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INSIDE

A New Therapy for Neuroleptic Malignant Syndrome

ABSTRACT & COMMENTARY

Source: Sato Y, et al. Efficacy of methylprednisolone pulse therapy on neuroleptic malignant syndrome in Parkinson's disease. *J Neurol Neurosurg Psychiatry*. 2003;74:574-576.

Neuroleptic malignant syndrome (NMS) presents several unique challenges for the treating physician. Although the disorder classically follows exposure to typical neuroleptics (often in young men given high-dose depot preparations of antipsychotics), any agent that blocks the D2 family of dopamine receptors, including metoclopramide or prochlorperazine, may trigger the disorder. It also occurs in patients with Parkinson's disease (PD) who decrease or discontinue their dopaminergic therapy. Symptoms of NMS include fever, rigidity, alteration of consciousness, autonomic dysfunction, and elevations in creatine kinase. However, a patient may present with NMS without florid signs of autonomic instability or high fever, and the diagnosis should be considered in any patient who presents with lethargy, fever, and elevation in creatine kinase.

In this paper, Sato and colleagues conducted a double-blind, placebo-controlled study of the effect of 3 days of treatment with steroid pulse therapy in NMS. Forty PD patients were enrolled in this trial and randomly assigned to receive either 1000 mg of methylprednisolone IV per day for 3 days or placebo. In all patients, NMS was triggered by discontinuation of dopaminergic agents, either because of hallucinations, dyskinesias, or on-off phenomena. For the duration of the trial, all patients were treated with oral levodopa (300 mg/d), bromocriptine (7.5 mg/d), and dantrolene (75 mg/d).

Symptoms and signs of NMS lasted 7 days in the steroid-treated group vs 18 days in the placebo group. Disseminated intravascular coagulation occurred in 3 patients in the placebo group (with 1 death); there were no deaths in the steroid group. Systolic and diastolic blood pressure normalized in 18 patients in the steroid group during or immediately after steroids were given, while blood pressure took at least 10 days to normalize in the placebo group. Ten days after enrollment, creatine kinase levels were normal in all patients in the steroid group but normal in only 6 patients in the placebo group.

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COMMENTARY

Despite the small sample size, this study demonstrates that the addition of 3 days of high-dose IV methylprednisolone substantially reduced morbidity and mortality in NMS. Most impressive, markers of NMS including creatine kinase, autonomic instability, and time to resolution of symptoms were all affected by the treatment. Based on this study, IV methylprednisolone should be administered to any patient suspected of suffering from NMS as soon as the diagnosis is considered.

Although this is an important study, *Neurology Alert* readers should be aware of several issues. In the 1980s, several PD patients were reported to develop fatal episodes of NMS after discontinuation of levodopa. This was observed following the practice of admitting patients to the hospital to withdraw their PD medications for a "levodopa holiday." After these reports, neurologists abandoned the practice of completely withdrawing dopaminergic stimulation in PD patients. Even in the setting of psychosis, severe dyskinesias, or motor fluctuations, most PD patients can be managed with a reduction in levodopa dose or the addition of other agents (such as atypical neuroleptics or amantadine). In practice, my colleagues and I never completely withdraw levodopa, particularly in advanced PD patients. More concerning, Sato et al gave each patient the same low dose of levodopa, bromocriptine, and dantrolene. In fact, the dose of levodopa and agonist required by a patient with NMS should be determined by their dopaminergic regimen prior to the development of NMS (ie, giving a patient 300 mg of levodopa when their usual daily dose is 1200 mg is insufficient and might be considered below an acceptable standard of care).

Although this trial yielded important results, readers should be aware that the treatment paradigm in this study is not appropriate for routine clinical care of PD patients who develop this devastating neurologic emergency. — **STEVEN FRUCHT**

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The Return of Mitral Valve Prolapse as a Cause of Stroke

ABSTRACTS & COMMENTARY

Sources: Avierinos JF, et al. Cerebral ischemic events after diagnosis of mitral valve prolapse. A community-based study of incidence and predictive factors. *Stroke*. 2003;34:1339-1344; Oppenheimer S. Editorial comment. Is MVP an MVP in ischemic cerebral events? *Stroke*. 2003;34:1345.

THE RELATIONSHIP BETWEEN MITRAL VALVE PROLAPSE (MVP) and ischemic neurological events remains controversial. Barnett and colleagues first reported the association between stroke and mitral valve prolapse mainly in young patients.[1] Subsequent publications could not identify any increased risk of cerebral embolism in patients with MVP,[2] and the condition ceased to be considered a major risk factor for stroke. Indeed, it has come to be considered a harmless variant that is common in the general population. Avierinos and colleagues at the Mayo Clinic have used the Olmstead County, Minn, Data Base to study the association between MVP and ischemic neurological events. They identified MVP patients diagnosed between 1989 and 1998. Patients were selected for echocardiography on the basis of auscultation findings (70%). The remaining 30% had cardiorespiratory or other symptoms that were reasons for echocardiography. The inclusion criteria were that the patients had no evidence of atrial fibrillation on ECG and no previous cardiac surgery or history of stroke or TIA. There were 777 eligible subjects. Their mean age was 49 ± 20 years, and 66% were women. The follow-up period averaged 5.5 years. Thirty patients (14 men, 16 women) experienced a first ischemic neurological event (12 TIAs, 18 cerebral infarctions). Seven of

those patients had recurrent ischemic neurologic events during the follow-up period. Twenty-eight symptomatic patients had carotid Doppler examinations. Only 2 patients, both of whom suffered cerebral infarcts, had ipsilateral cerebrovascular stenosis. Only 1 ischemic event, a TIA, occurred in a patient younger than 50 at diagnosis. Ischemic neurologic events occurred in 20 patients undergoing medical management and in 10 patients only after they had had cardiac surgery. Nine of these 10 patients had severe mitral regurgitation. In 16 patients, the first ischemic neurological event occurred after atrial fibrillation had been diagnosed, and in 14 patients, the first ischemic neurological event occurred without detected atrial fibrillation and under conservative management.

Compared with expected neurological events in the same community, subjects with mitral valve prolapse showed an excess risk of lifetime ischemic events (relative risk, 2.2; $P < .001$). The excess risk of TIA and stroke was observed in the high-risk subsets of patients undergoing medical management. These high-risk subsets included those with advancing age and thickened mitral leaflets at diagnosis. Subsequently, the need for cardiac surgery and the occurrence of atrial fibrillation in the course of the disease were independently associated with the risk of ischemic neurologic complications. The time-dependent risk factors or excess rates of ischemic neurologic events were related to the degree of mitral regurgitation resulting from MVP. In these patients, the subsequent need for cardiac surgery and the occurrence of atrial fibrillation in the course of the disease were independently associated with the risk of ischemic neurologic complications.

Avierinos et al conclude that the high-risk subgroups of MVP patients, namely those who are older and have mitral regurgitation, atrial fibrillation, and an enlarged left atrial diameter, require careful monitoring and therapeutic interventions to minimize the risk of stroke.

COMMENTARY

As noted by Oppenheimer in his editorial comment on this paper, this is a valuable study that helps to identify mitral valve patients at high risk of cerebral vascular events. The prognostic indicators for a high risk of stroke or TIA were older age (older than 50 years, atrial fibrillation, mitral valve thickening, and mitral regurgitation requiring cardiac surgery). It may be that older age is a marker for the fact that MVP in those patients is ischemic rather than congenital. Atrial fibrillation and an enlarged atrial dimension also are factors that are implicated in cardiogenic stroke apart from the presence of mitral valve prolapse. In the same way, cardiac surgery involving valve repair is an independent risk factor for stroke unrelated to MVP. Although the study makes no recommendations for treatment, clinicians must decide for themselves whether anticoagulation should be instituted in the higher-risk group, notably those older than 50 with atrial fibrillation, mitral valve thickening, or a previous history of stroke or TIA. In patients with mitral valve prolapse and an ischemic neurological event, there was a high recurrence rate that was 27% over the follow-up period. In contrast, patients younger than 50 without any of the high-risk factors probably do not need any prophylactic treatment to prevent stroke because their incidence of cerebral embolism was extremely low. Further studies of MVP patients in the high-risk categories will be required to determine the effect of medical intervention, namely antiplatelet or anticoagulant drugs on prognosis. **— JOHN J. CARONNA**

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SAH Risk May Be Reduced By Healthy Lifestyle

ABSTRACT & COMMENTARY

Source: Broderick JP, et al. Major risk factors for aneurysmal subarachnoid hemorrhage in the young are modifiable. *Stroke*. 2003;34:1375-1381.

Subarachnoid hemorrhage (SAH) due to a ruptured cerebral aneurysm is a disorder that is without apparent cause and is generally impossible to predict. This study suggests that there are a number of SAH risk factors related to lifestyle that are, in fact, modifiable.

The Hemorrhagic Stroke Project (HSP) compared 312 cases of aneurysmal SAH with 618 controls, without SAH, matched for age, sex, and race. Among cases, 66% were cigarette smokers compared with 30% of controls (generating an adjusted odds ratio of 3.73). Cocaine use was identified among 3% of cases and no controls (OR = 25). Other independent risk factors included hypertension, low body mass index, family history, low educational achievement, and caffeine or nicotine in pharmaceutical products.

COMMENTARY

These data from the HSP are important in that they emphasize that a seemingly unavoidable event, a sponta-

neous aneurysm rupture, may be influenced by modifiable lifestyle factors. While certain risk factors, such as family history or educational level, are difficult or impossible to change, other factors are associated with harmful behaviors and habits. Despite links with both atherosclerotic disease and cancer, young people continue to smoke cigarettes. These data, among individuals aged 18-49, further emphasize additional unrecognized deleterious effects of tobacco use. Similarly, for hypertension, the importance of treating blood pressure to prevent heart disease and stroke is well appreciated. This study further suggests that untreated hypertension in young people may also put them at increased risk for SAH. — **ALAN Z. SEGAL**

A True Clinical Application of Functional MRI: Predicting Dysnomia Following Left Temporal Lobectomy

ABSTRACT & COMMENTARY

Source: Sabsevitz DS, et al. Use of preoperative functional neuroimaging to predict language deficits from epilepsy surgery. *Neurology*. 2003;60:1788-1792.

Functional MRI (fMRI) has made tremendous strides as a research tool in providing insight into the anatomy and physiology of higher cortical function. Sabsevitz and associates report a correlation between fMRI results and language dysfunction following anterior temporal lobectomy (ATL) in the treatment of medically refractory epilepsy. They studied 24 patients who underwent left ATL (L-ATL) and compared them to 32 patients who underwent right ATL (R-ATL). All of the patients were evaluated with preoperative fMRI employing a language task, intracarotid amobarbital test (IAT, aka Wada test), and pre- and 6-month postoperative neuropsychological testing, including the 60-item Boston Naming Test (BNT). The fMRI study analyzed 8 region-of-interest (ROI) volumes for each hemisphere. Lateralization indices (LI) were calculated (LI = [L-R]/[L+R]), reflecting the interhemispheric difference between significantly activated voxel counts. An analogous LI was computed for the IAT based upon scores assigned for language performance for left vs right carotid injection.

Sabsevitz et al reported the following results. First, the L-ATL group had a significant ($P < .001$) decline in BNT score relative to the R-ATL group. Second, using Pearson correlation, the fMRI LI correlated with IAT LI, in concordance with prior studies. Finally, fMRI LI (to the left hemisphere) was significantly correlated (even more so than IAT LI in this series) with decrease in BNT. In analyzing specific ROIs, temporal LI was the best predictor of decline in BNT score. Specifically, using a > 2 standard deviation decline in BNT from the R-ATL group to define "poor outcome," fMRI temporal LI showed 100% sensitivity, 73% specificity, and 81% positive predictive value (PPV) with LI threshold set at 0.25. When poor outcome was defined as at least a 10-point decrease in BNT, temporal fMRI LI demonstrated 100% sensitivity, 57% specificity, and 63% PPV.

COMMENTARY

Neurology Alert has previously reported on fMRI as a tool for evaluation of patients undergoing epilepsy surgery.[1] Previously published data have been most concerned with validating noninvasive fMRI compared to the "gold standard" of the invasive IAT, in lateralization of language dominance.[2] The significance of the current study is the comparison of preoperative fMRI data to postoperative language deficit. Postoperative dysnomia could be considered a "platinum" standard, since it is a clinical outcome that relates directly to the functional risk of epilepsy surgery. If these results can be replicated, this study would represent the maturation of fMRI from a research instrument to a test that affects clinical decisions regarding assessing the risk of L-ATL in patients who have an intractable seizure focus localized to this region.

There are 2 caveats, however, in the interpretation of this study, and *Neurology Alert* hopes that Sabsevitz et al or others will provide us with further data. First, no information is presented regarding the results of other neuropsychometric testing other than the BNT. Certainly, non-naming language deficits can affect quality of life following epilepsy surgery. Exploring other language functions would provide important details about the PPV of fMRI for nondysnomic dysphasia. Second, and more importantly, Sabsevitz et al provide no data regarding the results of intraoperative or ictal electrocorticography (EcoG), nor EcoG functional mapping and how these results affected the "tailoring" of the anatomical boundaries of the resection margin. Knowledge of these data would obviously affect the robustness of fMRI as a predictor of neuropsychological risk of ATL for epilepsy. — **ANDY DEAN**

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Dr. Dean is Assistant Professor of Neurology and Neuroscience, Director of the Epilepsy Monitoring Unit, Department of Neurology, New York Presbyterian Hospital—Cornell Campus.

Maintenance Therapy for Vasculitis Associated with Antineutrophil Cytoplasmic Autoantibodies

ABSTRACT & COMMENTARY

Source: Jayne D, et al. A randomized trial of maintenance therapy for vasculitis associated with antineurotrophil cytoplasmic autoantibodies. *N Engl J Med*. 2003;349:36-44.

The treatment of a variety of forms of CNS vasculitis is difficult. Two types can characterized by positivity to antineutrophil cytoplasmic antibodies. These are Wegener's granulomatosis and microscopic polyangiitis. These illnesses share several common features including pulmonary capillaritis, glomerulonephritis, and the circulating antineutrophil cytoplasmic antibodies that are positive for either proteinase-3 or myeloperoxidase. Modern treatment for these illnesses was established in the early 1970s when Fauci and associates introduced a regimen combining daily cyclophosphamide therapy given for 1 year after remission was achieved with prednisone therapy initiated at a dose of 1 mg/kg of body weight per day and then tapered to an alternate day schedule.[1-2] This treatment has produced remission in 80-100% of patients and can result in long-term survival. One difficulty, however, is that many patients relapsed when they were discontinued from therapy. Relapse occurred in almost 50% of patients by 8 years. In the present report, Jayne and associates studied whether it was possible to substitute a regimen of azathioprine at 2 mg/kg per day for maintenance therapy in patients with generalized vasculitis. Both groups continued to receive prednisolone. In this study, the patients all received initially 3 months of oral cyclophosphamide and prednisolone and then were randomized to either 1.5 mg/kg per day of cyclophosphamide or 2 mg/kg per day of the azathioprine, which was then continued up to 18 months from study entry. Relapse was the primary end point. The number of serious adverse side effects was similar in the 2 groups. The relapse rate was lower among patients with microscopic polyangiitis than among those with Wegener's granulomatosis. The substitution of azathioprine after remission did not, however, increase the rate of relapse.

COMMENTARY

This appears to be a new and reasonable approach to more chronic treatment of patients with vasculitis. Exactly how long azathioprine therapy should then be maintained remains to be determined. Nevertheless, the lower toxicity of azathioprine as compared to cyclophosphamide makes it a reasonable alternative treatment once remission has been induced with cyclophosphamide. **— M. FLINT BEAL**

References

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Is 14-3-3 a Useful Diagnostic Tool for Sporadic Creutzfeldt-Jakob Disease?

ABSTRACT & COMMENTARY

Source: Geschwind, et al. Challenging the clinical utility of the 14-3-3 protein for the diagnosis of sporadic Creutzfeldt-Jakob disease. *Arch Neurol*. 2003;60:813-816.

The value of the 14-3-3 test for establishing a diagnosis of probable sporadic Creutzfeldt-Jakob disease (CJD) has been suggested to be as high as 96-100% in several reports. This has been established by reports from the World Health Organization, which revised its diagnostic criteria for probable sporadic CJD to allow substitution of a positive 14-3-3 test for a positive electroencephalogram, provided the disease has less than 2 years' duration. A number of other studies, however, has suggested that the test lacks both sensitivity and specificity. In the present report, 32 patients who had definite CJD established by biopsy or autopsy confirmation were studied for 14-3-3 reactivity. Seventeen of the 32 patients had a positive result. This yields a sensitivity of only 53%. Geschwind and colleagues concluded that the test was only moderately sensitive in establishing the diagnosis.

COMMENTARY

The present paper is consistent with that of a number of other studies, which suggest that the 14-3-3 test, although useful, is frequently insensitive in establishing a diagnosis of CJD. Another study showed a sensitivity

of 61%, yet a relatively high specificity if one used a cutoff of a value of more than 8 ng/mL. When a lower threshold was used, the sensitivity increased, but the specificity fell dramatically to only approximately 50%. The 14-3-3 protein is a marker for chronic neuronal damage. It can be increased by a variety of other illnesses such as rapidly progressive Alzheimer's disease, rapidly progressive frontotemporal dementia, Hashimoto's encephalitis, vasculitis, or diffuse intravascular lymphomatosis. The 14-3-3 protein is also increased in patients with multiple sclerosis with myelitis.[1] In our experience, we have had a number of biopsy-confirmed cases recently in which the test was negative. Findings of enhanced signal in the cortical ribbon on diffusion-weighted magnetic resonance imaging and a characteristic EEG may have greater diagnostic use. **— M. FLINT BEAL**

Reference

1. Satoh J, et al. *J Neurol Sci*. 2003;212:11-20.

Diagnosis of Autoimmune Autonomic Neuropathies

ABSTRACT & COMMENTARY

Source: Klein CM, et al. The spectrum of autoimmune autonomic neuropathies. *Ann Neurol*. 2003;53:752-758.

In this report by Klein and colleagues, the clinical features of a series of 18 patients (13 female, 5 male, 61.4 years of age ± 12.0 years) evaluated at the Mayo Clinic for autonomic dysfunction are presented. Ten patients had subacute onset of symptoms (6 with an antecedent viral illness), and 8 patients had a chronic progressive course. Patients with other definable causes such as diabetes, amyloidosis, or multiple system atrophy were excluded.

Patients were identified first with neurogenic orthostatic hypotension, defined as a systolic blood pressure reduction of at least 30 mm Hg that occurred within 3 minutes of head tilt up. Of 121 patients meeting that diagnosis, 18 were found to have autoantibodies against autonomic ganglion acetylcholine receptor (ganglionic AchR Ab). Additional autonomic testing was performed to assess postganglionic sudomotor, cardiovagal, and adrenergic functions, and a composite autonomic severity score (CASS) was calculated from 0 (no deficit) to 10 (maximal deficit). The mean score for the 18 patients was 7.5, indicating severe generalized autonomic failure. The patients with more severe cholinergic autonomic failure had higher levels of ganglionic AchR antibodies.

The clinical profile of cholinergic neuropathy included a spectrum of parasympathetic/enteric symptoms: sicca (dry eyes and mouth), abnormal pupillary responses to light (Adies), upper gastrointestinal symptoms (early satiety, postprandial nausea, and vomiting), constipation, neurogenic bladder, erectile dysfunction, and reduced sweating.

COMMENTARY

The diagnosis of autonomic neuropathy is often delayed over years if not considered by the alert clinician. The causes are heterogeneous and the term idiopathic autonomic neuropathy, or "pure autonomic failure," customarily categorizes those cases without a definable underlying pathology. This report documents the existence of an autoimmune etiology for a subset of patients, whose clinical profile appears to have both a subacute onset or a progressive course, some of whom might be confused with neurodegenerative autonomic failure. The therapeutic implications of identifying an autoimmune autonomic neuropathy were not addressed in this report by Klein et al. For example, was any attempt at immune modulatory therapy attempted in these patients (corticosteroids, plasmapheresis, IVIG), and was any benefit achieved? It is hopeful that neurologists may soon reliably identify and treat a previously untreatable disorder. **— BRIAN R. APATOFF**

Neurologic Complications of Bladder Cancer

ABSTRACT & COMMENTARY

Source: Anderson TS, et al. Neurologic complications of bladder carcinoma: A review of 359 cases. *Cancer*. 2003;97:2267-2272.

Among 359 patients with bladder cancer confirmed by tissue diagnosis and seen between 1962 and 2001 at the University of Kentucky Medical Center, 14% (n = 52) developed neurological complications. Overall, 5% developed neurologic metastases, with 2% each experiencing lumbosacral plexopathy (n = 7) or epidural spinal cord compression (n = 6), and 1% (n = 4) developing brain metastases. In 1 patient, brain metastases preceded diagnosis of the bladder cancer by 3 months. Nonmetastatic complications were the more

common and included metabolic encephalopathy in 24 (7%), peripheral neuropathy in 9 (2.5%), stroke in 6 (1.7%), and seizures in 5 (1.4%). One patient each was diagnosed with normal pressure hydrocephalus, subdural hematoma, and glioblastoma multiforme. Back pain was the most frequent neurologic complaint (n = 32, 9%), but in 25% (n = 8) it was unrelated to the cancer and in another 34% (n = 11) it was due to purely bony metastases. No patient developed infectious or carcinomatous meningitis. At autopsy, 67% of bladder cancer patients show metastases, usually to the liver (39%), lung (38%), or bone (28%). For the neurologist, however, local spread is more common than distant metastases. Back pain and metabolic encephalopathy, the latter usually due to renal failure, remain the most common incentives for neurologic consultation in such patients.

COMMENTARY

Paraneoplastic neurological syndromes may also, on rare occasions, occur with bladder carcinoma. Presumably a protein, normally restricted to the nervous system, is expressed by the tumor, inducing an immune response with production of onconeural antibodies both against the tumor and the nervous tissue. Evidence suggests that cytotoxic T cells are also involved. Among 34 patients with type 2 antineuronal nuclear autoantibody (ANNA-2 or "anti-Ri"), cancer was found in 24 (86%), including lung (n = 10), breast (n = 9), and 1 each with cervical and bladder cancer.[1] Opsoclonus-myoclonus was the predominant neurologic syndrome in the latter, presenting 1 year after cancer diagnosis, with other symptoms and signs comprising trochlear nerve palsy, tremor, dizziness, and memory problems. Dermatomyositis is also reported with transitional cell bladder carcinoma, and a causal relationship was suggested when treatment of the cancer resulted in resolution of the dermatomyositis.[2] Anti-Yo antibody (anti-Purkinje cell cytoplasmic antibody, APCA-1), paraneoplastic cerebellar degeneration, and bladder cancer comprise another syndrome. Tumor tissue demonstrated the presence of Yo antigen and antibody titers fell with removal of the tumor.[3] Lastly, among 12 patients with antineuronal nicotinic ganglionic acetylcholine receptor (AchR) antibodies, 5 had subacute autonomic neuropathy, 1 each with cancer of lung, rectum, or bladder. Neither healthy subjects nor 62 patients with myasthenia gravis and muscle AChR antibodies were positive for ganglionic AChR antibodies, implicating the latter in this paraneoplastic association.[4]

— MICHAEL RUBIN

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Selective Sympathicotomy Stops Sweaty Palms

ABSTRACT & COMMENTARY

Source: Yoon SH, Rim DC. The selective T3 sympathicotomy in patients with essential palmar hyperhidrosis. *Acta Neurochir*. 2003;145:467-471.

Among 54 patients with essential hyperhidrosis, 24 underwent T2/T3 sympathicotomy and were compared to 30 subsequent patients treated by selective T3 sympathicotomy. General anesthesia was used in all cases, and surgery, bilateral in all and lasting about an hour, was performed using a thoracoscope inserted into the midaxillary line at T6. T2/T3 sympathicotomy was accomplished by transecting the sympathetic chain above the second and third ribs, while for T3 sympathicotomy the sympathetic chain was cut only above the third rib. Patients were followed for a mean of approximately 17 months postoperatively, and statistical analysis was performed using the Mann-Whitney test and Fisher's exact test.

Palmar hyperhidrosis was relieved in all patients, without recurrence, during the observation period. Compensatory hyperhidrosis, involving the chest, back, abdomen, legs, or multiple sites, was reported in 11 (45.8%) of T2/T3 sympathicotomized patients but in only 5 (16.7%) of T3 sympathicotomized cases. Overall, 66% of the former but 88% of the latter reported "full satisfaction" with their procedure, while 25% and 13%, respectively, reported "satisfaction." Eight percent of the former, but none of the latter, were dissatisfied. Complications included chest pain (n = 6, n = 4, respectively), pneumothorax (n = 1 in each group), and Horner's syndrome (n = 4, n = 0, respectively). Length of hospitalization (mean, 2.4 days) was similar in both groups. T3 selective thoracoscopic sympathicotomy appears superior to T2/T3 sympathicotomy for the treatment of essential hyperhidrosis.

COMMENTARY

Favorable findings for an analogous procedure were reported earlier this year from the Mayo Clinic.[1] Ten consecutive patients with essential palmar hyperhidrosis who failed medical therapy underwent bilateral sympathotomy (simple disconnection) of the second thoracic

ganglion input into the brachial plexus. All 20 hands improved, with near-complete cessation or marked reduction in sweating documented by thermoregulatory sweat testing, in 11 and 8 hands, respectively. Neither pneumothorax, Horner's syndrome, nor moderate or severe postoperative hyperhidrosis occurred in any patient. Sympathotomy of the T2 ganglion input into the brachial plexus may be superior to T3 selective thoracoscopic sympathicotomy for the treatment of primary palmar hyperhidrosis, but longer-term follow-up for both procedures is needed for confirmation.

Open-label treatment of palmar and plantar hyperhidrosis using Botulinum toxin-A injection into the palms and sole was also found to be safe and effective.[2] Local side effects including hand weakness are not uncommon, but systemic side-effects, lasting up to 1 month, can also occur, including blurred vision, indigestion, and dysphagia with severe dry throat as reported with Botulinum toxin-B.[3] Preliminary controlled trials for the treatment of palmar hyperhidrosis using Botulinum toxin are under way but have yet to be reported.

Axillary hyperhidrosis, as well, appears to respond to Botulinum toxin-A.[4] Among 207 patients with primary bilateral axillary hyperhidrosis, 174 enrolled and completed a multicenter, double-blind study comparing placebo vs 50 U of Botulinum toxin-A injected per axilla. Blinded injections were given at study entry and followed by open-label injection every 4 months for a maximum of 12 months. Gravimetric assessment, 4 weeks following each treatment, of spontaneous sweat production of > 50 mg/axilla was the main outcome measure. Compared to placebo, Botulinum toxin-A was significantly more effective with response rates of 96.1%, 91.1%, and 83.3% following a first, second, and third treatment, respectively. Placebo response was 34.7%. Overall, 13.5% experienced side effects, compared to 4.1% in the placebo group, with increased nonaxillary sweating being most common (4.3%), followed by pain in the injection site (1.9%), hot flushes (1.4%), and muscle weakness (1%). No serious side effects (n = 11), including a single death from myocardial infarction, were felt related to study drug. Botulinum toxin-A is safe and effective for ongoing treatment of axillary hyperhidrosis. **— MICHAEL RUBIN**

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6. In patients with MVP, which of the following is associated with increased stroke risk?
a. Age older than 50 years
b. Atrial fibrillation
c. Mitral regurgitation
d. Enlarged left atrium
e. All of the above

7. Neurological complications of bladder cancer may include all of the following *except*:
a. lumbosacral plexopathy.
b. epidural spinal cord compression.
c. brain metastases.
d. sensory ganglionitis.
e. opsoclonus-myoclonus.

8. Which of the following is *false*? Autoimmune autonomic neuropathy:
a. is associated with antibodies against the acetylcholine receptor.
b. is characterized by a spectrum of orthostatic hypotension, gastrointestinal paresis, and urinary dysfunction.
c. does not affect pupillary responses.
d. can have a subacute or chronic presentation.

9. Treatment of essential hyperhidrosis may include:
a. Botulinum toxin-A injections.
b. Botulinum toxin-B injections.
c. sympathotomy (simple disconnection) of the second thoracic ganglion input into the brachial plexus.
d. T3 selective thoracoscopic sympathicotomy.
e. All of the above

Answers: 6(e); 7(d); 8(c); 9(e)

Readers are Invited

Readers are invited to submit questions or comments on material seen in or relevant to *Neurology Alert*. Send your questions to: Christie Messina—Reader Questions, *Neurology Alert*, c/o American Health Consultants, P.O. Box 740059, Atlanta, GA 30374. ■