Interventional Pain Management Reports
Volume1 , Number 5, pp 149-155

Case Series Report

Hemisomatic Central Sensitivity Pain Disorder ("Hemi-fibromyalgia Syndrome")

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Background: We describe a poorly recognized central sensitivity pain disorder (CSPD) presenting with moderate to severe chronic hemisomatic pain (limited to half of the body). In 7 patients, the syndrome developed spontaneously and masqueraded as common spinal or arthritic disorders, but none of these patients responded to standard therapies for the disorders they resembled. A key feature in the patients was the presence of hemisomatic myofascial tenderness reminiscent of fibromyalgia syndrome (FMS), but it was only present on half of the body. However, most patients did not meet current diagnostic criteria for FMS.

Objective: To describe a new (or poorly recognized) clinical entity characterized by chronic hemisomatic pain.

Study Design: An observational study and case series.

Observations: Seven patients exhibiting unilateral hemisomatic pain affecting the trunk and upper and lower extremities were identified at a subspecialty pain medicine clinic from 2013 to 2016. The pain was moderate to severe in 6 patients and mild to moderate in one patient. In contrast to FMS, the patients had minimal psychological comorbidities and low indexes for somatic complaints.

Conclusions: Despite its relatively high frequency, neurologists and pain specialists are unfamiliar with this syndrome of chronic hemisomatic pain. This entity appears to represent a CSPD of cryptic etiology rather than a somatoform or psychiatric condition. Although most of these patients had previously been evaluated at academic centers by different specialists, they frequently underwent invasive interventions which were not efficacious. Diagnostic criteria for its identification are proposed in this paper.

Key words: Chronic pain, fibromyalgia syndrome, central sensitization syndrome, central pain, myofascial pain

Generalized pain disorders represent a bridge between neurology and psychiatry with poorly understood neurobiological mechanisms. Among these, fibromyalgia syndrome (FMS) is a prototypical entity of pain centralization. FMS affects 3–8% of the population and is clinically characterized by diffuse pain (mainly myofascial tenderness), fatigue, sleep disturbances, and variable abnormalities of cognition and mood (1-3). In addition to a heightened response to non-painful stimuli, patients report bladder and bowel dysfunction (4), paresthesias (5), and unrefreshing sleep (6). Patients with FMS have a higher prevalence of depression, anxiety, and stress-related disorders such as posttraumatic stress disorder (7,8). Not all patients with FMS report all of these associations; some patients may be part of a spectrum disorder exhibiting only the pain components (9).

Here, we report a series of 7 patients afflicted with moderate to severe chronic hemisomatic myofascial pain masquerading as unrelated chronic pain disorders. Distinct to all of these patients was the complete absence of pain (subjectively and objectively on examination) in the contralateral side and the concomitant presence of widespread abnormal tenderness on the affected side (subjectively and objectively on examination). Although possibly related to FMS, most of these patients failed to meet the current

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American College of Rheumatology (ACR) criteria for this disorder, including the 1990, the 2010, and the subsequent 2011 and 2016 revisions (see discussion). In contrast with FMS, the patients exhibited limited psychological comorbidities. The recognition of this chronic pain condition is critical to avoiding misdiagnoses and unnecessary interventions.

Case Series (Presented in Summary Form in Table 1)

METHODS

The patients were selected from 154 consecutive cases of patients with FMS, seen at a subspecialty pain medicine clinic, from 2013 to 2016. All patients underwent comprehensive examinations by a board-certified neurologist and a board-certified pain medicine specialist, had magnetic resonance imaging (MRI) of the cervical and lumbar spine (except for patients 5 and 7), and underwent neurophysiologic studies including needle electromyography (EMG) examination (except for patients 5 and 6). Their evaluation included a widespread pain index (WPI), a symptoms severity scale score (SS), a McGill Inventory with pain drawings, a Brief Pain Inventory, the STOP-BANG questionnaire for sleep disorders, a physician assessment questionnaire (PHQ-9), and the Becker's depression and anxiety instruments. The WPI and SS were identical to those used in the 2010 ACR criteria for fibromyalgia, except that the SS included the 2011 modification to the somatic symptoms component of the SS (presence of headache, depression, and lower abdominal symptoms) (10). Also included were standard laboratory panels to exclude metabolic and inflammatory disorders and muscle enzyme levels (muscle aldolase and creatine kinase). Five of the patients had MRI examinations of the head to exclude brain structural pathology associated with central pain.

General Findings

None of the patients met the 1990 ACR criteria for the diagnosis of FMS, 2 patients met the 2010 ACR criteria, and none of the patients met the 2016 ACR revision of the criteria (11) (see below). The 1990 criteria were not met primarily because the patients lacked bilaterality of pain and the number of tender points was < 11/18 in all patients. Regarding the 2010 criteria, the patients showed a much lower incidence of fatigue, poor sleep, and cognitive problems than the average patient with FMS with a SS score of < 5 in the 5 patients not meeting the 2011 criteria for FMS diagnosis. Except for patient 7, none of the patients had a history of significant psychological or physical trauma associated with the onset of the symptoms. The presence of sleep or cognitive or mood abnormalities, fatigue, or somatic complaints is reported in table 1. Clinical "red flags" associated with lumbar spinal pain such as saddle anesthesia, history of malignancies, acute or chronic infections, or osteoporosis were negative in all patients. The pain was nondermatomal in distribution in all of the patients. Routine laboratory studies and muscle enzyme levels (muscle aldolase and creatine kinase) were normal in all of the patients. Needle EMG examinations which were negative for myopathic disorders. None of the patients had any history or findings of cardiovascular or cerebrovascular disease, and MRI examinations of the brain were normal in 5 patients and not obtained in 2 patients.

Patient 1 (NP)

The patient was a 41-year-old woman who presented with a complaint of pain in the right side of her body which began spontaneously during childhood. The pain increased substantially in the last 4 years. She was previously diagnosed with cervical and lumbar radiculopathy and lumbar discogenic pain. The worst pain was localized to the lumbar right paraspinal region. She had a history of depression, but the instruments for depression and anxiety showed normal scores. The patient had received multiple pharmacological treatments over many years and was currently taking nonsteroidal anti-inflammatory drugs (NSAIDs), which were ineffective. On examination, she showed subtle (but abnormal) myofascial tenderness conforming to the distribution outlined in the 1990 ACR criteria for the diagnosis of FMS, but it was only present on the right side of her body. The neurological examination was normal. Imaging studies of the spine showed no structural pathology and neurophysiologic investigations, including needle EMG, did not show any evidence of radiculopathy, compressive mononeuropathy, or myopathic conditions. Her visual analog scale (VAS) scores improved > 50% on amitriptyline 25 mg at bedtime. The patient declined any additional medications offered to further decrease her pain.

Patient 2 (SM)

The patient was a 51-year-old woman who presented with a complaint of left-sided pain lasting for 10 years. Prior diagnoses included cervical discogenic pain and cervical and lumbar radiculopathy. She had several interventions addressing these possibilities, without benefit. These interventions included epidural steroids and a cervical fusion. She also described dysesthesias and paresthesias affecting her left trunk for which she underwent a long thoracic nerve release in 2014, which was unsuccessful. Tender point examination revealed superimposed myofascial tenderness at typical FMS pressure points on the left side only. The neurological examination was otherwise normal. Imaging studies of the spine showed no structural pathology and a needle EMG of the painful extremities was normal. She was treated with amitriptyline 25 mg at bedtime followed by 60% improvement of her symptoms; this medication was switched at a later point to milnacipran, due to excessive drowsiness, followed by a dramatic improvement of her symptoms.

Patient 3 (BP)

The patient was a 38–year-old woman who presented with a complaint of left-sided cervicalgia and left lumbar spine pain lasting for approximately 2 years. The pain radiated to the left upper and lower extremities nondermatomally. The worst pain was localized to the left lumbar paraspinal region. She denied cognitive difficulties but reported sleep problems that she attributed to her pain. She saw several physicians, including orthopedic and pain medicine specialists, but remained undiagnosed. Ibuprofen 800mg daily was ineffective. On examination, there was widespread hemisomatic myofascial tenderness. The neurological examination was normal. Imaging studies of the cervical and lumbar spine were normal. A needle EMG showed an incidental left carpal tunnel syndrome. She was treated with amitriptyline 25 mg, followed by mild improvement, but attained more than 50% pain relief with the addition of gabapentin at a dose of 300 mg 3 times per day.

Patient 4 (RL)

The patient was a 45-year-old woman who presented with complaints of right lumbar stabbing pain radiating to the right leg and right neck pain for about 10 years. The patient stated that the lumbar pain was the most severe symptom. She denied a history of trauma around the onset of the symptoms, although she stated that the pain was exacerbated by several falls occurring over the prior 7 years. The patient was taking acetaminophen and NSAIDs, without efficacy. The patient was diagnosed with radiculopathy and underwent a series of epidural steroid injections, which were not beneficial. On examination, she presented with unilateral but widespread tender points conforming to the 1990 ACR criteria. A MRI of the lumbar spine showed severe stenosis of the right L4/5 foramen. The scores for depression and anxiety were within the range of moderate depression and anxiety. A needle EMG showed no evidence of radiculopathy. She was treated with amitriptyline 25 mg at bedtime, with initial mild improvement. The addition of pregabalin 150 mg twice per day resulted in marked improvement (80%).

Patient 5 (RP)

The patient was a 57-year-old man who presented with a history of lower back pain lasting for several years, localized to the right flank region radiating to the right thigh, right groin, and right testis. He described episodes of heavy lifting preceding the onset of symptoms. A L2-L3 disc herniation led to a discectomy surgery. He had some temporary improvement, but in June 2012 he had a recurrence of severe pain leading to a surgical revision. The second surgery decreased the severity of his pain only slightly and he continued to experience pain and paresthesias rated 4–5/10. Three epidural steroid injections, tramadol, and NSAIDs were ineffective. He was referred to one of the authors for consideration of spinal cord stimulation. He denied sleep or cognitive problems. There was no overt depression or anxiety. The examination revealed widespread myofascial tenderness present only on the right side of his body. Needle EMG and brain MRI examinations were not performed. He was placed initially on amitriptyline, which he did not tolerate due to excessive drowsiness, and was switched to milnacipran. He is currently pain-free on this medication.

Patient 6 (RG)

The patient was a 51-year-old woman who presented with left lumbar and left leg pain for 7 months. The worst pain was localized to the left hip and left trochanter area. She also complained of left shoulder girdle pain. The patient was taking ibuprofen, which was marginally effective. She also received a number

of intraarticular injections of steroids, which were ineffective. She denied cognitive problems but reported sleep abnormalities. On examination, she exhibited widespread abnormal tender points conforming to the ACR criteria for the diagnosis of FMS, but only on the left side. The neurological examination was normal. Imaging studies showed a disc herniation at L4-L5. A transforaminal epidural steroid injection at the left L4-5 foramen provided only minimal benefit. There was no depression or anxiety. Needle EMG examination was not performed. After 3 weeks of treatment with amitriptyline 25 mg at bedtime, the patient reported 60% improvement.

Patient 7 EJ

The patient was a 41-year-old woman who presented with a complaint of right hip and right neck pain in a nondermatomal distribution for 5 years. She reported a history of a fall around the onset of the symptoms. The worst pain was localized to the right sacroiliac joint area. The patient was taking tramadol, with minimal benefit. The patient had a series of epidural steroid injections, which were "mildly helpful" for a few weeks at a time but were otherwise ineffective. On examination, she exhibited widespread unilateral tender points conforming to the distribution outlined in the 1990 ACR criteria for FMS. The neurological and the needle EMG examinations were normal. Imaging studies were not performed because her pain resolved almost completely after initiating treatment with amitriptyline 25 mg at bedtime.

DISCUSSION

We report a series of 7 patients, 6 women and one man, affected with moderate to severe chronic hemisomatic pain exhibiting a distinctive pattern of hemisomatic pain distribution. All of the patients presented initially with symptoms simulating radicular, discogenic, or arthritic pathology. However, careful evaluation unveiled superimposed, abnormal hemisomatic myofascial tenderness present only on the affected side and generally corresponding to tender points as described in the 1990 ACR diagnostic criteria for FMS.

Unilateral pain syndromes have previously been mentioned only perfunctorily in the medical literature (11). The relationship of this syndrome to FMS is suggested by the typical distribution of tender points (although unilaterally), the lack of objective structural pathology in some of these patients, normal EMG examination, the response to the pharmacologic agents administered, the female preponderance, and in some of the patients, the presence of cognitive and sleep disturbances. Distinctive to these patients also, was the total absence of pain on the contralateral side, subjectively and objectively on examination. However, the 1990 or 2010/2011 criteria for FMS were not met in 5 of these patients as there was no bilaterality (1990), no identification of ≥ 11/18 tender points, and low scores for somatic complaints (see below). None of the patients met the widespread pain criteria required in the 2016 revisions (11).

In the recent past, FMS was often characterized as a psychological or psychiatric condition due to the absence of objective clinical or pathological findings. However, basic and clinical investigations have clarified some of the neurophysiologic bases for this condition that led to its current classification as a CSPD (12,13). This concept has been supported by functional imaging (fMRI) (14) and voxel-based morphometry MRI studies (15-17). Abnormal structural changes in the brain appear to support a more severe experience of pain for a certain stimulus in FMS patients compared to control individuals subjected to a stimulus of similar intensity. The introduction of the ACR FMS classification criteria in 1990 (18), as well as its more recent revisions (10,19), led to a heightened detection of this disorder.

Recognition of this unique presentation, for which we propose the names of hemi-CSPD or for simplicity, hemi-fibromyalgia syndrome, is important in avoiding misdiagnoses. Patients 4, 5, and 6 underwent epidural steroid injections, patient 5 had 2 spine surgeries, and patient 2 had a cervical fusion and a long thoracic nerve release. None of these procedures was followed by any meaningful clinical outcomes in these patients, except for partial temporary improvement in patient 5. Interestingly, this patient was referred to us, with a diagnosis of post-laminectomy syndrome, for a trial of spinal cord stimulation. However, because of the presence of hemisomatic myofascial pain with the typical tender point distribution, the patient received a trial of a tricyclic antidepressant and then was switched to milnacipran, which was followed by a complete resolution of his myofascial tenderness and pseudoradicular pain.

In FMS, despite the soft tissue pain and myalgia that patients experience, no intrinsic abnormalities

Table 1. Case series' characteristics & treatments.

Patient/ Case	Gender	Body Side Affected	Pretreatment VAS	Pain Descriptors	Severity Scale (SS)	Posttreatment VAS	Medication & Daily Dose
1	Female	Right	3–8	Shooting, burning	Sl-None C-None M-None F-W: None So: None	2–4	Amitriptyline 25mg
2	Female	Left	6–9	Throbbing	Sl-Mild C-Mild M-None F-W: None Sl: None	3–6	Milnacipran 50mg
3	Female	Left	3–8	Shooting, burning	S-Mod C-None M-Mild F:Mild W:Mod So:None	1–4	Amitriptyline 25mg Gabapentin 900mg
4	Female	Left	4–8	Throbbing, stabbing	Sl-Mod C-Mod M-Mod F-Mild W-Mod So-None	1–3	Pregabalin 300mg (after failing amitriptyline and gabapentin)
5	Male	Right	3–4	Burning	S-None C-None M-None F-None W-None So-None	0	Milnacipran 50mg
6	Female	Left	6–9	Burning	S-Mild C-None M-None F-None W-None So-None	2–4	Amitriptyline 25mg
7	Female	Right	6–8	Burning	Sl-Mild C-None M-None F-None W-None So-None	2–3	Amitriptyline 25mg

Sl-sleep disturbance; C-cognitive problems; M-mood abnormalities (depression or anxiety); F-fatigue; W-waking unrefreshed; So-somatic complaints

in muscle are present (20). This has held true with our patients as demonstrated by normal neurologic examinations and the absence of needle EMG abnormalities. It is interesting to recognize that the cluster of symptoms experienced by most of these patients (i.e., sleep, cognitive, memory, and chronic pain) are all nervous system functions which converge upon and are variably modulated in the thalamus. Therefore, we would like to propose that patients with this syndrome may exhibit an abnormality of contralateral thalamic nuclei. This possibility is supported by several studies in FMS showing reduced thalamic blood flow (21,22). However, the exact mechanisms may also involve interactions between central sensory processing and peripheral pain generators such as temporal summation of nociceptive impulses at the level of the spinal cord which occur in central sensitization (23).

The 1990 ACR criteria required tenderness on pressure (tender points) in at least 11 of 18 specific sites

(9 bilateral sites) and the presence of widespread pain for diagnosis (18). Widespread pain was defined as axial pain, left- and right-sided pain, and upper and lower segmental pain. However, a series of objections to the ACR 1990 criteria developed over time. First, the tender point count was almost never conducted in the primary care setting (19). Consequently, FMS diagnosis in practice has often been a symptom-based diagnosis. Second, symptoms that had not been considered by the 1990 Criteria became increasingly important and appreciated as fundamental traits of FMS. In addition, physicians caring for these patients considered that FMS was a variable condition not reflected in the dichotomous criteria established in 1990. These problems led to a revision and an introduction of a broad-based severity scale in 2010 that could identify patients depending on the degree of symptom severity (19). The new criteria eliminated the tender point examination component of the diagnosis and incorporated a SS as an instrument to quantify the symptoms and to follow up their evolution longitudinally on a same patient. This SS includes degree of cognitive impairment, fatigue, "waking unrefreshed," and somatic complaints. A WPI score was also included in the 2010 revision, which is centered on the occurrence of pain at 19 sites (10). The composite score does not include pain severity. Specifically, the 2010 criteria recommended a new case definition of FMS consisting of either a WPI > 7 and a SS > 5 or a WPI 3–6 and a SS >9. Thereafter, the 2010 criteria were revised twice. In 2011, the criteria eliminated the physician's estimate of the extent of somatic symptoms, substituted the sum of 3 specific self-reported symptoms, and added a FMS symptom scale (FS) (10). In 2016, the widespread criteria were expanded to 4 of 5 areas and the diagnosis of FMS was allowed irrespective of other diagnoses (11). Currently, the latest ACR criteria require a WPI = > 7 and a SS score = or > 5 or a WPI of 4–6 and a SS score = or > 9.

Unfortunately, the new ACR criteria have been subject to several pitfalls (24-26). In our opinion, partially shared by other cited authors, there are 3 main problems arising from the new criteria. The first one pertains to the choice of the symptoms. For example, the symptoms of fatigue, thinking or memory disturbance, non-restorative sleep, abdominal pain, depression, and headache represent depression as much as FMS and in fact, 4 of the 6 symptoms in the new criteria are part of the Beck II Depression Inventory (24). This results in very poor specificity for diagnosis of the syndrome without a tender point examination. The second problem is the lack of requirement for a physical evaluation (26). In addition to identifying tenderness, a lack of true muscle weakness and a normal neurological examination are critical to excluding neuromuscular disease. The third problem with the 2010 criteria and its subsequent revisions is that it also introduces complexities of its own into the patients' evaluation and as such, the system is of limited practical utility in a general clinical practice. Finally, few diseases start with a full-blown syndrome; in our opinion, shared by other experts, the ACR criteria miss the early stages and limited forms of the syndrome (27,28). Importantly, the application of newer ACR criteria would have precluded identification of the syndrome presented in this paper due to low scores for somatic complaints and widespread pain.

In our clinics, we have developed a simple approach which combines (and simplifies) the 1990 and the 2010/2011 ACR criteria which would be applicable to patients suffering from the CSPD presented here and, by and large, possibly to patients with diffuse myofascial pain disorders of cryptic etiology. Although the subject of a separate report, a brief outline of our criteria is as follows. For all patients, we require: 1) symptom duration of more than 3 months, 2) a lack of true muscle weakness and a normal neurological examination, to exclude intrinsic neuromuscular disease, and 3) the presence of myofascial tenderness on examination in at least 2 non-adjacent body quadrants, not readily explainable by another clinical condition. One additional cardinal symptom for a list of 4 as outlined below is required for a diagnosis of possible CSPD, 2 additional cardinal symptoms for a probable diagnosis, and 3 additional symptoms from this same list, for a definite diagnosis. Cardinal symptoms are: 1) fatigue, 2) cognitive complaints (thinking, concentration, or memory problems), 3) non-restorative sleep, or 4) somatic complaints (depression, headaches, or abdominal discomfort). Patients without any cardinal complaints are diagnosed as multifocal myofascial pain syndrome in our clinics. Following our criteria, 2 of the patients would have been diagnosed as definite CSPD and 4 patients as probable CSPD. However, if one is to follow the ACR 2010 criteria for FMS, 5 of the patients would not

have been diagnosed with FMS or CSPD. Patient 5 would have met our criteria for multifocal myofascial pain syndrome. Because of its simplicity, we follow our patients longitudinally with a Brief Pain Inventory (29), instead of a SS.

In conclusion, we present a poorly recognized syndrome of hemi-fibromyalgia, or hemi-CSPD, primarily characterized by chronic hemisomatic myofascial tenderness. Identification of this chronic pain syndrome is critical to avoiding misdiagnoses and unnecessary diagnostic and treatment interventions.

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