The following full text is a publisher's version.

For additional information about this publication click this link. 
http://hdl.handle.net/2066/59324

Please be advised that this information was generated on 2017-11-19 and may be subject to change.
Statin-associated exacerbation of myasthenia gravis

Michael S. Cartwright, MD; Douglas R. Jeffrey, 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. Repetitive nerve stimulation abnormalities were consistent with MG. The facial nerve showed a 50% decrement at baseline and ~50% decrement at 30, 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 remained on 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. Repetitive nerve stimulation abnormalities were consistent with MG. The facial nerve showed a 50% decrement at baseline and ~50% decrement at 30, 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.

From the Department of Neurology (Dr. Cartwright, Jeffrey, and Donofrio), Wake Forest University School of Medicine (G.R. Nuss), Winston-Salem, NC.
Received April 23, 2004. Accepted in final form July 8, 2004.
Address correspondence and reprint requests to Dr. Michael S. Cartwright, Department of Neurology, Wake Forest University Baptist Medical Center, Winston-Salem, NC 27157; e-mail: mcartwrr@wfebmc.edu

Copyright © 2004 by AAN Enterprises, Inc.

References

The fragile X premutation presenting as postprandial hypotension

P. Pugliese, MD; G. Annesi, PhD; N. Cutuli, MD; G. Abraida, MD; G. Nicoletti, MD; F. Annesi, PhD; P. Tarantino, PhD; A. Gambardella, MD; P. Valentino, MD; M. Zappia, MD; and A. Quattrom, MD

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 grandchildren 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 mild asymmetric (left greater than right) postural tremor in the distal upper extremities, which increased by action (without resting tremor). Tone, strength, sensation, deep tendon reflexes, 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 = 29/30), but speech and memory problems were evident. All cognitive 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.
Heterozygous Niemann-Pick disease type C presenting with tremor

Keith A. Josephs, MST, MD; Joseph Y. Matsumoto, MD; and Noralane M. Lindor, MD

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 neurology department with a 10-year history of tremor, initially a side-to-side 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 predominately 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 therapy, which she took for 3 months. Her family history was interesting because three brothers all developed tremor and an incurable neurologic disease.1 Her neurologic inventory was otherwise negative.

On examination, she was jocular. On the Short Test of Mental Status, she received a score of 31 of 38.2 Her cranial nerve examination was normal. She had a continuous “no-no” head tremor and mild lip and voice tremor. With mental activation, she developed a severe tremor in her upper extremities, worse on the right. With her arms held outstretched, she had a mild tremor. When her limbs were in a position of partial repose (e.g., with her left elbow on the armchair and her hand on her hips), she developed a severe tremor. Her gait was unremarkable, except for a moderate overflow tremor of both upper extremities. Her medical examination, including abdominal examination, was unremarkable. A complete radiologic examination, including EKG with transesophageal stimulation and study of R-R interval variability during deep breathing, echocardiography, and Doppler ultrasound studies of the carotid and vertebrobasilar systems, were otherwise normal. The administration of midodrine (2.5 mg TID) decreased postprandial symptoms. The molecular analysis of FMR1 gene revealed a premutation carrier status with 73 CGG repeats.

Discussion. The clinical presentation of this patient, who had severe postprandial hypotension associated with mild postural and intention tremor and who was carrying an FMR1 premutation, is atypical for FXTAS. Cases of FXTAS described thus far have consisted of intention tremor and/or ataxia, variously associated with cognitive decline, peripheral neuropathy, parkinsonism, and autonomic dysfunction;3,4 moreover, MRI showed generalized brain atrophy and/or T2 hyperintensities of the middle cerebellar peduncles,5 although the absence of this sign is not unusual, being present in only 59% of patients with FXTAS.5 Most important, all the reported cases of FXTAS were identified from families with known cases of FXS.6 Nevertheless in our patient, even if a family history for FXS was absent, a clinical diagnosis of “possible” FXTAS could be made because, in addition to the mandatory criterion of the FMR1 premutation status, he had intention tremor (one clinical major criterion) and moderate brain atrophy (one radiologic minor criterion).3 However, his main disturbances were postprandial symptoms caused by decreases in BP after meals; moreover, he had a reversed circadian BP rhythm and a mild orthostatic hypotension. This autonomic profile, although nonspecific, could identify an autonomic impairment, such as the dysfunction occurring in atypical Parkinson disease or multiple system atrophy.4 This autonomic dysfunction has not been previously described in patients with FXTAS, in whom dysautonomia has been mainly reported as impotence, hypertension, or bladder dysfunction.1,3

There is growing evidence that the clinical phenotypes of FXTAS may be more heterogeneous than previously thought. FMR1 premutations have been reported in patients with essential tremor and/or3 and in cases of sporadic ataxia without a family history for FXS.7 Our report adds further evidence to the clinical spectrum of FXTAS and suggests that DNA testing for the FMR1 premutation may reveal additional carriers among patients with BP dysautonomia. Nevertheless, further studies on more FMR1 premutation carriers are needed to confirm whether BP dysautonomia is a clinical feature of these subjects.

References


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).

From the Institute of Neurology (Drs. Pugliese, Arabia, Valentino, Gambardella, Zappia, and Quattrone), University “Magna Gracia,” Catanzaro; Laboratory of Molecular Genetics, Department of Services (Dr. Cutuli), University of Catania; and the Institute of Neurological Sciences (Drs. G. Annesi, Niccolotti, F. Annesi, Tarantino, Zappia, and Quattrone), National Research Council, Cosenza, Italy.

Received April 28, 2004. Accepted in final form July 6, 2004.

Address correspondence and reprint requests to Dr. Aldo Quattrone, Clinica Neurologica, Università “Magna Gracia,” Via T. Campanella, 88100 Catanzaro, Italy; e-mail: a.quattrone@isn.cnr.it

Copyright © 2004 by AAN Enterprises, Inc.
Radicular myoclonus induced by repetitive neck movements in a patient with cervical spondylosis

V. Di Lazzaro, MD; A. Oliviero, MD; P. Profice, MD; T. Tartaglione, MD; F. Pilato, MD; E. Saturno, MD; M. Dileone, MD; and P.A. Tonali, MD

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.1,2 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 started 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.

The patient arrived at our emergency department 6 hours later. On examination, he had rhythmic, involuntary jerks of the right shoulder on the horizontal plane and a slight lateral flexion of the head on the right side. Neurologic examination was otherwise normal. The involuntary activity was not affected by neck movements or by distraction or mental concentration. Blood count and chemistries (glucose, liver and renal function tests, electrolytes, and B12 level), rheumatologic screen (erythrocyte sedimentation rate, antinuclear antibody, anti-DNA, rheumatoid factor, complement factors C3 and C4, and antithrombin III antibody), copper and ceruloplasmin concentration, and thyroid function were normal. The EEG was normal. However, during activation with hyperventilation, the ongoing involuntary activity increased in frequency and amplitude in the absence of EEG modification.

EMG recording revealed cocontraction of several muscles with synchronous repetitive discharges of motor units occurring in trains lasting several minutes in right pectoralis major (clavicular head), teres major, pronator teres, and intermittently in biceps brachioradialis muscles (all supplied by the C6 root).

The involuntary activity in the neck muscles originated from a deep muscle and was not documented with EMG, but it is conceivable that it originated from the longus colli muscle that produces lateral flexion of the head and is supplied mainly by the C6 root. The duration of bursts of activity ranged from 350 to 410 ms. Subsequent recordings showed two different rates of involuntary movements, either 0.5 or 1.7 Hz. Hyperventilation either precipitated the involuntary activity or increased the amplitude of ongoing involuntary movements. When the frequency of involuntary movement 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.4 Cervical cord MRI revealed that the right C6 neural foramen was narrowed because of degenerative spondylotic changes, the spinal cord being normal.

The patient stopped the morning stretching activity of neck muscles. The movements resolved in the next 3 days.

Copyright © 2004 by AAN Enterprises, Inc.

References


Copyright © 2004 by AAN Enterprises, Inc. Unauthorized reproduction of this article is prohibited.
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 PM and DM but has only rarely been reported in IBM. 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 [MRC] score, 4) with asymmetric weakness of the forearm muscles (right, MRC 4; left, MRC 3). Muscle atrophy was most pronounced in 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.

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 PM and DM but has only rarely been reported in IBM. 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 [MRC] score, 4) with asymmetric weakness of the forearm muscles (right, MRC 4; left, MRC 3). Muscle atrophy was most pronounced in 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

N.C. Voermans, MD; M. Vaneker, MD; G.J.D. Hengstman, MD; H.J. ter Laak, PhD; C. Zimmerman, MD; H.J Schelhaas, MD; and M.J. Zwarts, PhD

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 PM and DM but has only rarely been reported in IBM. 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 [MRC] score, 4) with asymmetric weakness of the forearm muscles (right, MRC 4; left, MRC 3). Muscle atrophy was most pronounced in 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.

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 PM and DM but has only rarely been reported in IBM. 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 [MRC] score, 4) with asymmetric weakness of the forearm muscles (right, MRC 4; left, MRC 3). Muscle atrophy was most pronounced in 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.
Cerebral toxoplasmosis in a patient with common variable immunodeficiency

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

Cerebral toxoplasmosis is commonly seen as an opportunistic disease in patients with compromised cellular immunity. 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 facilitated by a humoral immune defect with combined immunoglobulin (Ig) A, IgG, and IgM deficiency.

and resulted in life-threatening respiratory failure. Only then the ventilatory support was started, and the vicious circle of respiratory muscle weakness, hypoventilation, hypercapnia, sleeping problems, deterioration of the general condition, weight loss, and severe respiratory failure was broken. Moreover, we started high-dose corticosteroid treatment, which involves a risk of serious adverse effects. In conclusion, primary respiratory failure can occur in patients with IBM, and awareness of this potentially life-threatening complication is warranted, especially for patients with signs and symptoms suggestive of hypoventilation.

From the Neuromuscular Centre Nijmegen and the Departments of Neurology (Drs. Voermans, Hengstman, ter Laak, and Schelhaas), Anesthesiology (Dr. Vaneker), Intensive Care Medicine (Dr. Zimmerman), and Clinical Neurophysiology (Dr. Zwarts), University Medical Centre Nijmegen, The Netherlands.

Received April 21, 2004. Accepted in final form July 8, 2004.

Address correspondence and reprint requests to Dr. H.J. Schelhaas, Neuromuscular Centre Nijmegen, Department of Neurology, University Medical Centre Nijmegen, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands; e-mail: h.schelhaas@neuro.umcn.nl

Copyright © 2004 by AAN Enterprises, Inc.

References


Copyright © 2004 by AAN Enterprises, Inc.

References

Alopecia and cutaneous atrophy after greater occipital nerve infiltration with corticosteroid

K.G. Shields, MRCP; M.J. Levy, MRCP; and P.J. Goodasy, 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, and a toxoplasma pseudocyst (e; original magnification, ×400). A high-power view of this pseudocyst (f; original magnification, ×1000).

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. R. Biancheri, MD; A. Rossi, MD; P. Tortori-Donati, MD; 4. Matharu MS, Bartsch T, Ward N, et al. Central neuromodulation in chronic migraine patients with suboccipital stimulators: a PET study. Brain 2003;126:1801–1813. 5. Jacobs MB. Local subcutaneous atrophy after corticosteroid injection. Postgrad Med 1986;80:159–160.
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.

From the Neuromuscular Disease Unit (Drs. Biancheri and Minetti, S. Stringera and S. Bonfigliino), University of Genova, and Department of Pediatric Neuroradiology (Drs. Rossi and Tortori-Donati), Istituto G. Gaslini, Genova, Italy.

Received May 23, 2004. Accepted in final form July 19, 2004.

December (1 of 2) 2004 NEUROLOGY 63 2195
References


Creative Expression Award Deadline Extended

The $2000 AAN Award for Creative Expression of Human Values in Neurology recognizes an outstanding poem, short story, or piece of creative nonfiction.

For information, visit http://aan.com/professionals/awards/award/awa_cre_exp.cfm.

The submission deadline for the 2005 award has been extended to Friday, December 31, 2004.