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Management of a rapidly progressing severe form of multiple sclerosis in a young man: a case report

Postępowanie w przypadku gwałtownie postępującej, ciężkiej postaci stwardnienia rozsianego u młodego mężczyzny: opis przypadku

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Abstract

Identifying risk factors for rapid progression of multiple sclerosis and initiating effective treatment are crucial for preventing disability, particularly in patients with relapsing remitting disease who develop a severe, rapidly progressive form. A 21 year old man presented with progressive lower limb weakness and gait disturbance, preceded by transient symptoms. Physical examination revealed pyramidal weakness, sensory impairment, and dysmetria (Expanded Disability Status Scale, EDSS 6.0). Magnetic resonance imaging showed more than 20 contrast enhancing T2/FLAIR lesions located cortically, periventricularly, in the corpus callosum, infratentorially, and within the spinal cord. Oligoclonal bands were present in cerebrospinal fluid. Steroid therapy led to improvement, but a relapse occurred one week later (EDSS 4.0), accompanied by new magnetic resonance imaging lesions. After initiation of natalizumab, remission was achieved at 12 months (EDSS 2.0). Risk factors for rapid progression include male sex, high early disease activity, motor or cerebellar symptoms, and extensive spinal cord involvement. Early recognition of a severe, rapidly progressive form of multiple sclerosis and timely initiation of high efficacy disease modifying therapy are essential to prevent disability.

Keywords: multiple sclerosis, relapsing remitting multiple sclerosis, rapidly evolving severe multiple sclerosis, aggressive multiple sclerosis

Streszczenie

Identyfikacja czynników ryzyka szybkiej progresji stwardnienia rozsianego oraz wdrożenie skutecznego leczenia są kluczowe dla zapobiegania niepełnosprawności, zwłaszcza u pacjentów z rzutowo-remisyjną postacią, u których rozwija się ciężka, szybko postępująca postać choroby. U 21-letniego mężczyzny z postępującym osłabieniem kończyn dolnych i zaburzeniami chodu, z wcześniejszymi przemijającymi objawami, badanie fizykalne wykazało niedowład piramidowy, zaburzenia czucia i dysmetrię (Expanded Disability Status Scale, EDSS 6,0). W obrazowaniu metodą rezonansu magnetycznego stwierdzono ponad 20 zmian w sekwencji T2/FLAIR, wzmacniających się po kontraście, zlokalizowanych korowo, okołokomorowo, w ciele modzelowatym, podnamiotowo oraz w rdzeniu kręgowym. W płynie mózgowo-rdzeniowym wykryto prążki oligoklonalne. Leczenie steroidami przyniosło poprawę, jednak po tygodniu nastąpił nawrót (EDSS 4,0) z nowymi zmianami w obrazowaniu metodą rezonansu magnetycznego. Po włączeniu natalizumabu uzyskano remisję po 12 miesiącach (EDSS 2,0). Do czynników ryzyka szybkiej progresji stwardnienia rozsianego należą płeć męska, wysoka aktywność choroby we wczesnym stadium, objawy motoryczne/móżdżkowe oraz rozległe zmiany w rdzeniu kręgowym. Wczesne rozpoznanie ciężkiej, szybko postępującej postaci choroby i zastosowanie skutecznej terapii modyfikującej przebieg choroby są kluczowe dla zapobiegania niepełnosprawności.

Słowa kluczowe: stwardnienie rozsiane, rzutowo-remisyjna postać stwardnienia rozsianego, szybko rozwijająca się ciężka postać stwardnienia rozsianego, agresywne stwardnienie rozsiane

AIM OF THE STUDY

Multiple sclerosis (MS) is a demyelinating, neurodegenerative, autoimmune disease of the central nervous system. It is characterised by axonal and myelin damage as well as chronic axonal loss in the brain and spinal cord (Kuhlmann et al., 2023). The course of the condition varies between individuals. The most common clinical form is relapsing-remitting MS (RRMS), which accounts for 85% of all MS cases (Haki et al., 2024). The Expanded Disability Status Scale (EDSS) is the most widely used tool for assessing the neurological status and progression of MS (Muros-Le Rouzic et al., 2023). However, some patients develop a rapidly evolving severe type of MS (RES MS), known as its aggressive form, with frequent and severe relapses that may lead to permanent disability and higher mortality (Huisman et al., 2017). Given this, it is crucial to recognise the early symptoms of RES MS to implement appropriate treatment, thereby aiming to decelerate the progression of the disease (Fernando and James, 2017). Disease-modifying therapies (DMTs) accessible for patients with MS have demonstrated high efficacy, provided that therapy is initiated at an early stage in the course of the disease (Claflin et al., 2019).

This article discusses potential early signs of RES MS in patients, aiming to identify individuals at risk and implement precise DMT to prevent rapid progression of MS. In light of the limited data on early indicators of RES MS, this case report may help fill a critical knowledge gap, raise awareness among healthcare professionals, and contribute to improved management strategies for high-risk patients.

CASE DESCRIPTION

A 21-year-old man was admitted to the neurology ward due to progressive muscle weakness of the limbs over the preceding two weeks, resulting in significant gait impairment. The weakness initially manifested in his right lower limb before spreading to other extremities. He also reported pain in the cervical and lumbar spine. Before this episode, seven months earlier, he had experienced transient weakness in both lower limbs and balance disturbances, which resolved spontaneously without intervention within three months. This incident had been preceded by vomiting and diarrhoea, which subsided after two days – the patient did not consult any medical professionals during this period. Additionally, he had suffered a spinal injury one month before hospitalisation, after being struck by a small fragment of concrete. The pain lasted one day and was not accompanied by focal neurological deficits. The exact location of the injury could not be determined due to a lack of available data. He had also had skin lesions for two years, most probably pityriasis versicolor. The patient had no pre-existing chronic conditions.

On admission, neurological examination revealed a subtle deviation of the tongue to the right. Aside from this, cranial nerves exhibited normal function. The patient presented with paresis of the left upper limb (III/IV on the Lovett scale), grade III paresis of the left lower limb, and grade III/IV paresis of the right lower limb. Deep tendon reflexes were exaggerated, with bilateral polyclonic Achilles reflexes, bilateral positive Babinski sign, bilateral positive pathological signs in the right upper limb, diminished superficial sensation in the left upper limb, reduced superficial sensation in both lower limbs, and a pronounced Lasègue sign on the right. His gait was brachybasic, unstable, and paraparetic, requiring assistance for distances up to 20 metres. The Romberg test yielded impaired results. On the EDSS, he was evaluated as 6.0 (0, 0, 4, 2, 3, 0, 0) (3).

INVESTIGATIONS

Brain magnetic resonance imaging (MRI) with gadolinium performed during the patient's hospitalisation revealed

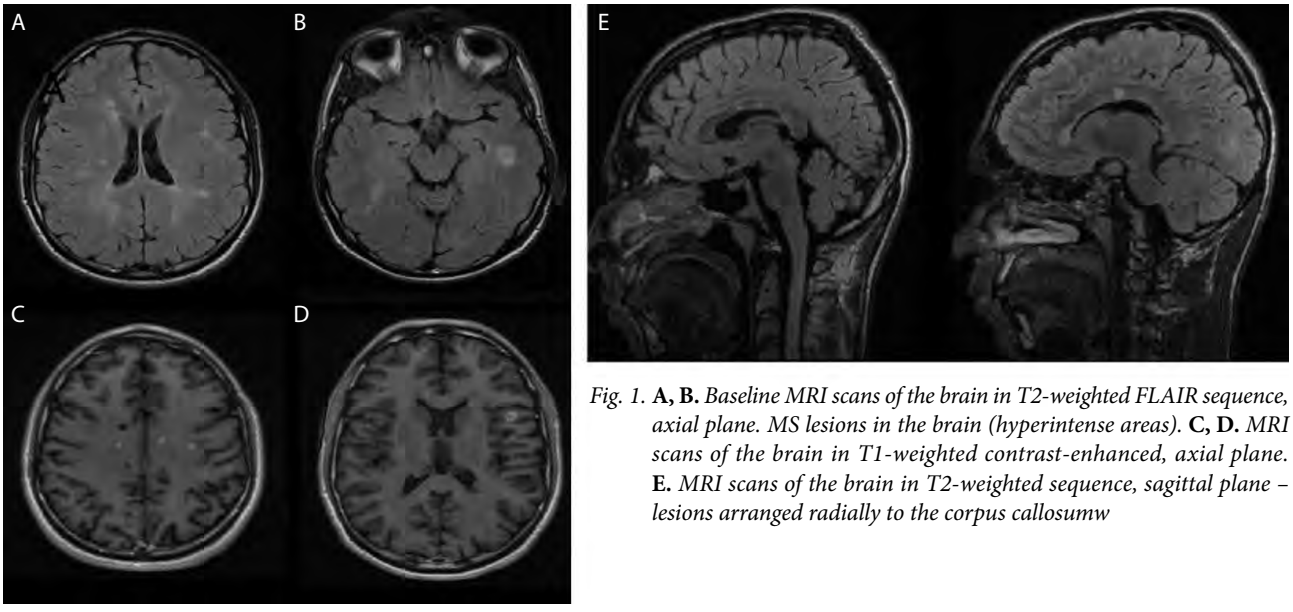

Fig. 1. **A, B.** *Baseline MRI scans of the brain in T2-weighted FLAIR sequence, axial plane. MS lesions in the brain (hyperintense areas).* **C, D.** *MRI scans of the brain in T1-weighted contrast-enhanced, axial plane.* **E.** *MRI scans of the brain in T2-weighted sequence, sagittal plane – lesions arranged radially to the corpus callosumw*

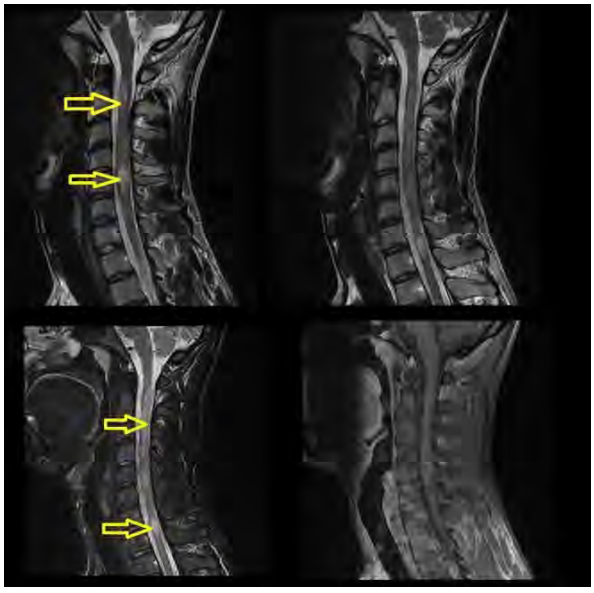

Fig. 2. Baseline MRI scan of the cervical spinal cord in T2-weighted, STIR, and T1-weighted contrast-enhanced, sagittal plane. MS lesions in the spinal cord

numerous (>20) high-signal areas in T2 and fluid-attenuated inversion recovery (FLAIR) sequences, measuring up to 13 mm, located in the white matter of both hemispheres (Fig. 1 A, B, C, D, E). Most of these lesions exhibited pathological contrast enhancement, with some displaying a ring-enhancing pattern. At least three morphologically similar areas were identified subtentorially. Some of the larger lesions in the left temporal and right frontal lobes exhibited partial suppression on FLAIR sequences, which intensified following contrast administration. A significant number of lesions were situated radially toward the corpus callosum, with MRI additionally detecting four high-signal areas within the corpus callosum on T2 and T2/FLAIR sequences (Fig. 1E).

MRI of the cervical spine revealed demyelinating lesions at the level of the odontoid on the right side at C2, as well as at C3–C5, and C7–Th1. All lesions showed contrast enhancement (Fig. 2).

Laboratory testing indicated the presence of oligoclonal bands in the distribution of cerebrospinal fluid (CSF) proteins, but none were found in the serum protein fraction. There was pleocytosis in the CSF at 8 cells per microliter. Serological testing for *Borrelia*, HIV (human immunodeficiency virus), HCV (hepatitis C virus), HBV (hepatitis B virus), AMPA 2 (AMPA 2 receptor antibodies), GABBR1 (gamma-aminobutyric acid type B receptor antibodies), LGI1 (leucine-rich glioma-inactivated 1 antibodies), NMDA (anti-*N*-methyl-D-aspartate receptor antibodies), CASPR 2 (contactin-associated protein-2 antibodies), and AMPA 1 (AMPA 1 receptor antibodies) was negative. The patient was tested for autoantibodies. A trace of ANA Ig IIFT (ANA Immunoglobulin Indirect Immunofluorescence Test) was found, while anti-PM-Scl 100 antibodies

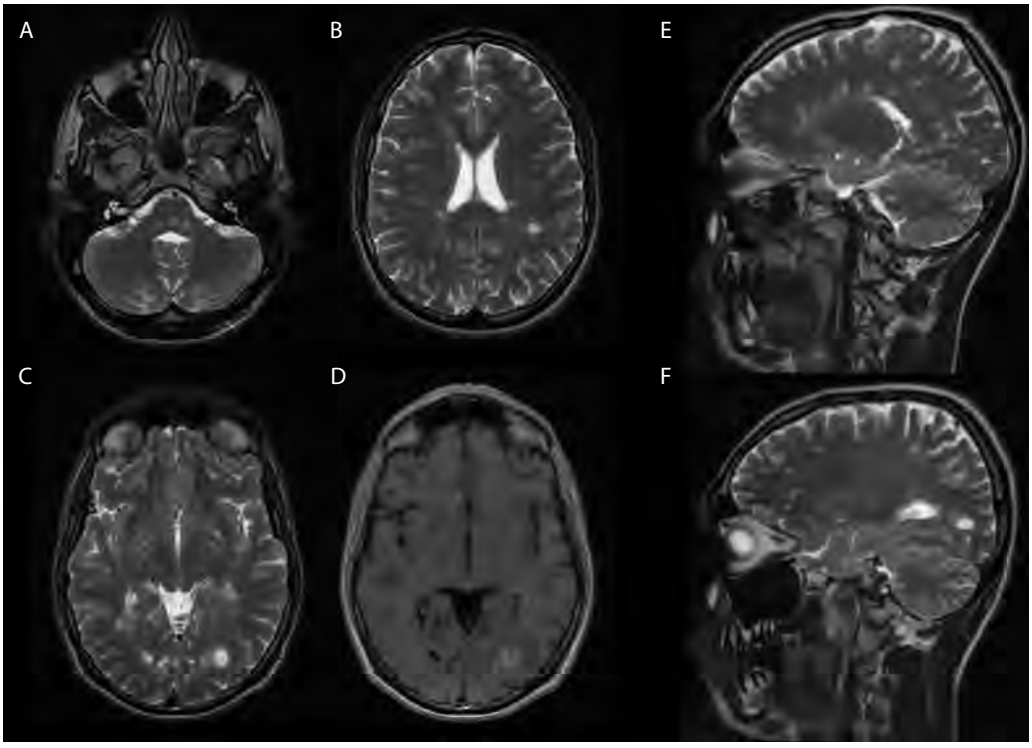

Fig. 3. **A, B.** *MRI scans of the brain in T2-weighted FLAIR sequence, axial plane, at four weeks. MS lesions in the brain (hyperintense areas).* **C, D.** *MRI scans of the brain in T1-weighted contrast-enhanced sequence, axial plane.* **E, F.** *MRI scans of the brain in T2-weighted sequence, sagittal plane – lesions arranged radially to the corpus callosum*

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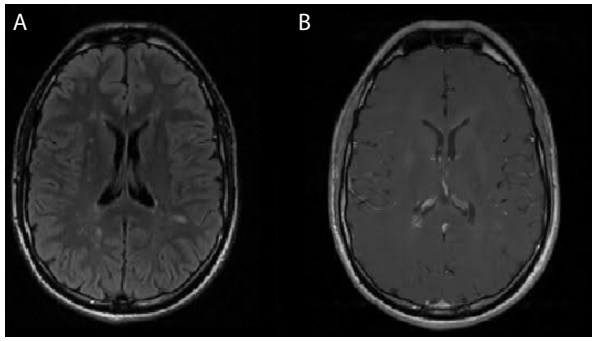

Fig. 4. **A.** *Follow-up MRI scan of the brain in T2-weighted FLAIR sequence, axial plane. MS lesions in the brain (hyperintense areas).* **B.** *Follow-up MRI scan of the brain in T1-weighted contrast-enhanced sequence, axial plane*

(associated with polymyositis/scleroderma) were positive. The John Cunningham virus (JCV) antibody test result was negative. Additionally, levels of alanine aminotransferase, aspartate aminotransferase, C-reactive protein, total bilirubin, cholesterol, gamma-glutamyl transpeptidase, and glucose were checked, revealing only elevated total cholesterol at 210 milligrams per decilitre (mg/dL) and low-density lipoprotein (LDL) cholesterol at 136.58 mg/dL. Urinalysis was normal. A chest X-ray did not reveal any abnormalities.

TREATMENT AND OUTCOME

The patient was treated with intravenous methylprednisolone (IVMP) at a dose of 1 g per day for five days. Consequently, a significant improvement in his clinical state was obtained. The sensory disturbances and coordination disorders subsided. His gait became unassisted, paraparetic, and without limitation in walking distance, with an EDSS score of 2.0 (0, 0, 2, 0, 1, 0, 0). Based on the data from his medical history, clinical course, results of additional tests, and improvement after the implemented therapy, the patient was diagnosed with RRMS. He met the McDonald 2017 diagnostic criteria (Thompson et al., 2017). Preliminarily, the patient was qualified for immunomodulatory treatment within a drug-prescription programme.

The patient was readmitted one month later due to another relapse of MS. As reported, the troubling symptoms indicating the relapse started one week after his previous hospitalisation. Neurological examination on admission revealed a subtle deviation of the tongue to the left. Aside from this, cranial nerves exhibited normal function. There was paresis of both lower limbs, more pronounced on the right (rated IV on the Lovett scale), paresis of both upper extremities (IV/V), inability to jump on his toes, bilateral foot clonus, exaggerated deep reflexes – polyclonic quadriceps reflex on the left, absent abdominal reflexes, no pathological signs, balance and coordination disorders, hypertonia in both lower limbs (more pronounced on the left), impaired diadochokinesia, ataxia in both upper extremities with intention tremor, reduced superficial sensation in both upper limbs, rachialgia, and pain in the left lower limb. His gait was brachybasic and rigid, with tandem walking. Walking distance was up to 500 m (progressing for two weeks).

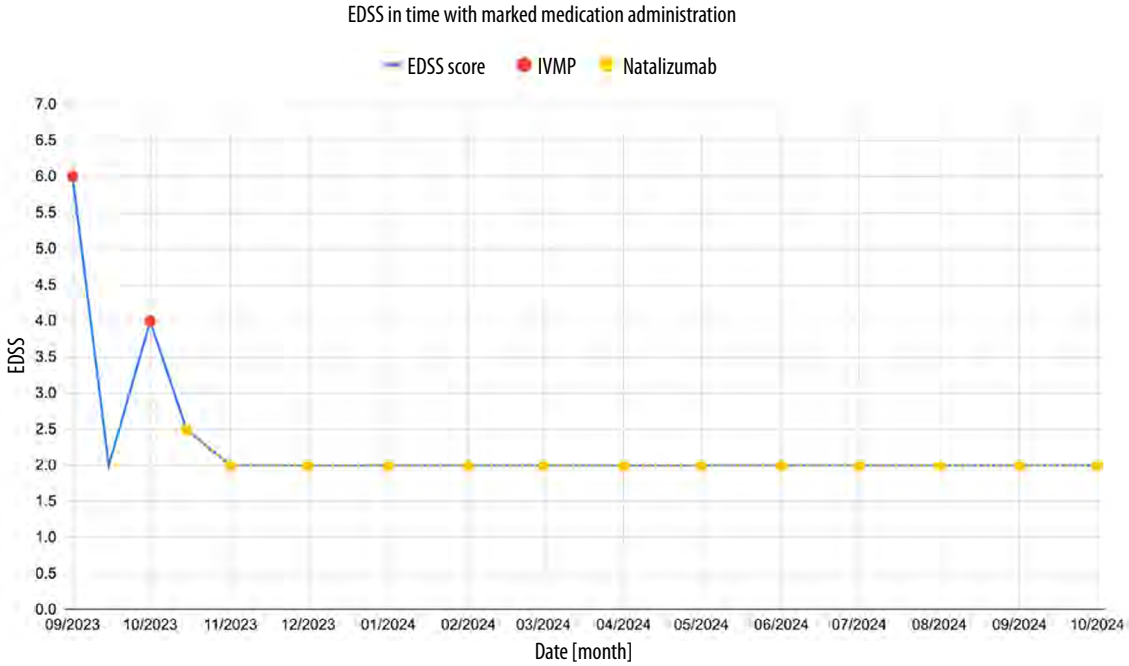

Fig. 5. Graph illustrating disease progression in the patient with rapidly evolving severe MS, based on EDSS scores, with marked points of medication administration

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He also reported urge incontinence. The EDSS score was 4.0 (0, 1, 3, 3, 3, 2, 0). Brain MRI revealed new demyelinated plaques in the cortical-subcortical location and paraventricularly with contrast enhancement, some displaying a ring-enhancing pattern (Fig. 3 A, B, C, D, E, F). Several plaques that were visible on the previous MRI scan appeared slightly reduced in size.

As during the previous relapse, he was treated with IVMP (1 g per day for five days), resulting in partial remission of neurological deficits. Hypoaesthesia in both upper extremities, ataxia, and gait difficulties improved. He had foot clonus, hypertonia in both lower limbs, micturition disorder, and brachybasic gait; the EDSS score was 2.5 (0, 1, 2, 2, 2, 2, 0). Given the patient's history of more than two relapses and the presence of multiple lesions on the MRI of the brain, including active plaques, a diagnosis of RES MS was made (Brola et al., 2022). Due to the aggressive course of the disease, the patient received the first dose of a high-efficacy treatment agent (HETA): 300 mg intravenous natalizumab. No adverse effects of the drug were observed during administration. He was discharged with a recommendation to continue treatment within a drug-prescription programme, with the next natalizumab administration scheduled in four weeks.

Four weeks later, he was admitted for the second dose of natalizumab. No adverse effects of the drug were observed. During hospitalisation, a follow-up MRI of the brain was performed (Fig. 4). No new lesions were identified in comparison to the previous scan. There was regression of earlier plaques, and progression was observed in the size and enhancement following contrast administration in the area posterior to the body of the right lateral ventricle. There was no clinical deterioration since the previous visit. The EDSS score was 2.0 (0, 0, 2, 1, 1, 0, 0).

In the following months, the patient was admitted for subsequent doses of natalizumab, which were administered without any observed adverse effects. Neurological examination did not reveal any new findings compared with the previous admission. After 12 months of treatment, the patient had no relapses and no neurological (EDSS 2.0) or radiological progression. The disease course of this patient with RES MS is presented below (Fig. 5).

CONCLUSIONS

This case highlights the need for heightened vigilance among neurologists when assessing male patients who present with severe symptoms, short intervals between relapses, and significant motor involvement, as these factors may indicate a more aggressive disease course (Correale et al., 2023; Dyczkowska and Kalinowska, 2024). Notwithstanding the general variability in MS course and progression, early identification of patients at high risk of severe disease is paramount.

However, there is no unified definition of RES MS, and the term "aggressive MS" has been used inconsistently in the literature, often overlapping with other subtypes like fulminant MS or tumefactive MS (Dyczkowska and Kalinowska, 2024). Despite initiatives such as the 2018 ECTRIMS Workshop, a universal, evidence-based definition remains elusive, complicating early recognition and management (Tur et al., 2023). Current definitions often rely on retrospective observations, highlighting the need for further research to identify predictive factors and standardise diagnostic criteria. Early, frequent relapses, particularly within the first two years of disease onset, and older age at onset are strong predictors of a more aggressive MS course (Iacobaeus et al., 2020). Additionally, a higher number of T2 lesions on initial MRI scans is a predictor of more severe disease progression (Hoffmann et al., 2024).

In this case, the patient presented with several early indicators of RES MS: male sex, frequent and severe relapses, and pronounced motor involvement. His primary symptoms included gait disturbances (brachybasia, instability, and paraparesis). His EDSS score was 6.0 at the first hospitalisation, and 4.0 following the second relapse. The interval between the two disabling relapses was four weeks.

Our findings align with previous studies suggesting that early initiation of high-efficacy DMTs (HETAs) can significantly alter the disease trajectory and improve long-term outcomes (Claflin et al., 2019; Fernando and James, 2017). This case underscores the importance of commencing DMT at an early stage. Evidence suggests that HETAs as natalizumab and alemtuzumab, and the moderately high-efficacy DMT fingolimod are effective in patients with high-risk, rapidly evolving RRMS, reducing the progression of the disease (Cañibano et al., 2024; Chapell et al., 2024; Dominguez-Mozo et al., 2025; Galota et al., 2025; Sainz-Amo et al., 2024). The choice of specific therapy should be tailored to be individual characteristics and needs of each patient (Kułakowska et al., 2024). In this case, the patient was treated with natalizumab for 12 months. At his most recent annual follow-up, his EDSS score had improved to 2.0, demonstrating significant symptom alleviation. Natalizumab is a humanised monoclonal antibody that targets the α4-integrin subunit of leukocyte adhesion molecules, thereby preventing their interaction with endothelial cells. This blockade inhibits the migration of autoreactive leukocytes into inflamed tissues, thereby reducing inflammation. The effectiveness of natalizumab in treating MS and Crohn's disease is due to its ability to prevent leukocyte adhesion and extravasation into the central nervous system and intestinal tissues, respectively (Khoy et al., 2020). However, another case study suggests that plasma exchange and a prolonged course of IV methylprednisolone (more than three days) may be more effective than a standard regimen in treating initial relapses, before implementing natalizumab (Fernando and James, 2017). Clinicians prescribing natalizumab must be aware of the risk of progressive multifocal leukoencephalopathy (PML) associated with its use. The most effective current management strategy involves screening patients for the JCV antibody index to assess risk

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and discontinuing treatment at the earliest signs suggestive of PML (Glenn et al., 2025; Saji and Gupta, 2025). Recent evidence indicates that switching from natalizumab to anti-CD20 therapy is both safe and effective. A transition period of up to four weeks, depending on the time needed to exclude PML, offers the best balance between safety and disease control (Bsteh et al., 2025).

To summarise, the present case demonstrates several significant features of RES MS. Although it concerns a single patient, it underscores that male sex, a high relapse rate, the presence of initial motor and cerebellar symptoms, a high number of T2-weighted lesions on baseline MRI, and infratentorial spinal cord involvement are all strong indicators of rapid MS progression. Early recognition of RES MS and the administration of a high-efficacy induction DMT (HETA) are crucial for preventing permanent disability.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organisations which might negatively affect the content of this publication and/or claim authorship rights to this publication.

Ethics approval

As this is case report describes clinical observations, ethics approval was waived. The patient provided written informed consent to participate in this study according to the principles of the World Medical Association's Declaration of Helsinki.

Author contribution

Original concept of study: AB. Collection, recording and/or compilation of data: AB, MR. Analysis and interpretation of data: AB, HB. Writing of manuscript: AB, HB, ME. Critical review of manuscript: MR, JS. Final approval of manuscript: MPO, JS.

References

Brola W, Adamczyk-Sowa M, Kułakowska A et al.: Highly active disease and access to disease-modifying treatments in patients with relapsing-remitting multiple sclerosis in Poland. Neurol Neurochir Pol 2022; 56: 256–260.

Bsteh G, Hoepner R, Gernert JA et al.: Switching from natalizumab to antiCD20 monoclonal antibodies: short transition interval is associated with improved outcome. Eur J Neurol 2025; 32: e16587.

Cañibano BG, Okar L, Baniamer YZ et al.: Real world experience with cladribine tablets in the management of relapsing multiple sclerosis in Qatar. Clin Neurol Neurosurg 2024; 247: 108615.

Chappell M, Sanderson A, Arun T et al.: Literature review and meta-analysis of natalizumab therapy for the treatment of highly active relapsing remitting multiple sclerosis in the 'suboptimal therapy' patient population. J Neurol Sci 2024; 464: 123172.

Claflin S, Broadley S, Taylor B: The effect of disease modifying therapies on disability progression in multiple sclerosis: a systematic overview of meta-analyses. Front Neurol 2019; 9: 1150.

Correale J, Rush CA, Barboza A: Are highly active and aggressive multiple sclerosis the same entity? Front Neurol 2023; 14: 1132170.

Dominguez-Mozo MI, Galán V, Ramió-Torrentà L et al.: A two-years real-word study with fingolimod: early predictors of efficacy and an association between EBNA-1 IgG titers and multiple sclerosis progression. Front Immunol 2024; 15: 1384411.

Dyczkowska K, Kalinowska A: Facts and myths about aggressive relapsing-remitting multiple sclerosis – current state of knowledge and future perspectives. Neurol Neurochir Pol 2024; 58: 548–556.

Fernando K, James M: Early predictors of rapidly evolving multiple sclerosis: a case report. J Neuroimmunol 2017; 307: 42–46.

Galota F, Marcheselli S, De Biasi S et al.: Impact of high-efficacy therapies for multiple sclerosis on B cells. Cells 2025; 14: 606.

Glenn T, Berger JR, McEntire CRS: Natalizumab-associated progressive multifocal leukoencephalopathy. Front Neurol 2025; 16: 1575653.

Haki M, AL-Biati HA, Al-Tameemi ZS et al.: Review of multiple sclerosis: epidemiology, etiology, pathophysiology, and treatment. Medicine (Baltimore) 2024; 103: e37297.

Hoffmann O, Gold R, Meuth SG et al.: Prognostic relevance of MRI in early relapsing multiple sclerosis: ready to guide treatment decision making? Ther Adv Neurol Disord 2024; 17: 17562864241229325.

Huisman E, Papadimitropoulou K, Jarrett J et al.: Systematic literature review and network meta-analysis in highly active relapsing-remitting multiple sclerosis and rapidly evolving severe multiple sclerosis. BMJ Open 2017; 7: e013430.

Iacobaeus E, Arrambide G, Amato MP et al.: Aggressive multiple sclerosis (1): towards a definition of the phenotype. Mult Scler J 2020; 26: 1031–1044.

Khoy K, Mariotte D, Defer G et al.: Natalizumab in multiple sclerosis treatment: from biological effects to immune monitoring. Front Immunol 2020; 11: 549842.

Kuhlmann T, Moccia M, Coetzee T et al.: Multiple sclerosis progression: time for a new mechanism-driven framework. Lancet Neurol 2023; 22: 78–88.

Kułakowska A, Mirowska-Guzel D, Kalinowska A et al.: Disease-modifying therapy in multiple sclerosis: recommendations of Multiple Sclerosis and Neuroimmunology Section of Polish Neurological Society. Neurol Neurochir Pol 2024; 58: 569–585.

Muros-Le Rouzic E, Ghiani M, Zhuleku E et al.: Claims-based algorithm to estimate the Expanded Disability Status Scale for multiple sclerosis in a German health insurance fund: a validation study using patient medical records. Front Neurol 2023; 14: 1253557.

Sainz-Amo R, Rodero Romero A, Monreal E et al.: Effect of alemtuzumab over sNfL and sGFAP levels in multiple sclerosis. Front Immunol 2024; 15: 1454474.

Saji AM, Gupta V: Progressive multifocal leukoencephalopathy. In: StatPearls [Internet]. StatPearls Publishing, Treasure Island, FL 2025–.

Thompson A, Banwell B, Barkhof F et al.: Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol 2017; 17: 162–173.

Tur C, Carbonell-Mirabent P, Cobo-Calvo Á et al.: Association of early progression independent of relapse activity with long-term disability after a first demyelinating event in multiple sclerosis. JAMA Neurol 2023; 80: 151.