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Bladder pain syndrome/interstitial cystitis as a functional somatic syndrome

John W. Warren

Department of Medicine, University of Maryland School of Medicine, 10 South Pine Street, #900, Baltimore, MD 21201, United States
Department of Epidemiology and Public Health, University of Maryland School of Medicine, United States

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ABSTRACT

Purpose: To determine whether bladder pain syndrome/interstitial cystitis (BPS/IC) has the characteristics of a functional somatic syndrome (FSS).
Materials and methods: There is no accepted definition of an FSS. Consequently, this paper reviewed the literature for common FSS characteristics and for reports that BPS/IC has these characteristics.
Results: Eleven articles met inclusion and exclusion criteria and yielded 18 FSS characteristics. BPS/IC patients manifest all but two: the exceptions were normal light microscopic anatomy (after hydrodistention under anesthesia, some BPS/IC bladders have Hunner's lesions and most have petechial hemorrhages) and normal laboratory tests (many BPS/IC patients have hematuria). Petechial hemorrhages and hematuria are probably related and may appear during naturally-occurring bladder distention. Without such distention, then, the 90% of BPS/IC patients without a Hunner's lesion have all the characteristics of an FSS. Comparisons in the opposite direction were consistent: several additional features of BPS/IC were found in FSSs.
Conclusions: This systematic but untested method is consistent with but does not test the hypothesis that BPS/IC in some patients might best be understood as an FSS. Like most conditions, BPS/IC is probably heterogeneous; hence only a proportion of BPS/IC cases are likely to be manifestations of an FSS. This hypothesis has several implications. Explorations of processes that connect the FSSs might contribute to understanding the pathogenesis of BPS/IC. Patients with FSSs are at risk for BPS/IC and may benefit from future preventive strategies. Therapies that are useful in FSSs also may be useful in some cases of BPS/IC.

Introduction

BPS/IC is a chronic disorder defined by pain perceived to be from the bladder plus the urinary symptoms of urgency, frequency and nocturia [1]. The condition was first described in the nineteenth century and came to be characterized by the presence of red, bleeding areas on the bladder wall, known as Hunner's lesions. Since then, BPS/IC has evolved to a diagnosis of symptoms, primarily pain which in the great majority of patients changes with bladder filling and emptying; most such patients do not have a Hunner's lesion. The prevalence of BPS/IC in the United States is 3–6% of women and 2–4% of men [2,3].

Since the recognition of BPS/IC, investigations of its pathogenesis have focused on the bladder. Candidate etiologies have included infections, autoimmunity, other inflammatory processes, mucosal abnormalities, urinary toxins, and local neuronal dysfunction. None have persuasively explained the syndrome and the lack of understanding of its pathogenesis has led to empiric and often inadequate therapies.

Recent studies have shown that significantly more BPS/IC patients than controls have other syndromes with symptoms well beyond the bladder, often numerous such conditions [4–9]. These non-bladder disorders include chronic fatigue syndrome (CFS), fibromyalgia (FM), irritable bowel syndrome (IBS), temporomandibular joint disorder (TMD), chronic pelvic pain (CPP), vulvodynia, migraine, low back pain, sicca syndrome, allergies, asthma, depression, and anxiety. Several of these are functional somatic syndromes (FSSs), the most venerable of which are CFS, FM, and IBS. Peter D. White, an expert on FSSs, recently remarked: "Probably the most replicated risk marker for an FSS is that having one is strongly associated with having another …" [10].

The fact that BPS/IC is associated with FSSs, then, generates the hypothesis that it too is an FSS. If so, then findings of mechanism(s), treatments and prevention of FSSs might be applicable to BPS/IC.

Testing the hypothesis that BPS/IC is an FSS is difficult, however, because there is as yet no pathophysiologic definition of an FSS nor even consensus as to which disorders are FSSs. Given this uncertainty, this paper outlines two available published features pertinent to the diagnosis of an FSS: 1) characteristics said to be common to FSSs and 2) statements that appear to define an FSS. It then assesses published knowledge of BPS/IC to determine whether this syndrome has these characteristics or meets these definitions.

E-mail address: jwarren@medicine.umaryland.edu.

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Materials and methods

PubMed was used for two searches of the MEDLINE database of the National Library of Medicine, for reviews and editorials on 1) *functional somatic syndromes*, and then 2) *chronic fatigue syndrome* AND *fibromyalgia* AND *irritable bowel syndrome*. The combined results were reviewed for articles that met the following inclusion and exclusion criteria. An article was included if it referenced all of the classic FSSs, i.e., CFS, FM, and IBS, and commented upon two or more characteristics considered by the authors to be common to the FSSs. Excluded articles were those that discussed symptoms but not syndromes (e.g., somatoform disorders), that primarily addressed more controversial or contested syndromes (e.g., chronic candidiasis or multiple chemical sensitivity) [11,12], or that mainly reviewed mechanisms or management. From each accepted article, two types of items were extracted: 1) characteristics stated by the authors as common to FSSs, and 2) if present, any statement that could be construed as a definition of an FSS. The first group, i.e., attributes said to be shared by FSSs, was then used to develop literature searches for studies of BPS/IC patients; those comparing BPS/IC patients to controls were preferentially reviewed. All searches were limited to studies of humans and in the English language.

Results

The literature searches yielded 157 reviews or editorials that discussed functional somatic syndromes and 71 that mentioned all of CFS, FM, and IBS. Of these, eleven articles met inclusion but not exclusion criteria and are listed by publication date in Table 1 [10,13–22]. Each of these referenced CFS, FM, and IBS, an inclusion criterion. The first, by Wessely et al. also listed the following conditions as FSSs: tension headache, TMD, atypical facial pain, atypical chest pain, hyperventilation syndrome, non-ulcer dyspepsia, globus syndrome, premenstrual syndrome, CPP, and multiple chemical sensitivity [13]. Subsequent articles [14,15,17,19–21] added others that those authors considered to be FSSs: insomnia, post-concussion syndrome, tinnitus, dizziness, pseudoseizures, neck pain, chronic whiplash, repetitive strain injury, low back pain, palpitations, mitral valve prolapse, vulvodynia, hypoglycemia, sick building syndrome, chronic Lyme disease, silicone breast implant effects, candidiasis hypersensitivity, food allergy, and Gulf War syndrome. Interestingly, several listed BPS/IC as an FSS [14,15,20,21].

Characteristics of functional somatic syndromes

Table 1 lists 18 characteristics of FSSs that were mentioned in at least one article, ranked as they might emerge during a patient work-up. Each characteristic is noted below, followed by findings from the literature search of that characteristic in BPS/IC patients.

Female predominance

In urology practices, most BPS/IC patients have been women [23]. Recent population-based studies suggest that about 60% of BPS/IC cases are female [2,3]. Given that some men diagnosed with BPS/IC also meet criteria for chronic prostatitis/chronic pelvic pain syndrome [3,24], the actual proportion of BPS/IC cases that are female might be higher.

Precipitating event

In some patients, an acute event appears to precipitate an FSS. Minorities of patients report physical trauma before FM and bacterial gastroenteritis before IBS, and several acute infections precede CFS onsets. Similarly, at the first medical encounter following the appearance of BPS/IC, 18%–36% of women had laboratory or clinical evidence of a urinary tract infection [25].

Pain

The pain of BPS/IC has been well described [26] and is a necessary component of its definition [1].

Fatigue

Clauw et al. found that 77% of female BPS/IC patients reported "fatigue" vs. 13% of control women of similar ages [4].

Overlap of defining symptoms of FSSs

Although this was introduced by Wessely et al. in their seminal article, each such symptom mentioned (abdominal pain, bloating, headache, and fatigue) overlapped ≤8 of the 13 listed syndromes [13]. Moreover, there is no overlap of the symptoms that define two classic FSSs, i.e., CFS [27] and IBS [28]. Hence, this FSS characteristic might not stand the test of time. Nevertheless, because Wessely et al. included abdominal pain as an "overlapping" symptom and the great majority of BPS/IC patients have lower abdominal, i.e., suprapubic, pain [26], BPS/IC appears to possess this characteristic.

Co-morbidity with FSSs

This is the characteristic that prompted this project. BPS/IC is associated with FSSs, as well as other conditions that are epidemiologically linked to FSSs: FM, CFS, IBS, temporomandibular disorder, CPP, migraine, depression, anxiety, low back pain, allergies, asthma, sicca syndrome, and vulvodynia [4–9].

Number of FSSs is a risk factor

Many BPS/IC patients have numerous FSSs [29]. Indeed, the greater the number of syndromes, the greater the odds of BPS/IC [9,29–32]. Two studies showed that the presence of multiple FSSs *preceded* and thus was a risk factor for BPS/IC [31,32]. The number of FSSs is by far the most powerful risk factor yet identified for BPS/IC [33].

Table 1
Characteristics stated or implied to be common to functional somatic syndromes (FSSs) in articles meeting inclusion and exclusion criteria

Author	Wessely	Aaron	Katon	Sharpe	Mayou	Henningsen	Masuko	Henningsen	Goldenberg	White	Harvey	BPS/IC
Year	1999	2001	2001	2001	2002	2003	2007	2007	2010	2013	2013	
Reference	[13]	[14]	[15]	[16]	[17]	[18]	[19]	[20]	[21]	[10]	[22]	
Characteristic												
Female	√			√				√	√	√	√	√
Precipitating event					√			√				√
Pain		√					√	√	√	√		√
Fatigue		√						√		√		√
FSS symptom overlap	√	√		√	√		√	√				√
FSS co-morbidity	√	√		√	√		√	√	√	√		√
No. FSSs = risk factor										√		√
Non-FSS symptoms	√	√	√					√	√		√	√
Depression	√		√	√	√	√	√	√	√	√	√	√
Anxiety	√		√	√	√	√	√	√		√	√	√
Adverse experience	√		√		√			√	√	√		√
Familial									√	√	√	√
Normal laboratory		√		√					√			±
Normal pathology			√	√			√	√	√			±
Chronic	√				√		√	√				√
Diagnosis of exclusion									√		√	√
Worsened by stress		√	√		√		√	√	√			√
Disability	√	√	√		√	√	√	√		√	√	√