Pentraxin 3 levels in women with fibromyalgia

Sirs,

Fibromyalgia (FM) is a common rheumatologic syndrome characterised by chronic widespread tenderness and muscular pain (1). It is one of the most common conditions seen in rheumatology clinics worldwide (1). The aetiology of FM remains obscure but neurochemicals may play a role. Spinal fluid levels of nerve growth factor and substance P were found elevated (2) and spinal fluid levels of serotonin products are decreased according to some controlled studies (2, 3). This is a disease that lacks objective markers to guide its diagnosis and treatment (1).

Pentraxine 3 (PTX3) is a long pentraxins produced by somatic and immune cells in response to proinflammatory stimuli and Toll-like receptor engagement, interacting with several ligands and exerting multifunctional properties (4). PTX3 blood concentration are low (about<2 ng/ml) in normal conditions (4). Its production is induced by IL-1, TNF and microbial moieties such as LPS (4) and unlike short pentraxines (C reactive protein-CRP and serum amyloid A) it is poorly induced by IL-6 (4).

To our knowledge, plasmatic levels of PTX3 have not been studied in FM. To verify its value in this disease we studied 94 women with FM according to American College of Rheumatology (ACR) diagnostic criteria (5) and 94 healthy women for controls paired for age. This study was approved by the local Committee of Ethics in Research and all participants signed consent. FM patients' median age was 51.5 years (range 26–65 years) and 55.3% were on amitriptyline; 27.3% on fluoxetine; 6.3% on both (amitriptyline and fluoxetine), 5.3% on cyclobenzaprine; 3.1% on duloxetine, 1.06% on pregabalin and 1.06% on venlafaxine. FM group had determination of BMI, lipid, glycaemia, hip/waist ratio and CRP serum levels. Depression level was measured by Beck instrument (6) and the disease impact by Fibromyalgia Impact Questionnaire (FIQ) (7); pain and fatigue were measured by a 0–10 visual analogue scale (VAS). Associated symptoms such as headaches, cognitive impairment, irritable bowel syndrome, paresthesias and non-restorative sleep where obtained through a Yes/No questionnaire. PTX-3 plasma levels were measured by a commercial kit using sandwich enzyme immunosorbent assay (ELISA) (R&D Systems, Minneapolis, MN, USA). Levels of plasmatic PTX3 in FM patients and controls are in Figure 1.

Studying PTX3 levels according to patients age, levels of total, LDL and HDL cholesterol; glycaemia, triglycerides, BMI, CRP, FIQ, depression, pain and fatigue scores, no correlation was found (p=NS; Spearman test). Also, no association could be found of PTX3 concentrations with presence of headaches, cognitive impairment, irritable bowel syndrome, paresthesias and non-restorative sleep (p=NS; Mann-Whitney test). We observed that PTX 3 plasma levels are higher in FM patients, but none of studied variable could be associated with this finding. Obesity and dyslipidaemia could not explain this elevation despite the fact that some studies have found association between PTX3 levels, BMI and atherosclerotic risk in otherwise healthy population (8). Also, none of the main FM symptoms could be linked to it.

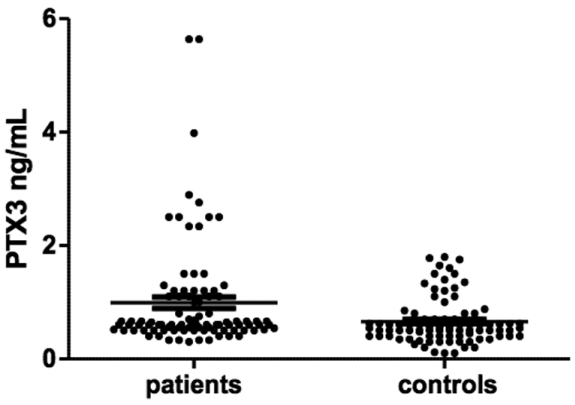

Fig. 1. PTX (pentraxine)-3 levels in patients with fibromyalgia (0.3–5.64 ng/mL; median 0.60; IQR=0.5–1.1 ng/mL) and healthy controls (0.1–1.8 ng/mL; median 0.56; IQR=0.4–0.7), p=0.0051 (Mann-Whitney test).

FM is considered a disease with abnormal pain processing at the central nervous system. Interactions between neurotransmitters, external triggers, behaviour patterns, hormones and some cytokines play a role in its appearance (1, 8). High levels of proinflammatory interleukins such as IL-8 and TNF-α have been detected in FM. IL-8 has been linked to modulation of sympathetic pain; TNF-α disrupts the blood-brain barrier and may have adverse effects on brain cell function, causing fatigue and anorexia that are seen in FM (1, 10). Unlike neuronal long pentraxins, PTX3 is not constitutively expressed in the central nervous system, but it can be found in neuronal cells and astrocytes after exposure to inflammatory signals (IL-1, TNF-α), infectious agents, autoimmune reactions or seizures (4). Studies in kainate-induced seizures in animal models suggested that PTX3 confers resistance to neurodegeneration, and its absence in brain tissue is associated with higher degenerating neurons (5). PTX3 may also interact with neuronal pentraxins and modulate their function; like them, its domain associates with AMPA-type glutamate receptors (5).

Summarising, we have found that PTX3 plasma levels are elevated in FM patients. Further studies are needed to confirm this finding and to better understand the role of PTX3 in FM.

T.L. SKARE[1]
A.C. PLAWIAK[1]
G. VERONESE[1]
E.S. PAIVA[3]
I. MESSIAS-REASON[3]
R. NISIHARA[1]

[1]Rheumatology Unit, Evangelical University, Curitiba, Paraná, Brazil;
[2]Department of Medicine, Positivo University, Curitiba, Paraná, Brazil;
[3]Immunopathology Molecular Laboratory, Clinical Hospital, Federal University of Paraná, Paraná, Brazil.

Address correspondence to:
Prof. Renato Nisihara, Evangelical Universtiy, R. Padre Anchieta 3230, 80320300 Curitiba, Paraná, Brazil.
E-mail: renatomitsu@yahoo.com.br

Competing interests: none declared.

References

1. BAZZICHI L, ROSSI A, GIACOMELLI C, BOMBARDIERI S: Exploring the abyss of fibromyalgia biomarkers. *Clin Exp Rheumatol* 2010; 28 (Suppl. 63): S125-30.
2. MILLAN MJ: The induction of pain: an integrative review. *Prog Neurobiol* 1999; 57: 1-164.
3. TROPY DJ,PAPANICOLAOUS DA, LOTSIKAS AJ, WILDER RL, CHROUSOS GP, PILLEMER SR: Responses of the sympathetic nervous system and hypothalamic-pituitary-adrenal axis to interleukin-6. *Arthritis Rheum* 2000; 43: 872-80.
4. GARLANDA C, BOTTAZZI B, BASTONE A, MANTOVANI A: Pentraxins at the crossroads between innate immunity, inflammation, matrix deposition, and female fertility. *Annu Rev Immunol* 2005; 23: 337-66.
5. WOLFE F, CLAUW DJ, FITZCHARLES M *et al*.: The American College of Rheumatology Preliminary Diagnostic Criteria for Fibromyalgia and measurement of symptom severity. *Arthritis Care Res* 2010; 62: 600-10.
6. MARQUES AP, SANTOS AMB, ASSUMPÇÃO A, MATSUNANI LA, LAGE LV, PEREIRA CAB: Validação da versão brasileira do Fibromyalgia Impact Questionnaire. *Rev Bras Reumatol* 2006; 46: 24-31.
7. BECK AT, STEER RA, GARBIN MG: Psychometric properties of the Beck Depression Inventory: twenty-five years of evaluation. *Clin Psychol Rev* 1988; 8: 77-100.
8. HOLLAN I, BOTTAZZI B, CUCCOVILLO I *et al*.: Increased levels of serum pentraxin 3, a novel cardiovascular biomarker, in patients with inflammatory rheumatic disease. *Arthritis Care Res* (Hoboken) 2010; 62: 378-85.
9. ENGLISH B: Neural and psychosocial mechanisms of pain sensitivity in fibromyalgia. *Pain Manag Nurs* 2014; 15: 530-8.
10. BAZZICHI L, ROSSI A, MASSIMETTI G *et al*.: Cytokine patterns in fibromyalgia and their correlation with clinical manifestations. *Clin Exp Rheumatol* 2007; 25: 225-30.