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More on Migraine Mechanism: Cortical Spreading Depression Revisited

ABSTRACT & COMMENTARY

Source: Ebersberger A, et al. Is there a correlation between spreading depression, neurogenic inflammation, and nociception that might cause migraine headache? *Ann Neurol.* 2001;49:7-13.

The pathophysiological mechanism of migraine remains a mystery. One possible clue has been the link between migraine aura and migraine headache. In the 1940s both Lashley's now infamous self reported scintillating scotoma moving at a rate of 2-3 mm/min and Leao's finding of spreading oligemia across the surface of a rabbit brain at the same 2-3 mm/min implicated this phenomenon of cortical spreading depression (CSD) as the crucial step in the initiation of migraine head pain. Indeed recent work by Michael Moskowitz on neurogenic inflammation suggests the importance of CSD in migraine pain. According to the Moskowitz model,CSD could induce the depolarization and antidromic activation of trigeminal afferents surrounding meningeal blood vessels inducing cerebrovascular pain and swelling. However, the link between the CSD and this neurovascular inflammatory event has never been proven. The current study by Ebersberger and associates is an attempt to accurately discern the relationship between CSD and neurogenic inflammation.

Twenty-one rats were studied. Intracortical, epidural, and brainstem trigeminal caudal nucleus (TCN) recordings were made. There was no significant increased activity in TCN during single or multiple induced CSDs. Furthermore, there was no increased sensitivity of TCN neurons when tested to heat, von Frey threshold, and spontaneous activity before or after CSDs.

Neurogenic inflammation (NI) was quantified by a measurement of NI mediators such as CGRP and prostaglandin E2 (PGE2) in plasma dural extravasation. Neither CGRP or PGE2 were increased following individual or serial CSDs.

Ebersberger et al conclude that CSD in the cortex in not sufficient to activate the release of neuroinflammatory peptides, nor is it sufficient to activate second order neurons in TCN. The results do not support the

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hypothesis that CSD could activate the trigeminalvascular system leading to the neurogenic inflammation that ultimately causes migraine headache.

COMMENTARY

This elegant study on rat brains brings up several important points on migraine in humans. Indeed a thoughtful editorial in the same publication by Goadsby preceding the article summarizes the critical issues (*Ann Neurol* 2001;49:4-6). As Goadsby notes, the clinical observation of CSD as a transient reversible neurologic phenomenon mainly experienced as visual obscurations has appeared to be a process not in series with migraine headache but rather one that is in parallel. For example, migraine aura only accompanies migraine headache in 15-20% of cases. Only 25% of the time does the aura actually precede the headache. Rather most of the time it is concurrent or follows the onset of the headache. And finally, 10% of migraineurs report migraine aura alone without headache. The Ebersberger et al study is important in proving the negative association experimentally between CSD and the other events more closely linked to migraine pain. So as future work will likely reveal, we are going to confirm what clinicians have known implicitly for a long time; the seminal events of migraine—the aura and pain—are a separate but equal phenomenon occurring not in series but in parallel. How they are linked remains to be determined. **—jeffrey b. reich**

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Childhood Headache and Stress Revisited

ABSTRACT & COMMENTARY

Source: Waldie KE. Childhood headache, stress in adolescence, and primary headache in young adulthood: A longitudinal Cohort Study. *Headache.* 2001;41:1-10.

The causal relation between stress and headache has not been adequately determined. Stressful life events can be risk factors for pain as well as consequences of pain. For example, it is not known whether frequent headaches in childhood influence the appraisal of life events or if prolonged stress affects future headache status of both. Previous attempts to study this issue have been fraught with methodological problems ranging from selection bias, to small sampling sizes, to a lack of standardized headache criteria.

Waldie reports on the results of a longitudinal study of 481 women and 499 men enrolled in the Dunedin Multidisciplinary Health and Development Study. This is a longitudinal study project looking at health and behavior of a birth cohort of children born in Dunedin, New Zealand, from April 1, 1972 to March 31, 1973. In this particular arm of the study headache frequency at ages 7, 9, and 11 was recorded. A total of 305 or 35.9% of children reported more than 1 headache per month and were defined as having a positive headache history.

At age 15 a stress assessment was obtained according to a 21-item "Feel Bad" scale listing items that could potentially cause stress in adolescents. Each item was then scored accordingly as producing "mild," "moderate," or "severe" stress. In the group with a positive headache history there was a 1.5 times more likelihood of reported stress at age 15 compared to children without a headache history before age 12.

At age 26 the cohort was evaluated to determine an IHS classifiable headache disorder. Of the 980 patients who were sampled at age 26, 72 (7.3%) fulfilled HIS criteria for migraine headache (MH), 109 (11.1%) for tension-type headache (TTH), and 42 (4.3%) for combined MH and TTH. In order to test the relationship between stress at age 15 and headache diagnosis at age 26, a multivariate analysis of variance was performed on mild, moderate, and high stress data. At age 26 study members who reported high stress at age 15 were 2.6 times more likely to be diagnosed with migraine than those who

were not. This group was twice as likely to have a combined headache disorder. Unexpectedly, study members with TTH were not found to experience increased stress during adolescence. Only when individual stressors were examined did a weak association emerge between the stress of changing bodily image in adolescence and the development of TTH later in life.

Waldie concludes that head pain in childhood may be a risk factor for experiencing high levels of stress in mid adolescence. In addition, stress in adolescence may contribute to the development of headache in young adulthood. From the current study it is not possible to determine a more specific cause and effect.

COMMENTARY

Several points can be made with regards to the findings of this study. First is the recognition that childhood headache can predispose children to the experience of stress later in life. Headache in this age group is notoriously under diagnosed and under treated and these findings should make proper headache diagnosis and treatment a more urgent matter. Second, the lack of association between adolescent stress and later development of TTH is notable and argues for a more fundamental physiological understanding of TTH. Waldie concludes that perhaps more recent stressors are important in the development of TTH but that still remains to be determined. And finally, a problem with this study, as with a lot of studies examining the role of "stress," is that they do not take into account the subjective nature of "stress." What is "stressful" for one individual may be exhilarating for another. Personality profiles and affective mood scores maybe be a helpful third variable to better discern the role stress plays in a person's life and subsequently, in any medical condition, not just headache. **—jeffrey b. reich**

Polio's Last Stand?

ABSTRACTS & COMMENTARY

Sources: Clarke T. Polio's last stand. *Nature.* 2001;409:278-280; Polio eradication: The end game. *Nat Med.* 2001;7:131; Watanabe M. Polio outbreak threatens eradication program. *Nat Med.* 2001;7:135.

Fifty years ago, poliomyelitis was the most dreaded infection that annually affected children and relatively young adults worldwide. The virus itself resides in the intestinal track of nonimmune persons and includes 3 distinct antigenic types, allowing it rarely to strike twice. Both antipolio vaccines discussed below, however, protect against all three types. Highly active viruses can kill large spinal anterior horn cells, thereby precipitating varying degrees of permanent muscular paralysis. A fraction of neurological victims also suffer potentially fatal attacks of acute brain stem encephalitis, which temporarily disrupts autonomic pathways as well as the ponto-medullary regulation of blood pressure, heart rate, breathing, swallowing, and bladder function.

By 1949, Enders and associates managed to cultivate the polio virus in tissue culture, a step awarded by the Nobel prize. Jonas Salk developed his killed virus inactivated poliomyelitis vaccine (IPV) in 1954. A year later Albert Sabin meticulously developed a vaccine comprised of alive, but attenuated non-paralytogenic, and delivered as orally polio viruses (OPV). Administration of the oral vaccination was far more easy to achieve and less costly. Used widely by the World Health Organization (WHO) and the Pan American Health Organization (PAHO), the OPV vaccine has been highly successful in reducing the incidence of poliomyelitis in 2nd and 3rd world countries around the globe. Thanks to these efforts, the disease has almost disappeared in the North and South Americas, Northern Europe, and Asia, plus almost the entire Pacific Asian coast, islands and continents. Global annual incidence of polio dropped from 320,000 p.a. before the advent of polio vaccination to a present ± 2000 p.a. Most of these latter cases come from Central Africa and Southwest Asia.

Against the above background, a small epidemic of acute paralytic poliomyelitis appeared last summer in the Dominican Republic and Haiti, both of which share the island of Hispaniola. Seven of the 9 paralyzed children were traced to a single mutant antibody of OPV pattern. By accident or staleness, this must have emerged from recipients who previously received either insufficient or too old vaccine, or have generated a wild mutant oral polio vaccine. The CDC suggests that the rogue OPV virus in the Dominican Republic may have kindled for 2 (or more) years before the present epidemic, spreading the diseased mutation via person to person from intestinal contents. Supporting this concept is that Clarke found that only 20% of Dominican children had ever even had one of the three OPV doses, an amount not sufficient to provide immunity. The remaining children and, presumably, adults never received preventive inoculation.

No fatalities have been reported, but *Nature* indicates that in the WHO international program, OPV vaccinations have occasionally had random hitches that averaged 1 case of paralytic polio for every 1/750,000 inoculated persons. Watanabe also indicates that Donald Henderson, Chairman of the Technical Advisory Group Pro-

gram of Immunization of the Americas, says there are an additional 39 suspected cases in Hispaniola. Whether paralytic is not commented upon.

Information from inner China several years ago suggested a small outbreak of persons presumably taking too little OPV. Watanabe also indicates that *Mortality and Morbidity Weekly* in its January 26 issue refers to an outbreak associated with OPV distribution in Egypt some years ago. Affected were a total of 32 polio cases in 1988 and 1993. Analysis suggests that a potentially malignant OPV virus may have been growing insidiously in the intestines of the affected population for as long as 11 years.

COMMENTARY

WHO and PAHO for many years have been struggling in efforts to eradicate poliomyelitis in the way that small pox apparently has been permanently conquered. *Nature Medicine's* editor, however, has cautions. Although the present breakthroughs of patients given OPV have involved only small numbers of paralytic disease, stronger mutations might cause larger and more frequent epidemics. He implies that if OPV can't block generating stronger mutations, there may come a day when such a mutation reproduces the acute severe crippling or killing illness that once came from wild viruses.

(*Editor's Note: When to be inoculated for poliomyelitis. Adults: For those younger than 40 years and never previously inoculated against poliomyelitis, take 2 doses of IVP sc 1 month apart and a third 6-12 months later. If urgent and anticipating immediate trips into Sub-Saharan Africa or Southwest Asia, take a single boost of either OPV or IVP even if either was completely or incompletely obtained several months or years earlier. For adults, see Cecil Textbook of Medicine, 21st ed. 2000: 44. For children's vaccination, consult Merck Manual, Centennial Edition. 1999:2342.*) **—fred plum**

CABG: Good for the Heart, Sometimes Bad for the Brain

ABSTRACTS & COMMENTARY

Sources: Newman MF, et al. Longitudinal assessment of neurocongitive function after coronary artery bypass surgery. *N Engl J Med*. 2001;344:395-402. Selnes OA, McKhann GM. Editorial: Coronary artery bypass surgery and the brain. *N Engl J Med*. 2001;344:451-452.

More than 500,000 coronary artery bypass grafting (CABG) operations are performed in the United States each year. Although effective for revascularizing the heart, CABG can have neurological complications. After CABG, postoperative delirium occurs in up to one-third of patients, stroke occurs in up to 5%, and short-term cognitive abnormalities in 30-80% depending upon the population tested and the tests used to evaluate cognition. Long-term cognitive changes following CABG are commonly reported by patients and their families but may be subtle or mainly affect mood and personality (*Curr Probl Cardiol.* 1997;22:449-480.)

Newman and associates from Duke Medical Center determined the course of long-term cognitive change during the 5 years after CABG. In 261 patients they performed neurocognitive tests before surgery, before discharge, and then 6 weeks, 6 months, and in 172, 5 years after CABG. Cognitive decline was defined as a reduction of 1 standard deviation (approximately 20% from the patient's preoperative baseline test score in 1 or more of 4 domains (verbal memory and language comprehension; abstraction and visuo-spatial orientation; attention, processing speed, and concentration; and visual memory). Factors predicting long-term cognitive decline were determined by multivariable logistic and linear regression.

Among study patients the incidence of cognitive decline was 53% at discharge, 36% at 6 weeks, 24% at 6 months, and 42% at 5 years. Cognitive function at discharge was a significant predictor of long-term function ($P > .001$) as were older age and lower level of education.

COMMENTARY

Newman et al found that a large proportion of CABG patients had cognitive decline when tested at the time of discharge. As pointed out by Selnes and McKhann in their accompanying editorial, the decline may reflect the fact that patients underwent neurocognitive assessment just days after major surgery. If the early cognitive decline is a valid finding, however, then cognitive change after CABG has a biphasic course of decline, improvement, and later decline. Since it is predicted by the presence of early postCABG decline, the later cognitive deterioration may be caused by perioperative events.

The mechanism of cognitive changes after CABG is probably multifactorial, including genetic and environmental factors, but intraoperative hypotension and microemboli are likely causes of cerebral injury. During CABG, ultrasonographic studies have demonstrated that showers of emboli enter the cerebral vessels especially when an atherosclerotic aorta is clamped and then unclamped (*Curr Probl Cardiol.* 1997;22:449-480.)

These findings underscore the importance of prevent-

ing or reducing perioperative brain damage in all patients, especially the elderly undergoing CABG. Patients in whom early postoperative decline is identified may be candidates for aggressive interventions to prevent later cognitive deterioration. **—john j. caronna**

Cerebellar Ataxia with Anti-glutamic Acid Decarboxylase Antibodies: A Potentially Treatable Condition

ABSTRACT & COMMENTARY

Source: Honnorat J, et al. Cerebellar ataxia with anti-glutamic acid decarboxylase antibodies. *Arch Neurol.* 2001;58:225-230.

Insidious cerebellar ataxia is usually an ominous clinical presentation. The differential diagnosis of a slowly progressive cerebellar disorder beginning in adulthood is not broad. Sporadic olivopontocerebellar degeneration (better known as OPCA), Jacob-Creutzfeldt disease, autosomal dominant spinocerebellar degeneration (SCA-1, 2, 3, 6, 8), paraneoplastic disease (mediated by anti-Yo antibody), and celiac disease are the most common causes of this clinical picture. There is currently no therapy that alters the natural history of OPCA, prion disease or the inherited spinocerebellar degenerations. While celiac and paraneoplastic cerebellar disorders may partially respond to treatment, improvements are usually modest at best.

There have been scattered case reports of cerebellar degeneration occurring in patients with antibodies to glutamic acid decarboxylase (GAD). Anti-GAD antibodies are present in a variety of immune-mediated disorders, including insulin-dependent diabetes mellitus, polyendocrine autoimmunity, and in the stiff-person syndrome, a neurologic disorder characterized by progressive muscle rigidity and painful muscle spasms. Stiff-person syndrome is a relentlessly progressive neurologic disorder that can respond dramatically to treatment with immuno-modulatory therapy. This paper is the first to link cerebellar ataxia and anti-GAD antibodies in a series of patients, implying a new and potentially treatable form of cerebellar dysfunction in adults.

Honnorat and colleagues describe 14 patients with anti-GAD antibodies and adult-onset cerebellar degeneration. The patients were identified by analyzing 9000 patient serum samples sent from 4 different European laboratories during screening for paraneoplastic antibodies. Thirteen of 14 patients were women, and their average age at the onset of cerebellar symptoms was 51 years. Ten patients had coincident insulin-dependent diabetes mellitus, and 6 had a family history of autoimmune disease. Autoimmune illnesses were common among this group of 14 patients, including thyroiditis (8 patients), pernicious anemia (2 patients), myasthenia gravis (1 patient), and psoriasis (1 patient). In virtually every case, cerebellar symptoms were slow and insidious. The predominant symptom was gait ataxia (10 patients), which could be severe. Limb ataxia was highly prevalent but mild. Twelve patients had nystagmus, 8 had dysarthria, and 2 had leg rigidity suggestive of a peripheral form of stiff-person syndrome.

Imaging of the brain was abnormal in 7 patients, demonstrating pure cerebellar atrophy. Cerebrospinal fluid examination was abnormal in 10 patients, with oligoclonal IgG bands present in the CSF. Radioimmunoassay and Western blot confirmed the presence of anti-GAD antibodies in all 14 patients, at levels that were similar to those seen in stiff-person syndrome.

COMMENTARY

This paper is important for several reasons. It suggests that neurologists who encounter patients with slowly progressive cerebellar symptoms should be aware of the possibility that anti-GAD antibodies are responsible for the condition. The neurologic features of these patients are identical to patients with sporadic OPCA, making it difficult to recognize them. Clues that may help the neurologist identify these patients include female gender, a history of insulin-dependent diabetes mellitus or other autoimmune disorders, and a family history of autoimmune disorders.

It is unknown how an antibody in the serum or CSF is able to access GAD, an intracytoplasmic antigen. Once present inside the cell however, anti-GAD antibodies have been demonstrated to reduce GAD enzyme activity, and GABA synthesis from glutamate. Glutamate is a known excitotoxin, and increased glutamate and decreased GABA may perhaps explain the loss of cerebellar neurons.

This paper does not comment about possible treatments for patients with cerebellar ataxia and anti-GAD antibodies. However, IVIG and plasmapheresis have both been reported to benefit selected patients with stiff-person syndrome, and presumably one of these approaches should be tried in autoimmune-mediated cerebellar disease. The importance of early recognition of this potentially treatable cause of cerebellar degeneration cannot be over-emphasized. **—steven frucht**

Welding-Related Parkinsonism

ABSTRACT & COMMENTARY

Source: Racette BA, et al. Welding-related parkinsonism: clinical features, treatment and pathophysiology. *Neurology.* 2001;56:8-13.

A variety of toxins can produce acute parkinsonism, including MPTP, organophosphate pesticides, carbon monoxide, carbon disulfide, cyanide, and methanol. Although all of these agents induce a parkinsonian state, MPTP produces an illness that is clinically indistinguishable from Parkinson's disease (PD). Patients with MPTP-induced parkinsonism are similar to PD in their response to levodopa and their propensity to develop motor fluctuations and dyskinesias. However, MPTP-induced parkinsonism differs from PD in several important ways. First, the parkinsonism is acute, evolving over hours to days to produce a typically severe akinetic-rigid state. Second, the pathology of MPTP parkinsonism is different from PD, as there are no Lewy bodies in the nigra. While the discovery of MPTP produced an explosion of interest in possible environmental triggers of PD, MPTP is clearly not responsible for sporadic PD. The search for environmental agents that are responsible for PD has been unsuccessful, until this report.

In their seminal paper, Racette and colleagues report 15 career welders who developed a parkinsonian state indistinguishable from PD. In their professional life, welders are exposed to particulate fumes and gases with high concentrations of F, Mn, Zn, Pb, As, S, Cr, Ni, CO, CO_2, F, and HF. All 15 welders in this series were men, with an average occupational exposure of 47,144 welding hours. They developed symptoms of parkinsonism at an average age of 46 years, and were evaluated 8.5 years into the course of their illness.

Parkinsonian welders were clinically indistinguishable from patients with sporadic PD. The incidence of asymmetry, bradykinesia, tremor, rigidity, and postural instability were the same. Thirteen of 15 welders treated with levodopa improved, and younger patients developed motor fluctuations and dyskinesias. Two patients underwent 18-fluro-dopa PET scanning, which measures the nigro-striatal dopaminergic projection. The scans showed selective reductions of dopaminergic innervation in the posterior putamen, a pattern indistinguishable from that seen in idiopathic PD.

Racette et al compared the clinical features of their 15 welders to a group of 100 sequential patients diagnosed with idiopathic PD, and to 6 patients that were age- and gender-matched to each welder. There were no differences between the welders and PD patients in any clinical features, with the exception that welders developed their first symptoms of parkinsonism an average of 17 years before sporadic PD patients.

COMMENTARY

This is the first report to directly link an environmental exposure to an illness that is indistinguishable with PD. What is the likely mechanism to explain the development of parkinsonism in welders? Racette et al speculate that a certain population of welders may be at higher risk for the development of PD. Given an adequate exposure to inhaled welding gases, a certain proportion of welders will likely develop PD. This report adds strong support to the argument that sporadic PD may result from exposure to low levels of environmental toxins in susceptible patients.

It is not known which element in welding vapor is responsible for the development of parkinsonism, although manganese is a likely culprit. Occupational exposure to manganese produces a syndrome called manganism, characterized by extrapyramidal signs of parkinsonism and dystonia. However, the response of manganism to levodopa is only partial and often transient, and such patients often have neuropsychiatric features that were not seen in PD welders. Nevertheless, the possibility exists that long-term, low-level manganese exposure in a susceptible patient population produces a syndrome that is indistinguishable from sporadic PD. **—steven frucht**

Vaccinations in Multiple Sclerosis and Risk of Relapse

ABSTRACTS & COMMENTARY

Sources: Ascherio A, et al. Hepatitis B vaccination and the risk of multiple sclerosis. *N Engl J Med.* 2001;344:327-332. Confavreux C, et al. Vaccinations and the risk of relapse in multiple sclerosis. *N Engl J Med.* 2001;344:319-326.

Ascherio and colleagues performed a case-control study in 2 large cohorts of nurses in the United States consisting of more than 230,000 women

followed for 11 to 24 years. For each person with multiple sclerosis (MS), 5 healthy controls and 1 person with breast cancer were selected as controls. The analyses included 192 women with MS and 645 matched controls, whose hepatitis B vaccination status was confirmed by vaccination certificates. The multivariate relative risk of MS associated with exposure to the hepatitis vaccine at any time before the onset of disease was 0.9 (95% confidence interval, 0.5-1.6), and within 2 years before onset of disease was 0.7 (95% confidence interval, 0.3-1.8). Thus, there was no association between hepatitis B vaccination and the development of MS.

Confavreux and associates conducted a case-crossover study in a European database for MS to assess if vaccinations for hepatitis B, tetanus, or influenza increased the risk of relapse in MS. Patients with an index relapse confirmed by a visit to a neurologist and preceded by a 12-month relapse-free period were included in the study. Of 643 patients with MS attacks, 15% reported having been vaccinated during the preceding 12 months (94% confirmed by medical records). In these patients, 2.3% had been vaccinated during the preceding 2-month period, vs. 2.8-4.0% that were vaccinated in the 3- to 12-month period prior to the index attack. The relative risk of relapse associated with exposure to any vaccine was 0.71 (95% confidence interval 0.4-1.2), indicating that vaccination did not increase the short-term risk of relapse in MS.

COMMENTARY

The safety of vaccinations in patients with MS has been debated for decades, with many reports of relapses and clinical onset of disease after vaccination. Small studies of influenza vaccination in MS patients have been reassuring (*Neurology.* 1997;49:312-314), yet clinicians remain reluctant to vaccinate persons with MS. Concerns increased following a mass hepatitis B vaccination program in France between 1995 and 1997, where several reports of new onset of MS were described a few weeks following immunization. However, as these carefully conducted case-controlled studies above appear to indicate, a significant increase in MS relapses with vaccination cannot be confirmed. One shortcoming of the European study by Confavreux et al is that the study design did not allow the index relapse to be the "first attack", or clinical onset of disease. Since only patients with established MS were retrospectively analyzed, they could not capture persons whose first episode might have been temporarially associated with vaccination.

Some clinicians may be convinced by their own anectdotal experiences with MS relapses following vaccination that there is cause and effect. Indeed, if MS attacks appear to correlate with a variety of viral infectious illness, it is a reasonable extrapolation that the viral antigenic stimulation of a vaccine could specifically or nonspecifically activate immune responses to trigger a relapse. However, the very unpredictable nature of this poorly understood relapsing disease makes it impossible to draw such conclusions. As the above reports indicate, the risk of relapse in MS with vaccination is small, and the public health benefits of mass immunization are great. **—brian r. apatoff**

Brief Alert

Floppy Head Syndrome in Parkinsonism

Source: Askmark H, et al. Parkinsonism and neck extensor myopathy: A new syndrome or coincidental findings? *Arch Neurol.* 2001;58:232-237.

Among 459 patients evaluated for parkinsonism between January 1997 and December 1999, 7 were found to have a dropped head with neck extensor weakness on examination. All 7 demonstrated dysautonomia and 6 did not respond to levodopa, consistent with a diagnosis of multisystem atrophy. Parkinsonism was the initial symptom in 5, head drop in 2. Five were found to have mild, moderate (n = 1 each), or profound (n = 3) neck rigidity. All 7 showed myopathic changes on needle electromyography of paraspinal or neck muscles (splenius, scalenus, semispinalis, trapezius) and muscle biopsy. The latter, performed in 5, showed noninflammatory myopathy, with mitochondrial abnormalities on electron microscopy in 2. Neck extensor weakness and a droopy head in parkinsonism may be caused by a primary myopathy and should raise the diagnostic possibility of multisystem atrophy.

COMMENTARY

Dropped head syndrome is an affliction of mixed etiology, resulting from disease anywhere along the motor unit, and beyond. Inflammatory myositis (polymyositis, dermatomyositis, inclusion body myositis), noninflammatory myopathy with or without necrosis, unspecified congenital myopathy, adult-onset nemaline myopathy, and muscular dystrophy (facioscapulohumeral dystrophy) may cause predominant weakness of neck extensors (*J Clin Neurosci.* 2000:7;334-336; *Neurology.* 1992;42;1625-1627; *J Child Neurol.* 1994;9;330-331; *Muscle Nerve.*

1999;22;115-118; *Ann Neurol.* 1986;20:133). Neuromuscular transmission defects (myasthenia gravis), neuropathy (chronic inflammatory demyelinating polyneuropathy), and anterior horn cell disease (amyotrophic lateral sclerosis) are also causative (*Ann Neurol.* 1986;20:133); *Muscle Nerve.* 1994;17:808-810). Hypokalemia, in addition to causing a vacuolar myopathy, may result in relatively acute neck muscle weakness (*Neurology.* 1993;43:846-847), and either hypothyroidism or hyperparathyroidism may cause a slowly progressive, severe dropped head (*Neurology.* 2000;55:896-897; *Rev Rhum Ed Fr.* 1993;60:467-469). Malignancy, postpolio syndrome, mitochondrial myopathy, and Cushing's syndrome are other associations (*Muscle Nerve.* 1999;22:115-118). Some remain cryptogenic. Serum creatine kinase is usually normal, though levels up to 4800 U/L are reported in secondary cases (*Neurology.* 2000;55:896-897). Needle electromyography of cervical paraspinal muscles shows low amplitude, short duration, polyphasic (myopathic) motor unit potentials with fibrillation potentials, and muscle biopsy in primary cases. These usually reveal nonspecific myopathy without evidence of inflammation. Treatment of an underlying condition, where present, is beneficial. Sometimes in cryptogenic cases, isolated instances of improvement have been reported following immunosuppression with azathioprine and prednisone (*Muscle Nerve.* 1999;22:115-118) or intensive physiotherapy (*Disabil Rehabil.* 1999;21:563-565). **—michael rubin**

CME Questions

18. Which of the following is correct?

a. Successive injections of IVP vaccine will give a lifetime of protection against poliomyelitis.
b. The recent epidemic of poliomyelitis in the Dominican Republic was the expression of a wild polio virus.
c. IVP vaccine should be repeated every year in adults for safe protection.
d. Other mid-American countries have had poliomyelitis epidemics in the last 10 years.

19. All of the following are associated with late cognitive decline after CABG *except*:

a. previous TIA.
b. cognitive decline at discharge.
c. older age.
d. fewer years of education.

20. An increased rate of MS attacks was seen with:

a. hepatitis B vaccine.
b. influenza vaccine.
c. tetanus vaccine.
d. a and c
e. None of the above

21. Cortical spreading depression is associated with each of the following *except*:

a. Migraine aura
b. Central pain sensitization
c. Prolonged neuronal depolarization
d. Glutamate excitation and extracellular potassium
e. Cerebral oligemia

Readers are Invited. . .

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