The association between benign fasciculations and health anxiety: A report of two cases and a systematic review of the Literature

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ABSTRACT

Background Benign fasciculation syndrome (BFS) is characterised by persistent spontaneous contractions of muscle fibres in the absence of a pathological cause. Patients with BFS often have concerns around having motor neuron disease (MND), in some cases fulfilling the criteria for health anxiety disorder. Research on how BFS and health anxiety relate to one another and how they should be optimally managed together is sparse.

Objective We report two cases of BFS associated with health anxiety. We also review the existing literature on the association between BFS associated with health anxiety.

Methods We systematically reviewed the literature using MEDLINE, Embase, PsychInfo, and OpenGrey for studies investigating benign fasciculation and anxiety symptoms up to August 2018.

Results Both cases were successfully treated for health anxiety disorder with cognitive behavioural therapy and antidepressant medication. We identified eight studies that met inclusion criteria describing a total of 384 patients. The majority of studies were of moderate quality. Patients with BFS tended to be male and in their 30s or 40s. There was an over-representation of clinicians. Anxiety symptoms were common and frequently coexisted alongside fasciculation symptoms. Health anxiety was overwhelmingly focused around MND.

Conclusion A proportion of individuals with BFS experience anxiety around having MND — to the point of developing health anxiety disorder. A bidirectional relationship may exist between BFS and health anxiety. Clinicians should be alert to the possibility of health anxiety in patients with BFS and have a low threshold to refer for psychiatric assessment. There is support for the role of psychological therapy, especially CBT, as well as pharmacotherapy, in the form of antidepressant medication. Furthermore, in severe or treatment-refractive cases, combined treatment may be indicated.

INTRODUCTION

Fasciculations are spontaneous, fast contractions of fine muscle fibres, which can be perceived as brief muscle 'twitches'(1). They are experienced by up to 70% of the healthy population,(2) and are associated with increased age, strenuous physical exercise, stress, and fatigue.(3) Fasciculations can be benign or associated with neurological disorders such as radiculopathy, peripheral nerve injury,(4) auto-immunity(5), and peripheral nerve hyper-excitability syndromes.(6) Fasciculations can also be the presenting symptom in Motor Neuron Disease (MND), a progressive neurodegenerative disorder.(7)

When fasciculations are persistent, but no pathological cause is identified, patients may be diagnosed with benign fasciculation syndrome (BFS). Diagnosis typically requires a normal neurological exam and electromyography (EMG), excluding fasciculation potentials. Since the first description of BFS, an association with anxiety around MND has been noted, (8) particularly in doctors and other healthcare professionals.(9) In some cases, it is sufficiently severe to fulfil the criteria for health anxiety. This is a psychiatric disorder characterised by a persistent preoccupation with having a serious physical illness leading to marked emotional distress, despite negative findings and reassurance(1). Safety behaviours, such as excessive checking and reassurance seeking are also defining features and depressive anxiety symptoms commonly coexist. The disorder is synonymous with the ICD-10 diagnosis of hypochondriacal disorder and in DSM-5 is divided into somatic symptom disorder (where marked somatic symptoms are present) and illness anxiety disorder (where somatic symptoms are mild, or absent). Research on how health anxiety and BFS relate to one another — and how patients suffering both disorders should be managed — is sparse. We systematically reviewed the literature and report two cases successfully treated with psychological and pharmacological interventions.

Cases

Case 1 was a 38-year-old male clinical neuroscientist with no significant medical history, who spontaneously developed twitching sensations in his left calf, spreading to other parts of his leg over two days. He became convinced that he was suffering from MND after noticing subtle muscle asymmetries. Approximately two weeks later, he developed swallowing and chewing difficulties, and twitching spread to different parts of his body, including his right leg, chest, abdomen, and face. A barium swallow was normal, except for some slight residual contrast agent in the pharynx, and functional endoscopy was normal. He was referred to a tertiary neurology centre, where initial neurological examination revealed fasciculations of his left gastrocnemius and a normal MRI of the head and cervical spine. Nerve conduction and electromyography (EMG) studies were also normal. He was diagnosed with BFS and health anxiety and referred to a neuropsychiatry clinic for assessment.

At the peak of his health anxiety symptoms, three months from symptom onset, he was unable to work, his relationship with his partner was severely strained, and he suffered with dysphoria and insomnia. He held intrusive over-valued ideas around having MND with ninety percent certainty. There was evidence of catastrophizing and rumination, as well as an excessive interest in news stories related to MND and he regularly consulted online BFS forums. Reassurance seeking from medical professionals, self-testing of muscular strength, inspection of his body for evidence of muscle wasting were also prominent. He also switched to eating semi-solid foods, and reduced exercise to avoid stimulating fasciculations.

He was initially trialled on fluoxetine 20mg, before being switched to mirtazapine 30mg. This transiently lead to insomnia but was otherwise well-tolerated. He underwent a course of cognitive behavioural therapy (CBT) for health anxiety following a semi-manualised approach (10) which focused around developing a shared understanding of his condition, cognitive restructuring, dropping of safety behaviours and exposure-response prevention. By the seventh session, in conjunction with mirtazapine, his health anxiety fully remitted, and he returned to work. There was also a subjective reduction of fasciculation symptoms by approximately 50%. At follow-up, eight months after the completion of CBT he remained in full remission.

Case 2 was a 41-year-old male who worked in finance as a manager. He had a medical history of irritable bowel syndrome and had no prior contact with mental health services. Health concerns emerged after an elaborate trick was played on him by colleagues to suggest that he had been infected with the Ebola virus. One month later, he became convinced that he was suffering from lung cancer, despite normal investigations, and was briefly admitted voluntarily to a psychiatric ward due to health anxiety. Approximately one year later, he noticed twitching in his right calf. After researching his symptoms on the internet, he became concerned that he had MND. An initial neurological exam and EMG study was normal, with no evidence of denervation or fasciculation potentials, and he was diagnosed with BFS. He was trialled on alprazolam, which temporarily reduced his muscle twitching symptoms. Whist briefly reassured, he subsequently sought multiple neurological opinions regarding the possibility of MND.

A trial of duloxetine was ineffective, and sertraline was discontinued due to a rash. He had two further informal psychiatric admissions over a one-year period due to increasing distress around having MND, and he openly contemplated euthanasia and assisted suicide. During the third admission, he was treated with escitalopram 10mg and CBT, which reduced his conviction that he had MND from approximately 95% to 50%. He discontinued medication after nine months and was subsequently referred to a specialist neuropsychiatry clinic.

On assessment, his main concern was a subjective experience of slurred speech and spasms of the tongue, suggesting bulbar onset MND to him. Safety behaviours included seeking reassurance from family and medical professionals, strength testing, visiting BFS websites and online forums, and visually inspecting his body dozens of times daily. Neurological examination was normal, however he was able to provide video evidence of intermittent fasciculations. He commenced a 12-week course of CBT for health anxiety, which was extended to 18 weeks due to the treatment-refractory nature of his symptoms. Medically unexplained subjective dizziness, especially upon standing, emerged and were interpreted as persistent postural perceptual dizziness(11). He developed a new concern that he had contracted Lyme disease and consulted several private clinicians, despite advice to limit this, resulting in further investigation and offers of various treatments, including antibiotics. We recommenced escitalopram 20mg for exacerbation of health anxiety. By the end of CBT and having been established on escitalopram, his conviction that he had MND had reduced by over 95% and his functional status had normalised (MRS 0). In addition to subjective reports of fewer fasciculations,

serial surface EMG measurements demonstrated a reduction in fasciculation potentials (figure 1). At follow-up, eight months after the completion of CBT he remained in remission of health anxiety disorder and dizziness and fasicualtions symptoms had also largely resolved.

[FIGURE 1: Timeline of health anxiety symptoms, fasiculations and treatment. Scores of the Health Anxiety Inventory demonstrated a reduction in symptom severity over time. Surface EMG over the right gastrocnemius reduced. Treatment focused on cognitive behavioural therapy, which was later augmented with escitalopram 5 - 10 mg]

SYSTEMATIC REVIEW

We reviewed the primary literature of BFS and anxiety symptoms using PRISMA guidelines (12) and prospectively registered the study on PROSPERO (CRD42018107211). We searched MEDLINE (PubMed), Embase, PsychInfo, and OpenGrey to identify articles and abstracts in all years, up to August 2018, using the following search terms: “anxiety” OR “hypochondria*” AND “fasciculation*” OR “twitch”. Studies were included if patients were assessed for benign fasciculations, and neurological examination and EMG had ruled out pathological causes. Patients were excluded if their diagnosis was subsequently revised. In addition, studies must have included an assessment of current, or past psychiatric symptoms. Two authors (HM and YC) independently screened the titles and abstracts of all identified articles. Full articles of the remaining studies were reviewed to confirm eligibility. Any dispute over the inclusion of a paper was resolved by a third author (GB). Where two papers reported the same dataset, the more comprehensive was selected. Data extracted included psychiatric and neurological characteristics, investigations, treatment, and outcome. Each publication was quality assessed independently two researchers (HM and YC) with any discrepancies resolved by a third author (GB) using a quality appraisal tool (13)

[FIGURE 2: PRISMA flowchart of systematic review search strategy]

RESULTS

The search of electronic databases yielded a total of 362 articles (figure 2). After screening titles and abstracts, 20 were reviewed in full. Two additional studies were included by reviewing the references of included studies. Our search yielded eight eligible articles (1, 2, 14-19) with a total of 384 patients (see supplemental information for table of included studies). Sample size ranged between 9 and 122 patients. All the studies were observational, with one cross-sectional (16) and the remaining studies adopted a case series design (1, 9, 14-19) . Quality appraisal identified six studies of medium quality and two studies of low quality (see supplemental information for details).

Clinical features

The mean age of included patients across the studies ranged from 39 (20) to 47 (17) years. In every study reporting gender (1, 15-19), there was a male predominance and where occupational status was recorded (1, 9, 17-19), there was an overrepresentation of clinicians. After fasciculations, the most common neurological symptoms were numbness or paraesthesia, cramps or spasms, and fatigue or subjective weakness. Neurophysiology investigations typically identified fasciculation potentials only.

Six studies reported previous psychiatric diagnosis, which varied widely between 0% (1) and 80%(9), and was most commonly an anxiety disorder. The presence of anxiety symptoms, including somatic complaints, coexisting alongside fasciculation symptoms was reported in seven studies. Their prevalence ranged between 29% (1) and 39% (15). In three studies, patient concern specifically around MND was reported, ranging between 14%, (18)and 100%. (18) Two studies reported anxiety measures (16, 19)and fasciculation potentials were found to correlate positively with patient-rated anxiety levels in one study. (16) One study clinically assessed patients for health anxiety disorder, which was endorsed in all cases.(1) An association between anxiety and fasciculations symptoms was noted in all five studies which reported factors related to exacerbation of fasciculations (1, 9, 15, 16, 18).

Treatment and outcome

Four studies reported an intervention for BFS or health anxiety, consisting of counselling (1), reassurance (17) or reassurance plus antidepressant medication (14, 15). Follow-up was assessed in six studies, ranging between 6 months (19) to 7 years. (1) An improvement, or resolution of BFS symptoms was reported in 11%(19) to 50%(18) of patients at follow-up. Counselling was associated with an improvement in health anxiety symptoms.(1) Reassurance and antidepressant medication was associated with an improvement in fasciculation symptoms(15), however reassurance alone was not(17).

DISCUSSION

Through a systematic review of the literature and two case reports, we explored the association between benign fasciculations and health anxiety. A consistent finding was the tendency for benign fasciculations to affect men in their 30s or 40s. Also notable was the association between being a clinician with benign fasiculations and having concerns around having MND, a finding highlighted as far back as 1951(9). Only one study specifically enrolled patients with BFS and health anxiety and notably health anxiety focused exclusively around MND. (1)

Health anxiety has a prevalence between 0.8 and 4.5% in primary care (21, 22). Recognised risk factors include increasing age(23), previous illness, and traumatic childhood experiences,(24) and it is often co-existent with other mental disorders, particularly anxiety disorders.(20) In our review, patients with BFS who developed health anxiety symptoms did so at a younger age compared to the age of onset normally seen in health anxiety. A plausible explanation for this is that health anxiety is temporally linked to the emergence of fasciculations.

BFS and health anxiety

Whilst apparent that fasicualtions may cause concern in some individuals, anxiety has also been postulated to play a causal role in benign fasicualtions (1, 2, 16, 18). Several mechanisms have been proposed to explain this relationship. Anxiety states are associated with heightened sensitivity to bodily sensations,(25) and the perception of fasciculations may be modulated, at least in part, by the degree of internally-focused attention. Alternatively, activation of the sympathetic nervous system during periods of emotional arousal, may lead to hyperventilation and motor axon excitability.(26)

Patients with BFS have been found to have similar levels of concurrent depressive and anxiety symptoms compared to patients with MND. However, they have been found to have higher rates of psychosomatic symptoms, stress, and previous psychiatric illness, leading some researchers to suggest that BFS may be a form of somatisation disorder.(15) Case 2 was notable in the patients propensity toward somatisation, including gastrointestinal, neurological and vestibular symptoms. Also notable was the co-occurrence of health anxiety and functional neurological symptoms, including persistent postural perceptual dizziness (27), highlighting the intersection between the two.

Whilst 77% of healthy individuals are estimated to have fasciculation potentials detectable on EMG, (16) they are symptomatic in only 50% to 61%, (26). Psychological variables may explain the discrepancy between the occurrence of fasciculation potentials and their perception in individuals.
In particular, anxiety may play an important role in the establishment of fasciculations. The cognitive behavioural model of health anxiety developed by Warwick and Salkovskis contends that exposure to, or knowledge about illnesses, are central to the formation of assumptions concerning symptoms, diseases, and health behaviours.(28, 29) These assumptions can lead to a tendency to misperceive bodily sensations as indications of an underlying disease process.

The association between being a clinician and developing health anxiety in the context of BFS is well-recognised, and has even attracted a specific term: fasciculation anxiety syndrome in clinicians (FASICS). (1) One possible explanation for this observation is that clinicians are more likely to have contact with patients with serious medical disorders associated with fasciculations, such as MND. In a study of 539 clinicians, Reed and colleagues found seventy percent reported experiencing fasciculations after watching a documentary about MND, highlighting the role of prior exposure.(2)

Additional variables, unrelated to occupation, also undoubtedly play a role in determining an individual's tendency towards interpreting fasciculations as evidence of a serious illness, such as perceived vulnerability and tolerance of uncertainty (30, 31). Furthermore, safety behaviours, such as reassurance seeking and self-monitoring, whilst serving to temporarily allay anxieties, ultimately heighten sensitivity toward internal bodily sensations and thereby plausibly exacerbate fasciculation symptoms. Taken together, we propose bidirectional relationship likely contributes towards maintaining both sets of symptoms (see figure 3).

[FIGURE 3: Hypothesized maintaining factors in patients with health anxiety and BFS] (28)

Management

The systematic review revealed a paucity of research assessing interventions to treat health anxiety in the context of BFS. Notably Of the four studies that described interventions, none utilised a

randomised control design. In the two studies that reported use of medication, one found fasciculation symptoms improved with treatment.(15) In the only study that assessed presence of health anxiety at follow-up, all the patients improved after counselling.(1) In the two case reports, CBT alongside antidepressant medication was associated with improvements in BFS and health anxiety symptoms.

Systematic reviews and metanalyses evaluating treatment for hypochondriacal disorder has consistently found CBT to be effective. There is also some evidence for other forms of psychotherapy, such mindfulness-based CBT (32) and acceptance and commitment therapy (33). Studies also support a role base for pharmacotherapy, however the evidence is more sparse,. The strongest evidence exists for antidepressant medication, primarily serotonin selective reuptake inhibitors (SSRIs), which have been shown to be more effective than placebo(34) and similar in effectiveness as CBT (35) . The only randomized placebo-controlled study to have assessed CBT and medication together, found they were more effective than either alone (36). No study we identified in the systematic review reported the effectiveness of medication on health anxiety; however, escitalopram (an SSRI) and mirtazapine (a noradrenergic and specific serotonergic antidepressant) were found to be effective and well-tolerated in the case reports.

In our experience, a '*vicious flower'* model of health anxiety is a useful tool for clinicians offering CBT.(37) Each component, or 'petal' reflects a feedback loop contributing towards the maintenance of health anxiety. It provides a shared understanding by which thoughts, emotions, behaviours and attentional focus that are erroneously perceived by the patient to help symptoms, ultimately have the effect of perpetuating health anxiety (see supplemental information for details). For example, in case 1 avoidance of exercise was an important safety behaviour and therefore identified as a 'petal' to be addressed. During therapy, exercise was actively encouraged, resulting in a transient increase in fasciculations. Through making a causal link between exercise and fasciculations (rather than between MND and fasciculations), over time this led to desensitisation and a sense of mastery over fasciculation symptoms. Case 2 was notable in the degree of internal self-monitoring that inadvertently maintained health anxiety. This was addressed in therapy through behavioural

experiments, in which systematic shifting of attentional focus could be demonstrated to modulate the severity of symptoms, such as dizziness. Thus, in both cases, identifying and addressing each 'petal' ultimately led to a reduction in distress levels.

In the absence of a specific biomarker to exclude MND, a concern for neurologists in the assessment of patients with new onset fasciculations is misdiagnosing a patient for BFS when they have MND. Evidence suggests this is rare, and where it does occur, patients typically have additional neurological features such as cramps,(38-40) or weakness.(1) It is notable that in both case reports, patients sought several neurological opinions and repeat investigations. Significant improvements in health anxiety symptoms were only demonstrated when these safety behaviours were addressed, highlighting the importance of continuity of care and avoiding over-investigation. Upon completion of a surveillance period to exclude MND, we suggest patients who do not respond to simple reassurance should be considered for a psychiatric review to assess for the presence of health anxiety.

Limitations and recommendations for future research

Whilst providing a valuable contribution to the field it is important to acknowledge some limitations. The overall quality of the studies identified were medium, and in some cases low. There was also high degree of heterogeneity with regards the design, patient population, and recorded variables. Only one study exclusively included patients with BFS and health anxiety,(1) and no study reported a clinical assessment by a psychiatrist. As such, it is difficult to ascertain the proportion of patients who met the diagnostic criteria for health anxiety disorder. Further research in a representative patient group using a prospective design (incorporating standardised instruments to assesses neurological and psychiatric features) is warranted. A randomised controlled trial would be particularly informative to address the optimal treatment in this patient group.

Conclusion

Health anxiety regarding MND in patients with BFS is an under-reported phenomenon, of which clinicians appear particularly prone. The relationship between BFS and health anxiety is complex, however a bidirectional relationship likely contributes towards maintaining both sets of symptoms. With the increasing prevalence of online patient forums and media coverage of MND (such as 'the Ice Bucket Challenge' of 2014) the number of patients who develop health anxiety around MND in the context of BFS can be predicted to increase. Neurologists should be alert to the presence of health anxiety coexisting with BFS and resist carrying out unnecessary investigations and consider referral for psychiatric assessment where reassurance is ineffective. A '*vicious flower'* model of health anxiety is a useful clinical tool in arriving at a shared understanding of the disorder with patients. From the available evidence, there is support for the role of psychological therapy, especially CBT, as well as pharmacotherapy, in the form of antidepressant medication. Furthermore, in severe or treatment-refractive cases, combined treatment may be indicated.

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