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EDITORIAL

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It is premature to categorize Hunner Lesion interstitial cystitis as a distinct disease entity

It is with some trepidation that I provide a contrary opinion on the differentiation of Hunner Lesion Interstitial Cystitis (HL-IC) from non-Hunner Lesion Bladder Pain Syndrome (BPS) published by some members of the European Society for the Study of Interstitial Cystitis (ESSIC) [1]. The authors representing this impressive group of prominent urologists, clinicians, advocates and patients interested in Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS) sought to explore if HL-IC differs from other BPS presentations in regard to symptomatology, physical examination findings, laboratory tests, endoscopy, histopathology, natural history, epidemiology, prognosis and treatment outcomes. This very comprehensive, yet biased (my opinion) review would like us to believe that IC/BPS patients can be categorized as black or white in a clinical world of infinite colors. While they may be correct (I personally believe that they are on the right track), it is important that the contrary view be available as well. The author's evaluation, when looked upon through an outside lens (the other side of this important debate was not presented by the authors), shows that their conclusions and recommendations based on the evidence they present are premature. In fact they have clearly shown that HL-IC does not differ from BPS presentations in almost all the parameters they assessed and the evidence clearly indicates that this is not the time to establish HL-IC as a distinct disease entity from BPS.

In regard to symptomatology, they confirm that while clinical phenotypes differ, the significant overlap means that symptoms cannot be used to differentiate HL-IC from BPS in individual patients [2]. They further confirm that there are no physical examination parameters to differentiate HL-IC from BPS. Furthermore, they report no readily available and validated laboratory tests to distinguish between either HL-IC or BPS diagnoses.

The authors are quite adamant that they can differentiate HL-IC from BPS on endoscopy but no one else in the world can do it properly. The authors accept the fact that we cannot actually call HL-IC a disease until we can all identify HL with a high degree of clinical accuracy. They recommend an international symposium to find consensus on how to actually diagnose a Hunner Lesion. It looks like the authors want to teach others how to readily identify HL patients on cystoscopy. That is very presumptuous, because I believe that even this experienced group of clinicians would have trouble finding consensus if actually put to a real world test. It is agreed by all, including myself, that we do need to try and find international consensus on how to properly diagnose HL on cystoscopy. Until that time, we cannot really call HL-IC a distinct disease but rather one end of a spectrum of cystoscopic conditions.

The authors describe the histological biopsy findings in HL-IC but do not describe the histopathology described for BPS, particularly when the histopathology is not as severe as that described in the article. The grey area in the spectrum between what the authors describe and the almost completely normal bladder seen at the other end of the spectrum (likely not a bladder pain syndrome at all but rather some other confusable condition such as pelvic floor dysfunction) can include inflammatory infiltrates in the mucosa, submucosa and deep muscle, increase in mast cell density, mucosal edema, small vessel fragility (sometimes see only acutely with hydrostatic bladder distention) and subtle neurogenic inflammatory signatures. The rationale for considering the more dangerous deep muscle biopsies to add to the diagnostic accuracy is not validated with data, only perception.

In regard to natural history, the authors make the point that there is no evidence that BPS evolves into HL-IC but since the natural history data is very limited they fail to mention that there is no evidence that it does not or that the progression could be bi-directional (such hypotheses have never been adequately tested). An important question that needs to be answered is whether Hunner Lesions appear in the bladder at the same time as the symptoms begin. Is there a prodromal phase where the bladder and its histopathology looks different than the late disease characteristics described by the authors. This will become clearer when we actually understand the mechanism and/or pathogenesis underlying IC/BPS. The authors acknowledge that epidemiological studies indicate the prevalence of HL-IC range wildly from a low of 3.5% to as high as 56%. That clearly shows that we as a urology profession (even the experts who do the studies) do not know how to clinically differentiate HL-IC from BPS. In regard to prognosis, long term studies are poor, small and inconclusive as to the long-term prospects of young or middle aged adults diagnosed with either HL-IC or BPS.

In regard to treatment outcomes, the authors present a well-documented argument that we have better surgically based "short term" therapies for HL-IC. Some patients do have significant benefits that can be durable for months or years, but for many there is no long term sustained cure with local therapy of the Hunner Lesions. The single rationale that some IC/BPS patients improve for a variable time after treating observable lesions in the bladder is not strong evidence to validate a differentiation between chronic disease

processes for which we have no long term management options.

The authors recommend classifying HL-IC as a separate disease entity (Hunner Lesion Disease or HLD) with its own ICD11 code. They have clearly shown that we are at a very early stage of understanding the disease processes in IC/BPS (HL-IC and BPS). Their excellent review of the science outlines that we know very little in regard to the mechanism, disease pathogenesis, diagnosis, treatment or prognosis in IC/BPS and even less about the relationship of HL with BPS. It is not only premature, but irresponsible, at this time to recommend that we are now ready to define these conditions as separate diseases as this could significantly impede the important scientific inquiry required to better understand these conditions and their relationship. In fact, there is concern that proceeding this way will only create more confusion in the field as the US FDA clearly believes there is not enough evidence (based on a similar review of the literature by unbiased scientists who are not as invested in the disease as the authors) to differentiate HL-IC from BPS in clinical trials [3]. In trying to understand enigmatic chronic urologic pain conditions, it is easy to misinterpret conjecture, opinion, consensus, and bias as fact or discussion as recommendations or conclusions. The authors have raised the appropriate questions in regard to HL and the relationship with IC/BPS. So, while we wait to validate the suppositions of the authors with real scientific and clinical evidence, we cannot ignore their valuable insights into this difficult (to understand and manage) condition. We should continue to differentiate as best we can IC/BPS patients with HL (and try to reach the consensus suggested by the authors on how to do this), manage this phenotype with evidence-based approaches but not completely discount the possibility that HL-IC and BPS represent a spectrum of IC/BPS disease. While I believe that the authors' hypothesis may eventually turn out to be correct, in their enthusiasm, they must not jump to unsubstantiated conclusions.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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