Is vestibulodynia a nociplastic pain syndrome? A commentary

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A recent consensus statement differentiated between persistent vulvar pain of at least 3-month caused by a specific disorder (e.g., inflammatory, neoplastic, traumatic) and vulvodynia, which is vulvar pain without clear identifiable cause.[1] The statement suggested using a pain-based system to characterize vulvodynia based on location (localized, generalized, or mixed), situations that elicit the pain (contact, spontaneous, or mixed), temporal pattern (intermittent or constant), and onset (primary or secondary).

Vulvodynia is a highly prevalent form of chronic genital pain in women, to such an extent that prevalence studies estimate ranges from 10% to 28% in reproductive-aged women.[2, 3] Localized provoked vulvodynia at the vestibule, known as vestibulodynia (VBD), is the most common manifestation of the disease (about 80%).[4]

Women with VBD often describe vulvar pain as a burning, stinging, irritation, rawness, and dyspareunia (difficult or painful intercourse). Most women with VBD described their pain as "hot," "burning," or "pricking" and that the vestibular area is sensitive to the touch (e.g. during sexual intercourse or tampon use) and that the pain would be increased by rubbing. The pattern of VBD responses is suggestive of sensory abnormalities in the form of evoked pain (e.g. hyperalgesia or allodynia), suggesting sensitization, an underlying manifestation of neuropathic pain.

This is consistent with biopsy studies that have demonstrated increased innervation of the vulvar vestibule and an increase in subepithelial heparinase activity and cytokines that have been linked to neuroinflammatory processes; patients with VBD also experience body changes in sensitivity, suggesting that sensory dysregulation might be involved the expression of this pain condition.[5]

Furthermore, the discomfort inherent in VBD is always associated with pelvic floor muscle overactivity.[6] This prolonged pattern can result in decreased tissue perfusion, muscle dysfunctional overactivity, and the development of myofascial trigger points, resulting in localized or radiating pain and/or intense tenderness. Neuropathic pain and hypertonicity can be considered a multifactorial and complex consequence of maladaptive neuronal plasticity.[7]

Neuropathic pain is defined as pain arising as a direct consequence of a lesion or disease affecting the somatosensory system.[8]According to this definition, VBD cannot be designated as a neuropathic pain, because a clear and evident lesion or a disease of the somatosensory system has not been identified as the cause of VBD pain. It may be argued that, by excluding VBD from the neuropathic pain syndrome, there is a risk of stigmatizing this group of patients as having a somatization disorder, one without a true and demonstrable abnormality, as opposed to the patients who have a "real" physical illness. The inability of this pain terminology to harmonize with the concepts of neuropathic pain has resulted in the use of other non-defined descriptors of VBD such as "dysfunctional" or "psychosomatic" pain, which not only give no insight into possible mechanisms but also carry implications that may stigmatize patients as only psychologically distressed. The International Association for the Study of Pain recently introduced the new pain descriptor "nociplastic pain," defined as "pain that arises from altered nociception, despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain," meant to cover cases not properly covered by neuropathic pain definition.[8]

The descriptor is primarily addressed to patients with chronic pain conditions characterized by evidence of altered nociceptive processing, such as VBD, where altered nociception is clinically documented. Therefore, the new descriptor does not apply to patients reporting pain without hypersensitivity. As such, it is neither a synonym for idiopathic pain nor pain of an unknown origin. A multifactorial aetiology, including infections, hormone disorders, neuroinflammation, atopic disease, gene polymorphisms that interfere with inflammation, and psychogenic factors, has been implicated in the development and maintenance of VBD.[8]

What is becoming increasingly apparent is that VBD is likely not one disease but rather several diseases, in which the common end point is vestibular hypersensitivity and pelvic floor hypertonic dysfunction. In my experience, VBD represents a summation and overlapping of various trigger factors (infections, hormonal disturbances, allergies, genetic aspects, psychological vulnerability, and others) with weight and predominance varying from patient to patient. It is impossible to say whether psychosexual factors are involved in the development or maintenance of VBD or whether they are the consequence of undiagnosed, persistent, and debilitating pain. Pain modulation by psychological factors is one of the most complex problems: in patients with VBD, psycho-neurobiological vulnerability plays a relevant role, and the experience of pain varies depending on the patient's psychological state.

In conclusion, I postulate that VBD results from diverse precipitating and trigger factors that ultimately promote and maintain a nociplastic pain syndrome. I believe these considerations provide the impetus for future work to identify responders of targeted treatments based on various subgroups of VBD.

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