

PEDIATRIC NEUROLOGY BRIEFS

A MONTHLY JOURNAL REVIEW

J. GORDON MILLICHAP, M.D., F.R.C.P., EDITOR

Vol. 27, No. 5

May 2013

NEUROMUSCULAR DISORDERS

SMALL-FIBER POLYNEUROPATHY AND PAIN SYNDROMES

Investigators at the Massachusetts General Hospital, Boston, MA, tested the hypothesis that acquired small-fiber polyneuropathy (SFPN) contributes to unexplained widespread pain syndromes in children and adolescents. Medical records of 41 consecutive patients were analyzed for objective diagnostic test data for SFPN. These included skin biopsy, nerve biopsy, and autonomic function testing, plus histories, symptoms and signs, and treatments. Healthy matched volunteers acted as normal controls for SFPN tests.

In this polyethnic patient sample, age at illness onset averaged 12.3 +/- 5.7 years; 73% were female, 68% chronically disabled, and 68% had been hospitalized. Objective diagnostic test results were definite for SFPN in 59%, probable in 17%, and possible in 22%. Only 1 had normal SFPN test results. Somatic complaints other than pain were reported in 98% patients and were consistent with SFPN dysautonomia (90% cardiovascular, 82% gastrointestinal, and 34% urological). Chronic fatigue was reported in 83% and chronic headache in 63%. Neurological examinations identified reduced sensation in 68% and vasomotor abnormalities in 55%, including erythromelalgia in 23%. Tests for causality of pain revealed only a history of autoimmune disease elicited in 33% and serologic markers of disordered immunity in 89%. Treatment with corticosteroids and/or IV immunoglobulin benefited 80% of patients (12/15), both objectively and subjectively. (Oaklander AL, Klein MM. Evidence of small-fiber polyneuropathy in unexplained, juvenile-onset, widespread pain syndromes. *Pediatrics* 2013 Apr;131(4):e1091-e1100).

COMMENT. Chronic, diffuse pain syndromes involving small nonmyelinated-C fiber peripheral nerves, especially in the extremities and feet, and the autonomic nervous system are a well-known but little understood disorder of the elderly, often referred to as

PEDIATRIC NEUROLOGY BRIEFS © 1987-2013, ISSN 1043-3155 (print) 2166-6482 (online), is published monthly and covers selected articles from the world literature. The editor is Pediatric Neurologist at the Ann & Robert H. Lurie Children's Hospital of Chicago; Professor Emeritus, Northwestern University Feinberg School of Medicine. PNB is a continuing education service designed to expedite and facilitate the review of current scientific information for physicians and other health professionals. Apply to PediatricNeurologyBriefs.com for Subscriptions (12 issues, January - December). Digital Edition PDF: \$72 (Residents/Fellows \$36); Print + Digital: \$96 within US/UK, \$128 outside US/UK. Institutions: Digital \$188, Print + Digital \$228. Mail: Pediatric Neurology Briefs Publishers, PO Box 11391, Chicago, IL 60611

“burning feet syndrome.” The cause may be nutritional, vitamin B deficiencies, diabetes, hypothyroidism, spinal stenosis, or genetic (Dyck PJ et al. Burning feet as the only manifestation of dominantly inherited sensory neuropathy. **Mayo Clin Proc** 1983 Jul;58(7):426-9), but often idiopathic (Ropper AH, Samuels MA eds. Diseases of the peripheral nerves. In: **Adams and Victor’s Principals of Neurology**. New York, McGraw Hill Medical, 2009, Chap 46;1296-7). SFPN in children is rarely reported. It appears to be an autoimmune disorder, but symptoms of dysesthesia and hyperesthesia are also encountered in children with ADHD and PDD, associated with an abnormal microarray, deletion 17p12 (Personal case report) (Grozeva D, et al. **Schizophr Res** 2012 Mar;135(1-3):1-7).

Diagnostic testing for small fiber neuropathy.

SFPN is characterized by loss of sensation (thermal and pinprick hypoesthesia) and positive sensory symptoms (burning pain, allodynia, hyperalgesia). Clinical neurological examination and routine neurophysiologic tests are often insufficiently sensitive, but skin biopsy and recent availability of normative reference values are of proven value in the diagnosis of damaged small nerve fibers (Lauria G, Lombardi R. Small fiber neuropathy: is skin biopsy the holy grail? **Curr Diab Rep** 2012 Aug;12(4):384-92). In an earlier study of 486 patients with SFPN, skin biopsy had a diagnostic efficiency of 88.4%, clinical examination of 54.6% and quantitative sensory testing of 46.9% (Devigili G, et al. The diagnostic criteria for small fibre neuropathy: from symptoms to neuropathology. **Brain** 2008 Jul;131(Pt 7):1912-25).

COATS SYNDROME IN FACIOSCAPULOHUMERAL DYSTROPHY TYPE 1

Investigators at University of Rochester Medical Center, NY; Hopital Archet-CHU de Nice, France; and Albert Einstein College of Medicine, NY, studied the frequency of Coats syndrome and its association with D4Z4 contraction size in 408 patients identified with facioscapulohumeral dystrophy type 1 (FSHD1). Three patients (0.8%) had a history of Coats disease, and 14 patients had FSHD and Coats syndrome confirmed by ophthalmologic examination. Median age at diagnosis of Coats syndrome was 10 years. The median D4Z4 fragment size was 13 kilobases. Close surveillance for retinal complications is recommended in FSHD1 patients with D4Z4 fragments <15kb. (Statland JM, Sacconi S, Farmakidis C, Donlin-Smith CM, Chung M, Tawil R. Coats syndrome in facioscapulohumeral dystrophy type 1. **Neurology** 2013 Mar 26;80(13):1247-50). (Response: Dr Statland: Jeffrey_Statland@URMC.Rochester.edu).

COMMENT. Coats disease, characterized by exudative retinitis and telangiectases of the retina, with slow progression to retinal detachment, may occur alone as an idiopathic form, unilateral, in males with onset at age 1-20 years, or as a syndrome, associated with FSHD1 and high-frequency hearing loss. FSHD1 is caused by a loss of D4Z4 repeat units on chromosome 4q35. Coats disease in the FSHD-associated syndrome is bilateral, it occurs at any age, and most frequently in female patients with FSHD and large contractions (allele size <15 kb). Contraction size (<15 kb) rather than age or FSHD severity should determine the need for annual retinal examinations for retinal vascular