].

When the first symptom is a headache in young people, there is often a misdiagnosis of migraine. Accompanying visual disturbances, periodically occurring paraesthesia or other focal deficits can be treated as migraine aura, which additionally hinders the proper differentiation of the disease. A particular type of migraine that may cause additional diagnostic difficulties is vestibular migraine. This connects vertigo and headache. Some patients report mild, transient hearing loss and visual distortions [39]. These symptoms are also quite frequent for SuS.

Therefore, for every patient with a headache (especially a migraine-like feature), every new, additional symptom (auditory, visual, and/or encephalopathic) should raise suspicions and result in referral of the patient for further diagnostics towards Susac's syndrome [40].

Cerebral venous and sinus thrombosis (CVST) is another disease where headache is the predominant symptom. As with SuS, it affects typically young adults, mainly females, which can lead to misdiagnosis [41]. CVST has a lot of varying clinical manifestations similar to SuS, but it is important to remember that the treatment differs significantly.

Also noteworthy in the differential diagnosis is spontaneous intracranial hypotension (SIH), which is dominated by headaches that intensify after standing upright. The orthostatic nature might become less obvious over time, and may become a chronic daily headache. In published case series, hearing change was present in about 70% of patients. In at least 50% of cases, headache was associated with nausea/vomiting and cochlear-vestibular signs. Additionally, mood disorders such as anxiety and depression have been observed [42]. These symptoms can also imitate SuS. The key to diagnosis seems to be establishing the initial, orthostatic, nature of the headache. It is also important to remember that hearing loss should be regarded as a vascular problem.

Treatment

To date, no detailed guidelines for the treatment of Susac's syndrome have been developed. The proposed regimens are based on the assumption that the essence of the disease is an autoimmune process, and thus the treatment should be immunosuppressive. Based on the case reports published so far,

the key seems to be early, aggressive and long-term treatment in order to protect against the recurrence of symptoms [14].

Most authors recommend starting treatment with high doses of steroids, administered intravenously, 1,000 mg of methylprednisolone for five days, and then orally at 1mg/kg body weight, with a gradual reduction under clinical control. This makes a correct diagnosis difficult, because such treatment is also helpful in MS relapse.

In severe cases, intravenous immunoglobulins also seem to be effective [43]. In the event of the recurrence of symptoms after steroid therapy or aggressive onset of the disease, high doses of cyclophosphamide, administered every four weeks [44], should be considered, or another immunosuppressive drug such as mycophenolate mofetil, rituximab or tacrolimus. Plasmapheresis treatments also seem worth considering [26].

Long-term treatment is clouded by the greatest uncertainty. It is very difficult to predict the individual course of the disease, and thus determine the appropriate time at which to cease treatment. It seems that any attempt to change the treatment should be carried out under the supervision of ophthalmological, audiological, neuropsychiatric and imaging examinations [45]. Regardless of the severity of the disease, treatment should usually last at least two years [46].

Prophylactic use of anticoagulants and acetylsalicylic acid is ineffective [47]. It is important to state that the vasoconstrictive agents used in migraine are contraindicated.

Prognosis

In most of the described cases, the disease is monophasic and self-limiting. However, there are relapses, as well as chronic and progressive courses [48]. Symptoms can return, even after many years of remission [49]. The severity of symptoms is also variable. They can be mild, moderate, severe or extremely severe; fatal cases are to be found in the literature [50, 51].

The course of the disease is individual for each patient, and it is difficult to predict the prognosis for a given patient, especially at the beginning of the disease. That is why early and aggressive immunosuppressive treatment is indicated. This prevents the emergence of new symptoms, and also reduces persistent deficits. In spite of treatment, some patients experience residual neurological symptoms, permanent hearing loss, and persistent cognitive impairment. There have also been persistent, mostly asymptomatic, changes in eye fluorescein angiography. Moreover, even with treatment, fatal cases may occur. There are published report cases of two women who died despite intensive immunosuppressive therapy (the first of them 12 weeks [50] after the onset of symptoms, and the second after seven months [51]).

Our experience

In our department, we diagnosed Susac's syndrome in a 23-year-old patient who had not been chronically treated so far. The first noticeable symptom was a sudden hearing loss in the left ear, accompanied by tinnitus and dizziness. After a thorough interview, it turned out that a few months earlier there had also been headaches of moderate intensity. The patient was then consulted by a laryngological specialist and treated with steroids, and then with a hyperbaric chamber, with partial improvement. About two weeks later, there was a 15-minute episode of aphasia and right-sided hemi-paraesthesia. At that time, an MRI of the head was performed, which showed small, multifocal lesions visible in T2 images, located in white matter in both hemispheres of the brain and in the corpus callosum. Differential diagnosis was performed in our department. We made a lumbar puncture, and in the cerebrospinal fluid were 7 cells/uL and an increased protein level to 78 mg/L. Oligoclonal bands were not detected in the CSF. EEG showed normal baseline function with a series of slow waves. Susac's syndrome was suspected, and therefore a 5-day course of methylprednisolone at a dose of 1,000 mg/day was prescribed, which resulted in a reduction of tinnitus and a subjective improvement in hearing. Then we referred the patient for ophthalmological consultation in order to perform fluorescein angiography. This examination confirmed branch retinal artery occlusion and dye leakage through the walls of the retinal vessels. Before the diagnosis was completed, hearing loss occurred in the right ear. Plasmapheresis was performed on the patient, which gave an improvement. Eventually, we diagnosed Susac's syndrome and introduced long-term treatment with mycophenolate mofetil.

Conclusions

Susac's syndrome is a disease that is still not fully understood and is often overlooked in the diagnostic process. In addition, during the first stage of the disease it is often misdiagnosed. Among young women, the first symptoms are often misread as migraine-like symptoms or MS-like symptoms. A major limitation in fully understanding the disease is its very rare occurrence. Most of the available information is based only on individual case reports or analyses of small groups of patients.

It must be underlined that early and aggressive treatment is crucial, and that delays in diagnosis of this disease, and as a result in the implementation of treatment, worsen the prognosis.

As our own experience shows, before making the correct diagnosis, a patient will have come into contact with various specialists: a laryngologist, a neurologist and/or an ophthalmologist. That is why it is so important to spread the knowledge published so far among doctors of all specialisations, in particular neurologists, ophthalmologists, and laryngologists, but also radiologists and general practitioners.

Conflict of interest: *None.*
Funding: *None.*

References

1. Susac JO, Hardman JM, Selhorst JB. Microangiopathy of the brain and retina. Neurology. 1979; 29(3): 313–316, doi: 10.1212/wnl.29.3.313, indexed in Pubmed: 571975.
2. Prakash G, Jain S, Gupta M, et al. Susac's syndrome: first from India and youngest in the world. Indian J Ophthalmol. 2013; 61(12): 772–773, doi: 10.4103/0301-4738.118446, indexed in Pubmed: 24088634.
3. Rennebohm R, Susac JO, Egan RA, et al. Susac's Syndrome--update. J Neurol Sci. 2010; 299(1-2): 86–91, doi: 10.1016/j.jns.2010.08.032, indexed in Pubmed: 20855088.
4. Susac JO. Susac's syndrome. AJNR Am J Neuroradiol. 2004; 25(3): 351–352, indexed in Pubmed: 15037453.
5. Susac JO. Susac's syndrome: the triad of microangiopathy of the brain and retina with hearing loss in young women. Neurology. 1994; 44(4): 591–593, doi: 10.1212/wnl.44.4.591, indexed in Pubmed: 8164809.
6. Aubart-Cohen F, Klein I, Alexandra JF, et al. Long-term outcome in Susac syndrome. Medicine (Baltimore). 2007; 86(2): 93–102, doi: 10.1097/MD.0b013e3180404c99, indexed in Pubmed: 17435589.
7. Dörr J, Krautwald S, Wildemann B, et al. Characteristics of Susac syndrome: a review of all reported cases. Nat Rev Neurol. 2013; 9(6): 307–316, doi: 10.1038/nrneurol.2013.82, indexed in Pubmed: 23628737.
8. Greco A, De Virgilio A, Gallo A, et al. Susac's syndrome--pathogenesis, clinical variants and treatment approaches. Autoimmun Rev. 2014; 13(8): 814–821, doi: 10.1016/j.autrev.2014.04.004, indexed in Pubmed: 24727151.
9. Magro CM, Poe JC, Lubow M, et al. Susac syndrome: an organ-specific autoimmune endotheliopathy syndrome associated with anti-endothelial cell antibodies. Am J Clin Pathol. 2011; 136(6): 903–912, doi: 10.1309/AJCPERI7LC4VNFYK, indexed in Pubmed: 22095376.
10. Gross CC, Meyer C, Bhatia U, et al. CD8 T cell-mediated endotheliopathy is a targetable mechanism of neuro-inflammation in Susac syndrome. Nat Commun. 2019; 10(1): 5779, doi: 10.1038/s41467-019-13593-5, indexed in Pubmed: 31852955.
11. Patel VA, Dunklebarger M, Zacharia TT, et al. Otologic manifestations of Susac syndrome. Acta Otorhinolaryngol Ital. 2018; 38(6): 544–553, doi: 10.14639/0392-100X-2166, indexed in Pubmed: 30623900.
12. David C, Papo T, Ba I, et al. Hunting for the genetic basis of Susac syndrome. Eur J Neurol. 2021; 28(7): e57–e59, doi: 10.1111/ene.14836, indexed in Pubmed: 33773011.
13. Kleffner I, Dörr J, Ringelstein M, et al. European Susac Consortium (EuSaC). Diagnostic criteria for Susac syndrome. J Neurol Neurosurg Psychiatry. 2016; 87(12): 1287–1295, doi: 10.1136/jnnp-2016-314295, indexed in Pubmed: 28103199.
14. Kleffner I, Duning T, Lohmann H, et al. A brief review of Susac syndrome. J Neurol Sci. 2012; 322(1-2): 35–40, doi: 10.1016/j.jns.2012.05.021, indexed in Pubmed: 22640902.
15. Pawate S, Agarwal A, Moses H, et al. The spectrum of Susac's syndrome. Neurol Sci. 2009; 30(1): 59–64, doi: 10.1007/s10072-008-0004-8, indexed in Pubmed: 19145401.
16. Roessler-Górecka M, Mendel T, Wiśniowska J, et al. Neuropsychological characteristics of encephalopathy in Susac's Syndrome - Case report. Neurol Neurochir Pol. 2017; 51(2): 174–179, doi: 10.1016/j.pjnns.2017.01.001, indexed in Pubmed: 28094021.
17. Barritt AW, Wickremaratchi M, Anderson SJ. Neuropsychological outcome of a case of Susac syndrome: A two-year follow-up study. Appl Neuropsychol Adult. 2019; 26(1): 89–95, doi: 10.1080/23279095.2017.1359178, indexed in Pubmed: 28922012.
18. Bolton C, Lacy M. Long-term neuropsychological and psychiatric outcomes in Susac's syndrome. J Neuropsychiatry Clin Neurosci. 2019; 31(2): 181–182, doi: 10.1176/appi.neuropsych.18080173, indexed in Pubmed: 31012828.
19. Saenz R, Quan AW, Magalhaes A, et al. MRI of Susac's syndrome. AJR Am J Roentgenol. 2005; 184(5): 1688–1690, doi: 10.2214/ajr.184.5.01841688, indexed in Pubmed: 15855140.
20. Susac JO, Murtagh FR, Egan RA, et al. MRI findings in Susac's syndrome. Neurology. 2003; 61(12): 1783–1787, doi: 10.1212/01.wnl.0000103880.29693.48, indexed in Pubmed: 14694047.
21. Raets I, Gelin G. Susac's syndrome: a clinical and radiological challenge. JBR-BTR. 2012; 95(6): 355–356, doi: 10.5334/jbr-btr.721, indexed in Pubmed: 23405486.
22. Kleffner I, Deppe M, Mohammadi S, et al. Neuroimaging in Susac's syndrome: focus on DTI. J Neurol Sci. 2010; 299(1-2): 92–96, doi: 10.1016/j.jns.2010.08.028, indexed in Pubmed: 20850137.
23. Kleffner I, Deppe M, Mohammadi S, et al. Diffusion tensor imaging demonstrates fiber impairment in Susac syndrome. Neurology. 2008; 70(19 Pt 2): 1867–1869, doi: 10.1212/01.wnl.0000280580.95671.01, indexed in Pubmed: 17959768.
24. Gross M, Banin E, Eliashar R, et al. Susac syndrome. Otol Neurotol. 2004; 25(4): 470–473, doi: 10.1097/00129492-200407000-00012, indexed in Pubmed: 15241223.
25. Susac JO, Egan RA, Rennebohm RM, et al. Susac's syndrome: 1975-2005 microangiopathy/autoimmune endotheliopathy. J Neurol Sci. 2007; 257(1-2): 270–272, doi: 10.1016/j.jns.2007.01.036, indexed in Pubmed: 17331544.
26. Grygiel-Górniak B, Puszczewicz M, Czaplicka E. Susac syndrome--clinical insight and strategies of therapy. Eur Rev Med Pharmacol Sci. 2015; 19(9): 1729–1735, indexed in Pubmed: 26004617.
27. Woolridge D, Stefanelli M, Hoppe B. Susac syndrome with frontal intermittent rhythmic delta activity (FIRDA). Can J Neurol Sci. 2006; 33(4): 403–406, doi: 10.1017/s0317167100005369, indexed in Pubmed: 17168166.
28. Papo T, Biousse V, Lehoang P, et al. Susac syndrome. Medicine (Baltimore). 1998; 77(1): 3–11, doi: 10.1097/00005792-199801000-00002, indexed in Pubmed: 9465860.
29. Papasavvas I, Teuchner B, Herbort CP. Susac syndrome (Retino-cochleo-cerebral vasculitis), the ophthalmologist in the role of the whistleblower. J Ophthalmic Inflamm Infect. 2020; 10(1): 27, doi: 10.1186/s12348-020-00217-z, indexed in Pubmed: 33125601.
30. Gass JD, Trattler HL. Retinal artery obstruction and atheromas associated with non-Hodgkin's large cell lymphoma (reticulum cell sarcoma). Arch Ophthalmol. 1991; 109(8): 1134–1139, doi: 10.1001/archopht.1991.01080080094039, indexed in Pubmed: 1867559.
31. Ringelstein M, Albrecht P, Kleffner I, et al. Retinal pathology in Susac syndrome detected by spectral-domain optical coherence tomography. Neurology. 2015; 85(7): 610–618, doi: 10.1212/WNL.0000000000001852, indexed in Pubmed: 26203089.
32. Brandt AU, Zimmermann H, Kaufhold F, et al. Patterns of retinal damage facilitate differential diagnosis between Susac syndrome and MS. PLoS One. 2012; 7(6): e38741, doi: 10.1371/journal.pone.0038741, indexed in Pubmed: 22701702.

33. Roeser MM, Driscoll CLW, Shallop JK, et al. Susac syndrome--a report of cochlear implantation and review of otologic manifestations in twenty-three patients. Otol Neurotol. 2009; 30(1): 34–40, doi: 10.1097/mao.0b013e31818b6ac2, indexed in Pubmed: 19108037.
34. Petty GW, Engel AG, Younge BR, et al. Retinocochleocerebral vasculopathy. Medicine (Baltimore). 1998; 77(1): 12–40, doi: 10.1097/00005792-199801000-00003, indexed in Pubmed: 9465861.
35. O'Halloran H. Microangiopathy of the brain, retina, and cochlea (susac syndrome) A report of five cases and a review of the literature. Ophthalmology. 1998; 105(6): 1038–1044, doi: 10.1016/s0161-6420(98)96005-5.
36. Turc G, Monnet D, Dupin N, et al. Skin involvement in Susac's syndrome. J Neurol Sci. 2011; 305(1-2): 152–155, doi: 10.1016/j.jns.2011.03.001, indexed in Pubmed: 21440909.
37. Allmendinger AM, Mallery RM, Magro CM, et al. Cauda equina involvement in Susac's syndrome. J Neurol Sci. 2014; 337(1-2): 91–96, doi: 10.1016/j.jns.2013.11.023, indexed in Pubmed: 24290499.
38. Algahtani H, Shirah B, Amin M, et al. Susac syndrome misdiagnosed as multiple sclerosis with exacerbation by interferon beta therapy. Neuroradiol J. 2018; 31(2): 207–212, doi: 10.1177/1971400917712265, indexed in Pubmed: 28644112.
39. Nowaczewska M. Vestibular migraine - an underdiagnosed cause of vertigo. Diagnosis and treatment. Neurol Neurochir Pol. 2020; 54(2): 106–115, doi: 10.5603/PJNNS.a2020.0031, indexed in Pubmed: 32285435.
40. Kowacs F, Ferreira Gomes M, Pigozzo T, et al. Migraine-like headache as presentation symptom in Susac syndrome. Headache. 2016; 56(10): 1667–1669, doi: 10.1111/head.12991, indexed in Pubmed: 27781269.
41. Domitrz I, Sadowski A, Domitrz W, et al. Cerebral venous and sinus thrombosis diagnosis: preliminary study of clinical picture and D-dimer concentration correlation. Neurol Neurochir Pol. 2020; 54(1): 66–72, doi: 10.5603/PJNNS.a2020.0006, indexed in Pubmed: 31965561.
42. Ferrante E, Trimboli M, Rubino F. Spontaneous intracranial hypotension: review and expert opinion. Acta Neurol Belg. 2020; 120(1): 9–18, doi: 10.1007/s13760-019-01166-8, indexed in Pubmed: 31215003.
43. Fox RJ, Costello F, Judkins AR, et al. Treatment of Susac syndrome with gamma globulin and corticosteroids. J Neurol Sci. 2006; 251(1-2): 17–22, doi: 10.1016/j.jns.2006.08.007, indexed in Pubmed: 17052732.
44. Klein M, Illies T, Georgi S, et al. [Aggressive immunotherapy in Susac's syndrome]. Nervenarzt. 2009; 80(12): 1502–1505, doi: 10.1007/s00115-009-2866-2, indexed in Pubmed: 19888559.
45. Rennebohm RM, Egan RA, Susac JO. Treatment of Susac's Syndrome. Curr Treat Options Neurol. 2008; 10(1): 67–74, doi: 10.1007/s11940-008-0008-y, indexed in Pubmed: 18325301.
46. Rennebohm RM, Asdaghi N, Srivastava S, et al. Guidelines for treatment of Susac syndrome - An update. Int J Stroke. 2020; 15(5): 484–494, doi: 10.1177/1747493017751737, indexed in Pubmed: 29319463.
47. Sauma J, Rivera D, Wu A, et al. Susac's syndrome: an update. Br J Ophthalmol. 2020; 104(9): 1190–1195, doi: 10.1136/bjophthalmol-2019-315597, indexed in Pubmed: 32029433.
48. Jarius S, Kleffner I, Dörr JM, et al. Clinical, paraclinical and serological findings in Susac syndrome: an international multicenter study. J Neuroinflammation. 2014; 11: 46, doi: 10.1186/1742-2094-11-46, indexed in Pubmed: 24606999.
49. Petty GW, Matteson EL, Younge BR, et al. Recurrence of Susac syndrome (retinocochleocerebral vasculopathy) after remission of 18 years. Mayo Clin Proc. 2001; 76(9): 958–960, doi: 10.4065/76.9.958, indexed in Pubmed: 11560310.
50. Saux A, Niango G, Charif M, et al. Susac's syndrome, a rare, potentially severe or lethal neurological disease. J Neurol Sci. 2010; 297(1-2): 71–73, doi: 10.1016/j.jns.2010.07.020, indexed in Pubmed: 20723912.
51. Agamanolis DP, Klonk C, Bigley K, et al. Neuropathological findings in Susac syndrome: an autopsy report. J Neuropathol Exp Neurol. 2019; 78(6): 515–519, doi: 10.1093/jnen/nlz031, indexed in Pubmed: 31100145.