

ORAL PRESENTATION

Open Access

Small-fiber polyneuropathy (SFPN), a common underlying diagnosis in syndromes involving unexplained chronic pain and multi-system symptoms

Anne Louise Oaklander^{1,2*}, Heather Downs¹, Zeva Daniela Herzog¹, Max Klein¹

From Seventh Scientific Meeting of The TMJ Association, Genetic, Epigenetic, and Mechanistic Studies of Temporomandibular Disorders and Overlapping Pain Conditions
Bethesda, MD, USA. 7-9 September 2014

Background

Syndromes involving unexplained chronic widespread pain (CWP) and multi-system symptoms are common, with 1-5% prevalence for fibromyalgia alone. They more often affect females and cause disability and high costs [1-3]. Other common syndromes include chronic fatigue, seronegative Lyme, and Gulf War Illness. Fragmentary syndromes include TMJD, POTS, CRPS, irritable bowel). These syndromes are particularly devastating in children and young adults, where they interfere with education and development and disrupt entire families [4-6]. SFPN is known to cause CWP and multi-system complaints in older adults. Unlike the syndromes above, SFPN can be objectively diagnosed by measuring innervation in lower-leg skin biopsies, and autonomic functions testing (AFT) of heart rate, blood pressure and sweating [7]. SFPN has several established causes including diabetes, infections, cancer, and toxins. Many causes are diagnosable, treatable, and sometimes curable [8]. Our work suggests that unrecognized SFPN contributes to several syndromes involving CWP and multi-organ symptoms.

Materials and methods

With IRB permission, we retrospective analyzed the medical records of 41 patients with onset of unexplained CWP and multisymptoms before age 21; most had objective testing for SFPN [9]. We also prospectively studied 27

adult patients with fibromyalgia and 30 healthy volunteers using history, examination, skin biopsies and AFT [10].

Results

Retrospective chart review identified definite (in 59%) and probable SFPN (in 17%) among the young patients with onset before age 21 [9]. We characterized the clinical features, diagnostic, and treatment options for this new early-onset SFPN. Studying children, who lacked the typical causes of late-onset SFPN, implicated autoimmune causality in most. Among patients treated with immunomodulatory therapies, pain and other symptoms improved in 2/3 [9]. Among adults with fibromyalgia, 41% of skin biopsies from subjects with fibromyalgia vs. 3% of biopsies from controls were diagnostic for SFPN, and symptom and examination scores were higher in fibromyalgia subjects than in controls (all $P \leq 0.001$) [10]. All fibromyalgia patients diagnosed with SFPN then had blood tests for all known causes [8]. None had diabetes but 62% had test-results consistent with dysimmunity, and some had genetic causes [10]. Other laboratories have now also linked fibromyalgia to SFPN [11-15].

Conclusions

Some patients with unexplained widespread pain and multi-system syndromes such as fibromyalgia have objectively diagnosable SFPN. SFPN can affect children and young adults, not just older adults. Multiple lines of evidence suggest that early-onset SFPN has novel causes that can be treated. The prevalence of SFPN among TMJD patients is unstudied.

¹Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA

Full list of author information is available at the end of the article

Disclosures

None of the authors have any conflicts of interest.

Acknowledgements

Supported in part by the NIH (NINDS K24NS059892, Department of Defense grant GW093049, and donations from the Bradley, Collman, and Cheever Powell family foundations.

Authors' details

¹Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA. ²Departments of Pathology (Neuropathology), Massachusetts General Hospital, Boston, MA 02114, USA.

Published: 15 December 2014

References

1. Lindell L, Bergman S, Petersson IF, Jacobsson LT, Herrstrom P: **Prevalence of fibromyalgia and chronic widespread pain.** *Scand J Prim Health Care* 2000, **18**:149-153.
2. White KP, Speechley M, Harth M, Ostbye T: **The London Fibromyalgia Epidemiology Study: the prevalence of fibromyalgia syndrome in London, Ontario.** *J Rheumatol* 1999, **26**:1570-1576.
3. White KP, Speechley M, Harth M, Ostbye T: **The London Fibromyalgia Epidemiology Study: direct health care costs of fibromyalgia syndrome in London, Canada.** *J Rheumatol* 1999, **26**:885-889.
4. Buskila D: **Pediatric fibromyalgia.** *Rheumatic Disease Clinics of North America* 2009, **35**:253-261.
5. van Geelen SM, Bakker RJ, Kuis W, van de Putte EM: **Adolescent chronic fatigue syndrome: A follow-up study.** *Arch Pediatr Adolesc Med* 2010, **164**:810-814.
6. Mikkelsson M, El-Metwally A, Kautiainen H, Auvinen A, Macfarlane GJ, Salminen JJ: **Onset, prognosis and risk factors for widespread pain in schoolchildren: A prospective 4-year follow-up study.** *Pain* 2008, **138**:681-687.
7. England JD, Gronseth GS, Franklin G, Carter GT, Kinsella LJ, Cohen JA, *et al*: **Practice Parameter: Evaluation of distal symmetric polyneuropathy: role of autonomic testing, nerve biopsy, and skin biopsy (an evidence-based review).** Report of the American Academy of Neurology, American Association of Neuromuscular and Electrodiagnostic Medicine, and American Academy of Physical Medicine and Rehabilitation. *Neurology* 2009, **72**:177-184.
8. England JD, Gronseth GS, Franklin G, Carter GT, Kinsella LJ, Cohen JA, *et al*: **Practice Parameter: Evaluation of distal symmetric polyneuropathy: role of laboratory and genetic testing (an evidence-based review).** Report of the AAN, AANEM, and AAPMR. *Neurology* 2009, **72**:185-192.
9. Oaklander AL, Klein MM: **Evidence of small-fiber polyneuropathy in unexplained, juvenile-onset, widespread pain syndromes.** *Pediatrics* 2013, **131**:e1091-e1100.
10. Oaklander AL, Herzog ZD, Downs HM, Klein MM: **Objective evidence that small-fiber polyneuropathy underlies some illnesses currently labeled as fibromyalgia.** *Pain* 2013.
11. Üçeyler N, Zeller D, Kahn AK, Kewenig S, Kittel-Schneider S, Schmid A, *et al*: **Small fibre pathology in patients with fibromyalgia syndrome.** *Brain* 2013.
12. Albrecht PJ, Hou Q, Argoff CE, Storey JR, Wymer JP, Rice FL: **Excessive peptidergic sensory innervation of cutaneous arteriole-venule shunts (AVS) in the palmar glabrous skin of fibromyalgia patients: Implications for widespread deep tissue pain and fatigue.** *Pain Med* 2013, **14**:895-915.
13. Serra J, Collado A, Sola R, Antonelli F, Torres X, Salgueiro M, *et al*: **Hyperexcitable C nociceptors in fibromyalgia.** *Ann Neurol* 2013.
14. Giannoccaro MP, Donadio V, Incensi A, Avoni P, Liguori R: **Small nerve fiber involvement in patients referred for fibromyalgia.** *Muscle Nerve* 2013.
15. Caro XJ, Winter EF: **Evidence of abnormal epidermal nerve fiber density in fibromyalgia: Clinical and immunologic implications.** *Arthritis Rheumatol* 2014.

doi:10.1186/1744-8069-10-S1-O12

Cite this article as: Oaklander *et al*: Small-fiber polyneuropathy (SFPN), a common underlying diagnosis in syndromes involving unexplained chronic pain and multi-system symptoms. *Molecular Pain* 2014 **10**(Suppl 1):O12.

Submit your next manuscript to BioMed Central and take full advantage of:

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit

