

Department of Neurology, Medical University of Lublin, Lublin, Poland
Katedra i Klinika Neurologii, Uniwersytet Medyczny w Lublinie

ALEKSANDRA WASZCZUK, ALEKSANDRA WIETESKA,
KATARZYNA BRODKO, OLIVIA KOPERA,
MAGDALENA WASZCZUK, MARTA TYNECKA-TUROWSKA,
MAREK KAMIŃSKI, MOJDEH SAMZADEH, KONRAD REJDAK

Devic's disease – the pathogenesis, diagnosis and treatment

Choroba Devica- patogeneza, diagnostyka i leczenie

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INTRODUCTION

Devic's neuromyelitis optica(NMO) is a rare idiopathic inflammatory demyelinating disease of the central nervous system that preferentially affects the optic nerve and spinal cord. The probable cause of this disorder is the presence of antibodies which the target is aquaporin – 4. Recently, NMO was considered as a variant of multiple sclerosis(MS) but nowadays it is qualified as a distinct disease entity. Moreover, the diagnosis of Devic's disease is difficult to establish due to the presence of other demyelinating symptoms which include: neuromyelitis optica, myelitis and demyelination. NMO has been reported all over the world, in all continents and races but disease incidence is higher in the areas of Black, Asian and Indian populations. Although the gender distribution is variable, the prevalence rate in women is nine times higher than men [57, 41, 13, 19]. In turn, the average age of onset is about 39 years, nevertheless Devic's disease can be also diagnosed in children and people over 50 years of age [18, 15, 12].

HISTORICAL OVERVIEW

The first case report of the disease was described by Albutt in 1870 [1]. After a few years, Erb [28] reported the man with recurring optic neuritis in whom occurred transverse myelitis in three months. In America the first case was reported in 1880 [48]. After that, in 1884 the french neurologist Eugene Devic [14] and his student Ferdynand Gault reported the case of the 45 years old french woman with the monophasic and relapsing course of neuromyelitis optica. They also found 16 similar cases in the literature and named the syndrome „neuro-myelite-optique”. In 1907 Acchiote suggested the eponym „Devic’s disease” for those symptoms. Next 51 cases were described by Golden [20] in 1914 which he complied with Devic’s diagnostics criteria. In 1927 Beck [5] reviewed 71 case reports and he emphasised differentiation NMO with multiple sclerosis(MS).

In addition, the discovery performed by Stansbury [50] in 1949 made it possible to determinate the age range of disease. Based on over 200 cases, they ascertained that the disease is present between 3 and 5 decade but it can appear at every age. Moreover, Stansbury noticed that at the beginning of the disease, in equal measure there appear disturbances including the optic nerve and spinal cord. Among the characteristic symptoms of NMO, he [ascertained](#) the binocular blindness more often than monocular, also the prognosis of the disease was unfavourable, because most of the patients died several months after the diagnosis.

In turn, Scott [47] in 1952, as opposed to Stansbury, noticed good functional recovery. He described cases with minimal dysfunction of the spinal cord connected to the loss of vision or even blindness only without spinal disorders. Over 300 cases of Devic’s disease had been found by 1958 and it was more common than expected [42].

At the beginning, the criteria made by Devic’s and Galut included bilateral neuromyelitis optica and acute myelitis, which appear at the same time or within a few weeks apart. Next, Mandler [29] in 1994 extended diagnosis criteria for imaging CSF and pathological features(necrosis, cavitation of the spinal cord with the presence or absence of inflammatory infiltrates). In 1996, O’Riordan [41] defined Devic’s disease as a complete acute and severe transverse myelitis associated with acute unilateral or bilateral optic neuritis without signs of brain involvement beyond the optic nerves. In turn, the clinical investigations at the Mayo Clinic changed the point of view and helped to understand a number of issue concerning its immunological mechanisms, pathology, imaging and clinical features [57, 27, 26, 44, 28].

In 2002, Luccinetti et al. [28] broadened knowledge about NMO and MS. The main characteristic feature of NMO was a pronounced perivascular deposition of immunoglobulin and complement, eosinophilic infiltration and prominent vascular fibrosis and hyalinization within the lesions. Additionally, they deduced that humoral immunity plays an important role in pathogenesis of NMO.

In 2004 serum autoantibody marker of NMO has been identified and called NMO-IgG by Lennon et al. [26]. Therefore, there is a possibility to distinguish NMO from MS and other demyelinating disorders. The year after, Lennon et al.,

displayed selective binding of the NMO – IgG to aquaporin – 4. Finally, nonspecific brain MRI lesions were found in most of the patients by Pittock et al. [44].

PATHOGENESIS

Until the present times the pathogenesis of Devic's disease has not been completely understood, determining the factor which causes production of antibodies against aquaporin-4 still fails. The inflammatory process causing damage to the blood brain barrier gives the ability to connect to anti - AQP – 4 with channels aquaporins 4. Besides in the presence of complement factor, MAC(membrane attack complex) is activated [23]. The pathology of the spinal cord in the acute phase of disease is dispersed by swelling, softening comprising a plurality of segments of the spinal cord and sometimes even the entire length of the spinal cord.

Histopathologically, there is necrosis of both gray and white matter. Moreover, perivascular inflammatory infiltration consisting of neutrophils and eosinophils occurs, resulting from activation of complement factor. Then in the course of disease it comes to cavitation and atrophy, the affected segments of the spinal cord and optic nerve ensue with marked gliosis and cystic degeneration [25].

GENETICS

Coexistence of NMO with the systemic autoimmune disease or the presence of circulating antibodies, may indicate genetic susceptibility to autoimmunity and amplified humoral immune response. However, significant genetic risk factors determining NMO have not been discovered [43].

The literature reported only five pairs of familial cases suffered from NMO. McAlpine in 1938 described case of identical twins with bilateral optic neuritis and severe myelitis. Post- mortem examination revealed a significant demyelination of both optic nerves and the spinal cord with mild or without inflammatory infiltrates. Then Chlen et al. reported the case of two sisters who developed NMO at the ages of 3 years and 2 years 9 months. In both of them bilateral optic neuritis and myelitis occurred in the period of five months. Older Japanese sisters with onset at the age of 62 years and 59 years is another reported case. In turn the first mother-daughter pair was reported by Bradley. Unlike the other previous cases, they were affected in different stages of life: the mother at 62 years of age, while the daughter at the age of 29 years. Interestingly enough, the daughter underwent previous thymectomy for myasthenia gravis, after which NMO was diagnosed [25].

AUTOANTIBODIES

Gathering evidence of humoral mechanisms involved in the pathogenesis of NMO, specific IgG autoantibodies(NMO-IgG) can be identified [27]. The NMO-IgG generates a characteristic immunohistochemical pattern of binding in the indirect immunofluorescence that is evident in mice's pia, subpia, as well as the Virchow-Robin space and micro vessels in white and grey matter of the midbrain, cere-

bellum and spinal cord. Moreover, it binds to the area of the astrocytes' foot process, specifically to an antigen in the luminal face of cerebral microvessels.

According to the literature, the Japanese investigators [53] used human AQP – 4 – transfected cells to clarify if non-human substrates could be affected its sensitivity and specificity. They tested 148 plasma samples of patients suffering from MS, clinically isolated syndrome in the course of MS, NMO, high risk syndrome and miscellaneous diseases. Compared to the non-human test antigen, the specificity was 100% for NMO, in turn the risk factors and sensitivity were about 91% for NMO and 85% for high risk syndrome respectively [32].

AQUAPORINE - 4

Aquaporine 4(AQP4) is an integral protein of astrocytes' plasma membranes and is highly concentrated in the astrocyte foot processes which exhibit the biggest expansion in the optic nerves, brain stem and gray matter of the spinal cord. AQP4 forms water channels in the CNS and is also responsible for the regulation of water and electrolyte balance in the central nervous system(CNS). In addition, water channels regulate transport of water in other organs including kidneys, gastrointestinal tract, secretory glands, inner ear and muscles [3].

AQP 4 is a protein found in the excitable tissues(brain and spinal cord, inner ear, retina and skeletal muscles) however, it is not generally expressed in excitable cells and also occurs in supporting cells(astrocytes and ependyma) in the central nervous system, Müller cells in the retina, Hensen's and inner sulcus cells in the ear [52]. Moreover, aquaporin 4 is concentrated in the blood-brain barrier, anchored in the astrocytes' foot process membrane by the dystroglycan complex and particularly in the mammals' brain [2]. AQP4 is also present on ependymal and endothelial cells. It is highly expressed in the supraoptic nucleus of the hypothalamus, the area of postrema and the vascular organ of lamina terminalis. What is important, there is no blood brain barrier in these locations and additionally, osmosensitive neurons regulating the fluids homeostasis are located [6]. Besides AQP4 co-localizes with potassium channel and the glutamate transporter-1 (GLT-1) [61], what makes the event of loss of aquaporin-4 damage to the myelin sheath and axons in sensitive areas such as the spinal cord and optic nerves and can lead to brain oedema in other regions of the brain, such as: hypothalamus and periventricular structures [7]. [Perivascular location gives the ability to](#) bi-directional flow of water which plays an [important role in the pathogenesis of cerebral oedema](#) [21]. Hypoxia, brain injury, meningitis and encephalitis causes that AQP4 is up-regulated in the astrocytes, which increases the possibility of cerebral oedema. Mice in which the absence of AQP4 expression at astrocyte has been demonstrated are relatively resistant to the formation of cerebral oedema due to hypoosmolarity or stroke [31]. Distribution of AQP4 rich areas in the central nervous system, especially in the central part of the spinal cord, hypothalamus, periventricular area and periaqueductal areas is closely related to the changes occurring in NMO [36, 40, 45]. In this disease, two basic types of pathology are observed. The first type includes the most common spinal cord and optic nerves and comes to the deposition of immune complexes, active demyelination and vascular

hyperplasia with hyalinization, while [the second type](#) is located [mainly in the spinal cord](#), where the inflammatory process occurs. [Although it has been suggested that antibodies against the aquaporin-4 are the cause of NMO, acting through inhibition of AQP4](#) [26, 53, 35]. Moreover, it still not explained why other organs(lung, inner ear, intestine) in which also aquaporin 4 occurs, are not affected by disease process. It remains unknown why the dominant changes affect the spinal cord and optic nerve although AQP4 is ubiquitously expressed throughout the nervous system.

CLINICAL FEATURES

Neuromyelitis optica manifests as the acute transverse myelitis and optic neuritis. Those symptoms appear independently as well as in indefinite time interval. Devic's disease could follow monophasic(no relapses in the future), or recurrent course as attacks of transverse myelitis, optic neuritis, or both at the same time. Relapsing course is more frequently connected with predisposing factors including: female sex, later age of onset, less pronounced motor symptoms after the first myelitis attack, longer period of remission and coexistence of systemic autoimmune diseases [56].

Clinical signs of optic neuritis as visual field defects, color vision deficiency and eye pain appear in both NMO and MS, while bilateral optic neuritis is more characteristic for NMO. Visual field defects manifest usually as central scotoma. The occurrence of bitemporal hemianopsia and paracentral scotoma is also possible. Compared to MS, atrophy of the optic nerve and the optic disc pallor is more pronounced in Devic's disease than in multiple sclerosis [29, 16]. Furthermore, NMO symptoms are more severe and leave much greater neurological deficit [23]. In turn, symptoms such as: symmetrical paresis, sensory disorder and sphincter dysfunction are effected by complete tranverse myelitis [57]. In contrast, the MS lesions are asymmetrical and milder, due to acute partial transverse myelitis [49]. Extension of the disease into the brainstem is manifested by nystagmus, persistent hiccups, vomiting, trigeminal neuralgia, facial paralysis and even breathing problems. In 15% of patients there appear encephalopathy, hypothalamic dysfunction and cognitive disorders. Lhermitte's signs, paroxysmal tonic spasms and radicular pain concern to certain cases(about 30% recurrent cases). Additionally, paroxysmal tonic spasms appear more often in NMO, than MS [57].

Symptoms such as transverse myelitis, optic neuritis, recurrent inflammation of the spinal cord and optic nerve may also occur during other autoimmune diseases, particularly in systemic lupus erythematosus or Sjogren's syndrome. Detection of anti-nuclear antibodies may lead to the identification of these diseases, however, antinuclear antibodies are also common in patients with neuromyelitis optica, which have no clinical symptoms of systemic autoimmune disease. International criteria for the diagnosis of systemic lupus erythematosus or Sjogren's syndrome correspond to only 3% of patients with NMO [53, 56, 54].

Undoubtedly, this indicates the association of NMO with systemic autoimmune disease, and even more frequently with the presence of circulating autoantibodies in

the absence of symptoms underlying disease. Besides, among other autoimmune diseases accompanied with NMO are mentioned: hypothyroidism, ulcerative colitis, primary sclerosing cholangitis, myasthenia gravis, immune thrombocytopenic purpura or pernicious anemia [54].

The diagnosis of Devic's disease is difficult and requires a lot of experience, as the symptoms may resemble the beginning of the MS [23]. As a result of the disease, patients often lose the ability to walk unaided good vision - even to complete blindness. Undiagnosed and untreated disease can lead to death due to neurogenic respiratory failure, caused by the involvement of medullary neuromuscular respiratory centers [57]. Early mortality rate reaches approximately 20% of patients.

NMO requires the differentiation of the other like inflammatory and demyelinating diseases including: aforementioned multiple sclerosis (MS) as well as acute disseminated encephalomyelitis(ADEM) or longitudinally extensive transverse myelitis(LETM) [57].

CEREBROSPINAL FLUID

In most patients with NMO some irregularities in the cerebrospinal fluid(CSF) have been detected, mainly concern cell count, protein level and oligoclonal bands. Moreover, in the case of 14-79 % of patients occurred pleocytosis(rich up to 1000 leukocytes / mL) consisting primarily of neutrophils [11]. [In addition, higher concentration of proteins in the cerebrospinal fluid with the present of interleukin\(IL\)-18, IL-17, IL-6, IL-5, IgG and IgM-secreting cells were observed in 46-75% of patients](#) [11, 22].

The incidence of oligoclonal bands(OCB) ranges from 0 % to 37 % of patients with NMO, furthermore the presence of OCB may be transient in contrast to MS [41, 8, 57]. In the case of MS patients, cerebrospinal fluid analysis rarely shows pleocytosis(about 50 % of patients) , but in approximately 90% of them oligoclonal bands are present. An additional difference is significantly higher concentration of neurofilament(NfH) and fibrillar acidic protein(GFAP) in the CSF of NMO as compared to MS patients [37]. In contrast, IgG index remained at normal levels in patients with NMO, while in individuals suffering from MS is significantly elevated [39]. Likewise, the concentration of matrix metalloproteinase 9 is higher in MS patients [30]. In conclusion, all differences in the cerebrospinal fluid analysis are very useful to distinguish NMO from MS.

MRI ABNORMALITIES

Neuroimaging studies have expanded considerably as for Devic's disease concept by describing typical spinal cord lesions as well as revealing brain lesions in asymptomatic patients. Furthermore, [it is the most credible element used by clinicians for the diagnosis of NMO and allows for differentiation NMO from MS.](#)

MRI scans of the spinal cord in patients with Devic's disease reveal pathologic, gadolinium- enhanced lesion of several vertebral segments described as longitudinally- extensive transverse myelitis, which is associated with cord swelling or atrophy during acute phase of disease [41, 17]. NMO diagnosis based on finding at least

three or more segments of the spinal cord lesion which is mainly localized in the cervical and thoracic spinal cord [58]. The preference for the location of lesions in gray matter of the spinal cord results from its structure including opulent in AQP4 glial cells adjacent to the cells lining the central canal of the spinal cord [38, 24]. In contrast to NMO in MS patients, spinal cord lesions encompass a maximum of two vertebral segments in length, do not lead to cord swelling or atrophy and are not located in the spinal cord transverse area [49, 10].

In one [study conducted by](#) Nakashima et al. the MRI features associated with opticospinal MS were correlated with the NMO- IgG serpositivity. [Antibodies against AQP-4 occurred in 25 out of 28 patients with](#) longitudinally extensive spinal cord lesions(LESCL) [and in 12 of 17 opticospinal MS patients with](#) extensive [atrophy of the spinal cord](#). [Despite, the fact that LESCL is more often observed in the case of opticospinal MS than in conventional MS,](#) the [some authors](#) [9, 51, 34] [found the presence of LESCL in 25% of Asian patients with conventional MS indicating a](#) receptivity [of Asian population to severe, extensive damage to the spinal cord](#) [40, 32]. Moreover, in the case of conventional MS both short spinal cord lesions and LESCL are most frequently localized [in the cervical spine](#) and mainly occupy the peripheral area of the spinal cord. [The differences in the pathogenesis of LESCL may result from the presence of anti-AQP4 antibodies. In the case of](#) patients with [anti-AQP4](#) antibodies positive, [primary humoral response plays main role, while in](#) the case of patients with LESCL and [absence of AQP4 antibodies](#) the most [essential is the role of cellular response](#) [32].

For a long time it was believed that brain lesions detected by MRI exclude Devic's disease. However, the development of Wingerchuk criteria gave a new insight on this issue [44]. Analysis of 60 cases of patients which fulfilled above criteria demonstrated that in approximately 60% of them, the brain abnormalities were visualized in MRI scan. In 30 % of patients the initial brain MRI was normal but in a half of them, pathological lesions within cerebral hemispheres, thalamus, hypothalamus, region around the fourth ventricle, and the cerebral peduncle or cerebellum were noticed. In another study [45] in 9 of 89 patients suffering from NMO, lesions were visualized in the hypothalamus and within the third and fourth ventricle with high expression of AQP4. Moreover, only in one of this group, the symptoms were not associated with participation of optic nerve and spinal cord. These studies showed that in the course of NMO, damage to the brain is not specific phenomenon, however, location of lesions in the brain stem and hypothalamus are characteristic for NMO [54, 46].

DIAGNOSTIC CRITERIA

In the years between 1950 and 1993 in the Mayo Clinic 71 cases of NMO patients were examined, which subsequently in 1999 were reviewed by Wingerchuk et al. Diagnostic criteria for Devic's disease were selected, taking into account the laboratory, clinical and imaging data. As a result, the diagnosis of NMO consisted of three absolute criteria(optic neuritis, myelitis and the absence of clinical signs of

disease beyond the optic nerve and spinal cord) and six additional criteria (including three major and three minor criteria). Major criteria included: a negative brain MRI at onset (does not meet criteria for MS), spinal cord MRI with signal abnormality extending over ≥ 3 vertebral segments and CSF pleocytosis of > 50 WBC/mm³ or > 5 neutrophils/mm³. In turn, the minor criteria involved following features such as: bilateral optic neuritis; severe optic neuritis with fixed visual acuity worse than 20/200 in at least one eye; severe, fixed, attack-related weakness (MRC \leq grade 2) in one or more limbs [57].

In 2006 the diagnostic criteria for Devic's syndrome have been updated by D. Wingerchuk et al. The absolute criterion considered simultaneous optic neuritis and transverse myelitis. Moreover, it should be noted the presence of at least one of the following three additional criteria (adjacent spinal MRI lesions lasting three vertebral segments in length or greater, or MRI, which do not meet the diagnostic criteria for MS, or AQP4 IgG positive) [58].

TREATMENT

PROPHYLACTIC TREATMENT

In patients with acute attacks of NMO or high-risk syndrome and who are NMO-IgG-seropositive the early prophylactic treatment is recommended due to an increased risk of relapses in the future after isolated transverse myelitis [55].

At the beginning of longitudinal therapy it is recommended to use azathioprine (2.5-3mg/kg/daily) associated with oral prednisone (1mg/kg/daily) which effectiveness has been proved over a period of 18 months. Moreover, rituximab as a chimeric anti-CD20 monoclonal antibody is also applied in the initial treatment. Each patient receives four infusions of intravenous rituximab (375 mg/m²) once per week for four weeks or 1000mg infused twice with a 2-week interval between the infusions. In study conducted by Cree BAC et al. six of eight patients have not experienced the attack during 12 months rituximab therapy and in seven out of eight patients the recovery of the neurologic function has been observed.

In turn, immunosuppressant treatment in the form of mitoxantrone (12mg/m²), methotrexate (50mg weekly) or mycophenolate mofetil is recommended in case of first line treatment failure or contraindication to the use of first line drugs [33]. Whereas in children and patients with contraindications for immunosuppressant therapy intravenous immunoglobulins are effective. In the most severe cases of patients, third line therapy can be applied using recombinant monoclonal antibodies directed against the receptor for IL-6 (tocilizumab) [4].

TREATMENT OF ACUTE ATTACKS

In patients with acute course of NMO it is recommended to introduce high-dose intravenous methylprednisolone (1 g daily for five days) as the initial treatment. Then, if the patient's condition does not improve, plasmapheresis or immunoadsorption should be performed. Whereas in children and patients with contraindications for immunosuppressant therapy, intravenous immunoglobulins in a dose of 0.7g/kg daily for three days are recommended [60].

CONCLUSIONS

Devic's disease is one of the numerous demyelinating diseases, which the course and symptoms make for clinician both diagnostic and therapeutic difficulties. Therefore, it is very important to differentiate NMO from other demyelinating disorders such as multiple sclerosis. Unilateral or bilateral optic neuritis with transverse myelitis in the absence of clinical evidence of disease elsewhere in the CNS are the main diagnostic criteria of NMO. The literature describes two forms of Devic's disease – monophasic and relapsing. Monophasic is more severe but enjoys a better long-term prognosis, whereas relapsing often leads to severe disability where the use of immunosuppressive therapy is essential. Despite numerous studies, the pathogenesis of NMO is not well known yet, but further studies on understanding the mechanisms responsible for the disclosure of NMO may contribute an important element for the correct diagnosis of Devic's disease and develop appropriate treatment.

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ABSTRACT

Devic's disease (neuromyelitis optica, NMO) is a severe idiopathic demyelinating disease of the central nervous system (CNS), which mainly affects the spinal cord and the optic nerves. For a long time NMO was considered as a variant of multiple sclerosis (MS), however in terms of laboratory, clinical and immunological features they constitute two different disease entities which require separate treatment. Extremely important was the discovery (2006) of aquaporin-4 (AQP-4) water channel, which by binding to IgG antibodies in the central nervous system plays an essential role in damage to the myelin sheath. Devic's disease is more common in women

than men and the average age of onset is about 39 years. The aim of this article was to present Devic's disease and the role of aquaporin - 4 in its pathogenesis. This article has been written on the basis of Pub Med articles and other resources. Recent studies have increasingly captured the important role of NMO antibodies aquaporin-4 in the pathogenesis of Devic's disease. AQP-4 is a component of water channels in the CNS, located on the feet astrocytes. NMO - IgG antibodies recognize a fragment of the extracellular aquaporin 4 and come to the immune response. The diagnosis of NMO requires two absolute criteria(optic neuritis and acute myelitis) and at least one of the three auxiliary features(the presence of NMO- antibodies AQP-4, brain MRI not meeting diagnostic criteria for MS and contiguous spinal cord MRI lesions occupying at least three adjacent vertebral segments). Typical treatment of MS is ineffective in Devic's disease, and it exacerbates symptoms. In patients with acute course of NMO, high-doses of intravenous corticosteroids are recommended. However, immunosuppressive treatment is important in the prevention of relapses, which should be treated as main goals in the NMO therapy. The distinction of Devic's disease and MS is very important for clinical practice and application of the appropriate therapeutic treatment. On the basis of clinical, serological and neuroimaging features it is possible to distinguish NMO from other demyelinating diseases. Despite numerous studies on the participation of antibodies in the NMO pathogenesis, their role has not been confirmed yet, but their detection has allowed for the extension of diagnostic criteria. Further studies on understanding the mechanisms responsible for disclosure of NMO may constitute an important element for making correct diagnosis of Devic's disease and develop effective treatment.

STRESZCZENIE

Choroba Devica(zapalenie nerwu wzrokowego i rdzenia, NMO) jest idiopatyczną chorobą demielinizacyjną ośrodkowego układu nerwowego (OUN) o ostrym przebiegu, dotyczącą przede wszystkim rdzenia kręgowego i nerwów wzrokowych. Przez długi okres czasu NMO uważane było za wariant stwardnienia rozsianego(SR), jednakże pod względem parametrów laboratoryjnych, klinicznych i immunologicznych są to dwie różne jednostki chorobowe, które wymagają zastosowania odrębnego leczenia. Niezwykle ważnym okazało się odkrycie w 2006 roku kanału wodnego akwaporyny-4 (AQP-4), który poprzez wiązanie się z przeciwciałami IgG w obrębie ośrodkowego układu nerwowego pełni zasadniczą rolę w uszkodzeniu mieliny. NMO występuje z większą częstotliwością u kobiet niż u mężczyzn, a średni wiek zachorowania wynosi około 39 lat. Celem artykułu było omówienie choroby Devica oraz roli akwaporyny-4 w jej patogenezie. Artykuł ten został napisany w oparciu o wiadomości zaczerpnięte z bazy PubMed i innych źródeł. Najnowsze badania coraz częściej podkreślają ważną rolę przeciwciał przeciwko akwaporynie-4 w patogenezie choroby Devica. AQP-4 jest składnikiem kanałów wodnych zlokalizowanych w ośrodkowym układzie nerwowym(OUN) na powierzchni astrocytów. Przeciwciała NMO-IgG rozpoznają fragment zewnątrzkomórkowy akwaporyny-4, co w efekcie wywołuje odpowiedź immunologiczną. Do rozpoznania NMO

konieczne jest spełnienie dwóch bezwzględnych kryteriów klinicznych (zapalenie nerwu wzrokowego i rdzenia kręgowego) oraz co najmniej jednego z trzech kryteriów pomocniczych (obecność przeciwciał przeciw AQP4, obecność zmian w MRI niespełniających kryteriów SM oraz uszkodzenie rdzenia kręgowego zajmujące co najmniej 3 segmenty rdzeniowe). Typowe leczenie stosowane w SM jest nieskuteczne w przebiegu NMO, a ponadto zaostrza objawy choroby. W przypadku pacjentów z ostrym przebiegiem choroby zalecane jest stosowanie wysokich dawek kortykosteroidów podawanych dożylnie. Z kolei leczenie immunosupresyjne jest niezwykle ważne w celu zapobiegania nawrotom schorzenia, co powinno stać się główną domeną terapii NMO. Rozróżnienie choroby Devica i SM jest niezmiernie ważne w praktyce klinicznej, jak również implikuje możliwości włączenia odpowiedniego leczenia. Na podstawie objawów klinicznych, badań serologicznych i neuroobrazowych możliwe staje się wyłonienie NMO z grupy wielu innych chorób demielinizacyjnych. Pomimo licznych badań dotyczących udziału przeciwciał w patogenezie NMO ich rola nie została jeszcze do końca poznana, aczkolwiek pozwoliło to na rozszerzenie kryteriów diagnostycznych choroby. Dalsze badania nad zrozumieniem mechanizmów odpowiedzialnych za ujawnienie się NMO stanowią istotny element w dokonaniu prawidłowej diagnozy i opracowaniu skutecznego leczenia choroby Devica.

Artykuł zawiera 38155 znaków ze spacjami