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Statin-associated exacerbation of myasthenia gravis

Michael S. Cartwright, MD; Douglas R. Jeffery, MD, PhD; Geoffrey R. Nuss, BA; and Peter D. Donofrio, MD

Myasthenia gravis (MG) can be exacerbated by a variety of medications, which increase weakness by interrupting neuromuscular junction transmission. Statins, which lower lipids by inhibiting 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, are not commonly known to worsen MG or have activity against the neuromuscular junction. One report suggested that statin therapy produced ocular myasthenia. However, based on the case description, it is not clear that this patient had MG. We present a patient with well-documented MG who experienced worsening of his condition after taking different statins on four separate occasions.

Case report. A 55-year-old man with hyperlipidemia and borderline hypertension was evaluated for a 1-year history of intermittent dysarthria. He first noticed dysarthria ~1 week after the initiation of atorvastatin. At that time, MRI and blood work revealed no evidence of a stroke or elevation in his creatine kinase (CK) level. He stopped atorvastatin, and within 1 week the dysarthria resolved. During the next 8 months, he tried three other statins (lovastatin, pravastatin, and simvastatin). With each statin, the dysarthria returned in ~1 week and resolved after stopping the medication. There was no elevation in his CK after the use of any of the statins. When he sought treatment in our medical center, he had experienced several weeks of dysarthria despite avoiding statin therapy for the previous 4 months. The dysarthria was worse in the evening and after prolonged periods of talking. On examination, he was markedly dysarthric. He had normal tongue movements and was not hypophonic. No cranial nerve abnormalities or proximal muscle weakness was detected. Retinerve stimulation abnormalities were consistent with MG. The facial nerve showed a 50% decrement at baseline and >50% decrement at 50, 60, 120, and 180 seconds postexercise. The ulnar nerve showed a 6 to 7% decrement, and the spinal accessory nerve showed a 10 to 12% decrement postexercise. His acetylcholine receptor antibody level was >7.5 nmol/L (normal, <0.4 nmol/L). EMG did not reveal a myopathy, and CT of the chest did not show a thymoma. He was started on pyridostigmine (60 mg TID) and experienced rapid improvement in his speech.

Discussion. To our knowledge, the only report in the literature associating statin use with worsening myasthenic symptoms involved a patient who developed ocular and systemic weakness on four separate occasions: three times with statins and once with a fibrate. However, it is not clear that this patient had MG because no laboratory testing verified the diagnosis. Our patient's history, repetitive nerve stimulation results, acetylcholine receptor antibody levels, and response to pyridostigmine substantiate the diagnosis of MG. It appears likely that statin use exacerbated his symptoms, given that dysarthria occurred on four separate occasions after four different statins, and each time he improved after discontinuation of the medication.

Medications that exacerbate MG are thought to interrupt transmission in the neuromuscular junction. Statins, which block HMG-CoA reductase, are not known to interfere with neuromuscular junction transmission, but we propose three ways that statins could potentially worsen MG. First, it is now understood that statins have immunomodulatory properties, including the ability to induce production of the Th2 cytokines interleukin (IL)-4, IL-5, and IL-10. Animal and human studies suggest that these Th2 cytokines play a role in the development of MG; therefore, it is possible that by up-regulating Th2 cytokine production, statins could lead to worsening MG.

Second, statins have been postulated to cause mitochondrial dysfunction by depleting endogenous coenzyme Q10. The presynaptic nerve ending and the postsynaptic junction are rich in mitochondria. For this reason, statin-induced mitochondrial dysfunction could interrupt transmission in the neuromuscular junction and worsen MG.

A third theory is that a statin myopathy could exacerbate the underlying weakness of MG. Myopathy is a well-described side effect of statins, and it ranges from mild without CK elevation to overt rhabdomyolysis. It is possible that in addition to having MG, the patient described in our case also experienced a statin myopathy. This dual-hit hypothesis may explain why the association between statin use and exacerbation of MG has not been extensively documented.

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References


The fragile X premutation presenting as postprandial hypotension

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The fragile X-associated tremor/ataxia syndrome (FXTAS) is a neurodegenerative disorder consisting of progressive intention tremor and cerebellar ataxia recently described in men with the premutation (55 to 200 CGG repeats) in the promoter region of the fragile X mental retardation 1 (FMR1) gene and with grandchilden with fragile X syndrome (FXS). We describe here a patient with postprandial hypotension and intention tremor carrying an FMR1 premutation allele and without a family history for FXS.

Case report. A 73-year-old man was referred to our clinic for episodes of blurred vision, dizziness, and weakness appearing after meals and associated with low blood pressure (BP) values. These episodes began 1 year before our visit, but the patient also had bilateral hand tremor with onset at age 71 years, mostly pronounced with posture and action. His family history was unremarkable for peculiar neurologic disorders: he had two healthy sons aged 42 and 39 years and two healthy grandchildren. Moreover, he had only two sisters: one died at age 38 years during delivery, and the other died at age 80 years from bronchopneumonia and had healthy children and grandchildren (two males and one female). Neurologic examination revealed facial hypomimia and plantar responses were normal. There was no ataxia, and stance and gait were normal, including tandem gait. A general cognitive screen was normal (Mini-Mental State Examination score, 25/30), but speech and memory problems and executive function deficits could not be excluded because a more complete neuropsychological testing was not done. EEG, EMG, and nerve conduction studies were normal, as was sympathetic skin response recorded...
carriers are needed to confirm whether BP dysautonomia is a
nomia. Nevertheless, further studies on more
may reveal additional carriers among patients with BP dysauto-
FXTAS and suggests that DNA testing for the
reported cases of FXTAS were identified from families with
function occurring in atypical Parkinson disease or multiple
orthostatic increase in heart rate: these changes of systolic BP were
progressed, involving her right hand and 1 year later, the left. The
tremor in her upper extremities predominantly occurred at rest;
however, she also stated that occasionally she would experience a
tremor in her hands while holding a cup of coffee or a deck of
cards. She carried a diagnosis of Parkinson disease, but her
tremor did not improve with 1,000 mg of L-dopa/carbidopa ther-
apy, which she took for 3 months. Her family history was interest-
There is growing evidence that the clinical phenotypes of FX-
TAS may be more heterogeneous than previously thought. FMRI
premutations have been reported in patients with essential tremor
and in cases of sporadic ataxia without a family history for
FXTAS. Our report adds further evidence to the clinical spectrum of
FXTAS and suggests that DNA testing for the FMRI premutation
may reveal additional carriers among patients with BP dysautono-
ma. Nevertheless, further studies on more FMRI premutation
carriers are needed to confirm whether BP dysautonomia is a
clinical feature of these subjects.

Heterozygous Niemann–Pick disease type C
presenting with tremor

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Tremor is defined as rhythmic oscillation of a body part. The
differential diagnosis of tremor is extensive; however, when there
is a family history of tremor, the diagnosis most likely will be
essential tremor. We describe a woman who sought treatment for
tremor, had a family history of tremor, and was found to have a
unique diagnosis.

Case report. A 75-year-old woman was referred to the neuro-
ology department with a 10-year history of tremor, initially a side-
to-side head tremor. Five years after onset, her tremor had
progressed, involving her right hand and 1 year later, the left. The
tremor in her upper extremities predominantly occurred at rest;
however, she also stated that occasionally she would experience a

Figure. A 24-hour noninvasive ambulatory recording of
blood pressure and heart rate. Systolic blood pressure values
are on the top (continuous line); diastolic blood pressure
values are in the middle (dashed line); and heart rate
values are on the bottom (dotted line).
Radicular myoclonus induced by repetitive neck movements in a patient with cervical spondylosis

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Myoclonus results from abnormal activity in many different parts of the CNS. Only a few cases of peripheral nervous system-generated myoclonus have been reported in patients with spinal root lesion. We report a patient who developed a cervical segmental myoclonus immediately after prolonged repetitive flexion-extension neck movements.

Case report. A 67-year-old man developed neck pain and tension. In an attempt to reduce neck tension, he started to perform repetitive flexion-extension neck movements for ~10 minutes every morning. After a few days, he developed involuntary jerking of the right shoulder immediately after repetitive flexion-extension neck movements. The general practitioner, who thought that this was a simple partial seizure, injected the patient with 2 mg diazepam ~30 minutes after the onset of symptoms and again 2 hours later, but the treatment was ineffective. Subsequent recordings showed two different rates of involuntary movements. When the frequency of involuntary movements was 0.5 Hz, it changed to 1.7 Hz after hyperventilation. No signs of denervation were found. The blink reflex and its recovery cycle were normal. Motor evoked potentials and somatosensory evoked potentials (SEPs) after stimulation of radial, median, and ulnar nerve were normal. The recovery cycle of the spinal SEPs evoked by pairs of stimuli to the radial nerve, which distributes to the C6 and C7 dermatomes, was normal. This test may reveal excitability changes within the dorsal horn in segmental myoclonus of spinal origin. Cervical cord MRI revealed that the right C6 neural foramen was narrowed because of degenerative spondylopathic changes, the spinal cord being normal. The patient stopped the morning stretching activity of neck muscles. The movements resolved in the next 3 days.

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originated at the peripheral level, conceivably from the C6 root. It is likely that the repetitive flexion-extension neck movements had determined a transient mechanical irritation of this root. Ephaptic transmission or ectopic excitation of the spinal root may cause the involuntary movements in spinal root lesions. However, this mechanism could not explain the sensitivity to hyperventilation of the myoclonus and the presence of two definite frequencies. One possibility is that it originates from retrograde impulse propagation along the relatively intact motor root consequent to the mechanical irritation. The abnormal activity originating from mechanical irritation is known as back-discharge. A similar abnormal retrograde activity may trigger the repetitive discharge of the anterior horn cells of the corresponding segmental spinal cord. The interaction between the ongoing activity in the segmental spinal cord circuitry (that oscillates continuously in response to segmental and suprasegmental inputs) and the retrograde activation would determine the frequency and amplitude of involuntary movements, and would justify the presence of more than one pattern of involuntary activity. Hyperventilation could produce an increment in the involuntary activity through the alkalosis that increases neuronal excitability.

Myoclonus associated with a root lesion has been reported in two cases that showed clinical findings similar to those of the present patient with involuntary movements confined to muscles supplied by a single root. In the first patient, who had a tumor mass in the intervertebral foramen between the fourth and fifth thoracic vertebrae, the involuntary movement disappeared after local radiotherapy. The second patient, who had an L3 degenerative radiculopathy, was successfully treated with valproate and clonazepam.

Primary respiratory failure in inclusion body myositis

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The idiopathic inflammatory myopathies are a group of disorders characterized by acquired muscle weakness and presence of inflammatory infiltrates in skeletal muscle. The three most common diseases within this group are dermatomyositis (DM), polymyositis (PM), and inclusion body myositis (IBM). Respiratory muscle weakness with respiratory failure is a well-recognized complication in DM and IBM but has only rarely been reported in PM. Symptomatic respiratory failure in IBM is considered to be secondary to coincidental pulmonary disease. We report a patient with IBM who developed subacute respiratory failure caused by primary respiratory muscle weakness.

Case report. A 58-year-old woman sought treatment for slowly progressive muscle weakness, dysphagia, and weight loss. Her medical history was unremarkable, and she did not use any myotoxic drugs. Physical examination revealed normal speech, mild facial weakness, dysphagia without aspiration, and generalized muscle weakness (Medical Research Council score, 4) with asymmetric weakness of the forearm muscles (right, MRC 4; left, MRC 3). Muscle atrophy was most pronounced in the forearm muscles. Creatine kinase was mildly increased (285 U/L; normal, MRC 3). Muscle atrophy was most pronounced in the quadriceps muscles. By EMG, the presence of severe respiratory failure made us reconsider her diagnosis. Empirical treatment with prednisone (50 mg daily for 4 weeks) resulted in minimal increase in muscle strength. Needle-conduction studies of the phrenic nerve demonstrated low amplitudes of the compound motor action potential of the diaphragm bilaterally. EMG revealed poor recruitment without spontaneous activity of the diaphragm and intercostal muscles. Muscle biopsy from the tibialis anterior showed myopathic changes with invasion of non-necrotic muscle fibers by mononuclear cellular infiltrates, basophilic rimmed vacuoles, and sarcocellular HLA-1 antigenicity of all muscle fibers, consistent with the diagnosis of IBM (figure). Pulmonary function testing revealed mildly impaired vital capacity (1.87 L; normal, 2.60 L) and decreased mouth pressures (maximal expiratory pressure, 3.01 kPa = 307 mm H2O; normal, 8.90 kPa; maximal inspiratory pressure, 1.90 kPa = 193 mm H2O; normal, 6.90 kPa), reflecting an extraparenchymal restrictive pattern. It was concluded that the patient had IBM with respiratory muscle weakness, which had resulted in primary respiratory failure.

Discussion. Respiratory failure in patients with IBM is generally believed to occur only secondary to aspiration pneumonia or coincidental pulmonary or cardiac disease. Primary respiratory failure has, to the best of our knowledge, been reported only twice in literature. One of these reported patients had a concomitant human T-cell lymphotropic virus type 1 infection. In our patient, respiratory failure resulted from hyperventilation caused by weakness of the diaphragm and intercostal muscles. Our limited awareness of this manifestation of IBM delayed its recognition.

References


The rarity of radicular myoclonus contrasts with the high incidence of radiculopathies, and it is possible that a genetic or other factor may contribute to its development.
Cerebral toxoplasmosis in a patient with common variable immunodeficiency

Martin Holtkamp, MD; Ali Fuat Odahucu, MD; Randolf Klingebiel, MD; and Christoph J. Ploner, MD

Cerebral toxoplasmosis is commonly seen as an opportunistic disease in patients with compromised cellular immunity.1 Thus far, purely humoral immune defects, as seen in common variable immunodeficiency (CVID), have not been described to facilitate cerebral toxoplasmosis. Here, we present a patient with intracerebral mass lesions caused by toxoplasmosis, which were apparently facilitated by a humoral immune defect with combined immunoglobulin (Ig) A, IgG, and IgM deficiency.

Case report. A 52-year-old woman subacutely developed gait difficulties, impaired upper limb coordination, and swallowing and articulation difficulties. The patient had a history of CVID, which had been substituted with 10 g Igs every month. Four weeks before neurologic symptoms, an attack of autoimmune hemolytic anemia was managed with prednisolone in a dosage that was tapered from 100 to 30 mg/d.

Clinically, the patient had moderate spastic tetraparesis and severe dysarthria and dysphagia. C-reactive protein was slightly elevated to 1.1 mmol/L. Temperature, white blood cells, and differential hemogram revealed no abnormalities. Lymphocytic subpopulations were normal, except for an elevation of CD19+ B cells to 0.63×10⁹/L (normal range, 0.1 to 0.4). Igs were decreased with IgA <5 mg/dL (normal range, 70 to 400), IgG 214 mg/dL (normal, 700 to 1,600), and IgM <10 mg/dL (normal, 40 to 230). The patient tested negative for HIV-1 and -2. MRI showed bilateral hemorrhagic lesions in the basal ganglia with irregular contrast enhancement and marked perifocal edema (figure), suggestive of cerebral toxoplasmosis. CSF showed lymphocytic pleocytosis with 108 leukocytes/μL. Serologic and PCR examinations in serum and CSF were negative for neurotropic viruses of the herpes group and tuberculosis. Serologic examinations in serum and CSF were negative for Aspergillus, Candida species, cryptococcus, Borrelia burgdorferi, toxoplasmosis, and Treponema pallidum. Molecular diagnosis for these agents was not performed.

There was no evidence of systemic lymphoma on whole body CT scan, immunofixation, and bone marrow examination.

Initial treatment was polypragmatic with acyclovir, ceftriaxone, and cotrimoxazole. Dexamethasone was given for marked perifocal edema. Because diagnosis was unclear, stereotactic brain biopsy was obtained from the left basal ganglia lesion. Histology revealed an inflammatory reaction with necrotic areas, and immunohistochemical staining showed pseudocysts containing Toxoplasma gondii organisms and extracellular parasites especially in necrotic areas (see figure). Treatment with pyrimethamine and sulfadiazine was initiated. Six and 14 weeks after antitoxoplasmosis treatment was started, CSF cell count was normal. The tetraparesis had resolved, and dysarthria had moderately improved; however, dysphagia was still prominent. Clinical improvement correlated with marked shrinkage of the bilateral perifocal edema, although lesions in the basal ganglia remained unchanged (see figure).

Discussion. In this patient, neuroimaging could not differentiate between lymphoma and toxoplasmosis. Serology for toxoplasmosis was negative, but antibody production was limited by the known CVID. Brain biopsy was performed and showed pseudo-
Alopecia and cutaneous atrophy after greater occipital nerve infiltration with corticosteroid

K.G. Shields, MRCP; M.J. Levy, MRCP; and P.J. Goadsby, MD, PhD

Greater occipital nerve (GON) infiltration is used as a treatment for patients with primary and secondary headache disorders, including migraine and cluster headache. This procedure has several advantages, including ease of performance and a relative lack of complications. As the physiology of the trigeminocervical neurons is better understood and possible brain modulatory roles of greater occipital nerve stimulation are explored, the procedure may gain increased usage. In our experience, GON infiltration is highly efficacious for certain patients, particularly those with tenderness over the nerve, and it remains a valuable intervention for the management of headache disorders. It is generally without side effects. Here we report two cases in which the procedure has been complicated by a previously unreported side effect of alopecia and cutaneous atrophy. These patients represent 2 of the last 100 patients we have injected for various headache indications.

Case reports. Case 1. A 27-year-old man sought treatment for a history of headaches from childhood consistent with a diagnosis of migraine with aura. He now had chronic daily headache, with frankly migrainous exacerbations twice weekly, and was consuming compound analgesic preparations daily.

On examination, he had tenderness in the region of the right GON.

A nerve block was performed with 80 mg methylprednisolone acetate in 2 mL and 3 mL of 2% lidocaine, resulting in anesthesia [51x99]1

Figure. (A) Cross-sectional MR scans at the level of the basal ganglia. (a) Fluid-attenuated inversion recovery (FLAIR) study showing hyperintense signals within the basal ganglia bilaterally, predominantly on the left side, extending into the internal capsula and thalamus. T1-weighted unenhanced (b) and gadolinium-enhanced (c) images at the same level as in (a). Hyperintense hemorrhagic lesions are depicted within the basal ganglia and irregular contrast enhancement. (B) Neuropathologic findings from the biopsy specimens of the left basal ganglia lesion. (a) Inflammatory infiltration including histiocytes and lymphocytes (H-E, original magnification, ×400). (b) Pseudocyst within inflammation (arrow; H-E, original magnification, ×1000). (c) Giemsa-stained slide shows a pseudocyst (arrow; original magnification, ×1000). (d–f) Immunohistochemical staining for Toxoplasma gondii. Numerous extracellular organisms are present in necrotic area (d; original magnification, ×400). Inflammatory cells, an extracellular organism (arrow), and a toxoplasma pseudocyst (e; original magnification, ×400). A high-power view of this pseudocyst (f; original magnification, ×1000).
Syntelencephaly was described in 1993 as a fourth subtype of middle interhemispheric variant (MIH) of holoprosencephaly or S. Stringara, MSc; S. Bonifacino, MSc; and C. Minetti, MD.

Discussion. We describe alopecia with underlying fat atrophy after GON infiltration with lidocaine and depo-corticosteroids for the management of primary headache. This is a commonly used procedure in headache clinics, and patients and clinicians need to be aware of this possible complication. Although corticosteroids are not universally used during GON blockade, relief of headache may be prolonged after their use. This issue now needs to be revisited and defined for each headache type treated so the real risk-benefit assessment can be made.

A variety of corticosteroid preparations and doses have been used, but this side effect was not reported. The estimated occurrence of cutaneous atrophy after corticosteroid injection ranges from 1 to 14%, although there may be under-reporting. It appears to be more common in premenopausal women. Mixing corticosteroids with other solutions, such as saline or local anesthetic, should only be done if the solutions are miscible—if solubility is altered, it may result in a subcutaneous depot injection. Resolution of cutaneous atrophy is reported to occur after 6 to 7 months, although it may persist up to 24 months.

GON infiltration is undoubtedly an effective and useful treatment for certain patients. At times, it may be the only intervention to offer a patient symptomatic relief. There are currently no firm guidelines concerning patient selection or clinical features predictive of a successful outcome. There is no clear consensus on the efficacy of the procedure itself. However, given the lack of severe side effects associated with GON infiltration, it should still be considered as a useful therapy for the management of headache pain. We have described two examples of this novel complication, alopecia with fat atrophy, in a relatively small series of patients.

In light of this, we would suggest that all patients, especially women, should be advised of this cosmetic side effect when consenting to the procedure. Moreover, it seems inadvisable in general to inject the supraorbital nerve unless there is a specific indication to do so.

References


Middle interhemispheric variant of holoprosencephaly: A very mild clinical case

R. Biancheri, MD; A. Rossi, MD; P. Tortori-Donati, MD; S. Stringara, MSc; S. Bonifacino, MSc; and C. Minetti, MD

Middle interhemispheric variant (MIH) of holoprosencephaly or syntelencephaly was described in 1993 as a fourth subtype of holoprosencephaly (HPE), in addition to the three classic types of alobar, semilobar, and lobar HPE. MIH consists of an abnormal midline continuity of the posterior frontal and parietal regions of the cerebral hemispheres, with separation of the basal forebrain, anterior frontal lobes, and occipital regions. Although MIH and classic HPE share a number of similarities, they are related to different embryologic mechanisms. Classic HPE is caused by a defect in the formation of the embryonic floor plate, whereas MIH is secondary to a disturbance of formation of the roof plate. The ZIC2 gene plays a critical role in differentiation of the roof plate of the developing embryo in the dorsal midline of the neural tube. In mice, decreased levels of ZIC2 result in the failure to form midline CNS structures. In humans, mutations in the ZIC2 gene have been found in ~3 to 4% of HPE cases, including individuals with MIH, confirming that MIH is a variant of HPE.

The clinical manifestations of MIH patients have been recently reported in detail and compared with classic HPE. Neurologic developmental functions were similar to the lobar subtype of HPE.
In particular, speech and oromotor development were delayed in all MIH cases; mild to moderate spasticity, hypotonia, and dystonia occurred in a high percentage of cases, as did seizures. Facial dysmorphisms were moderate or even mild. Severe midline craniofacial anomalies, choreoathetosis, and endocrine dysfunction were absent in MIH cases.5

Case report. A 14-year-old boy was referred to us because of muscular hypotonia and weakness. He is the first child of healthy, nonconsanguineous parents. He was born at term after an uneventful pregnancy with normal delivery. Birth weight was 2,800 g. Motor development was slightly delayed (unsupported walking acquired at age 18 months). He never had seizures. Despite the presence of a mild reading disorder, his academic skills were within the normal range.

Neurologic examination showed no facial dysmorphism (namely, no hypotelorism or hypertelorism or single central maxillary incisor), normal head circumference, mild weakness of eye closure, a slightly reduced muscular tone and trophism, rigid spine, proximal limb weakness mainly of the shoulders, and normal osteotendinous reflexes. He was able to walk independently with lordosis. Cardiac and respiratory functions were apparently normal. Endocrine functions and temperature regulation were normal.

Laboratory investigations, including creatine kinase, transaminases, and karyotype, were normal. EKG was normal. EMG (deltoid muscle) showed myogenic signs. Nerve conduction velocity was normal. Muscle biopsy of quadriceps revealed only mild myopathic changes, as increasing of the percentage of central nuclei and type I fiber predominance, without specific degenerative or inflammatory features.

IQ assessed with the Wechsler Intelligence Scale for Children—Revised scale was normal (total IQ, 103; performance IQ, 101; verbal IQ, 106).

Brain MRI revealed a middle interhemispheric variant of holoprosencephaly (figure).

Genetic analysis for sonic hedgehog was not performed. Results of mutational analysis for ZIC2 gene are not yet available.

Discussion. The severity of HPE correlates with the degree of neurologic impairment and developmental delay. In the most severe type (alobar), there is only a minimal developmental progress, whereas the developmental outcome is more favorable in milder forms of HPE (semilobar and lobar).6 Despite similarities with lobar HPE, MIH represents a distinct cliniconeuroradiologic subtype of HPE.6 The frequency of seizures, hypotonia, and dystonia was comparable, whereas spasticity occurred more frequently in MIH than in lobar HPE. Developmental neurologic abnormalities, including mobility, upper extremity function, and expressive language, were similar to those of lobar HPE. The degree of dysfunction of these variables has been correlated with the nonseparation of deep gray nuclei (caudate, lentiform nuclei, and thalamus).6 Language development is poor in lobar HPE and MIH, and patients are usually able to pronounce only single words or short sentences.5,6

However, expressive language and intelligence of our case are completely normal, and his academic skills are in the normal range, except for a mild reading disability. In conclusion, this case contributes to the further definition of the phenotype of MIH, indicating that the clinical variability of this disorder is wider than expected, also including a very mild clinical phenotype.
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