Original article

Characteristics and electrocauterization of Hunner's lesions associated with bladder pain syndrome

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A B S T R A C T

Objective: This study was conducted to investigate patients with bladder pain syndrome (BPS) and cystoscopic findings of Hunner's lesion. The treatment and pathological findings related to Hunner's ulcers are unclear. The purpose of this study is to clarify the characteristics and to develop a new method for the diagnosis and treatment of Hunner's lesions in patient with BPS.

Methods: From 2005 to 2011, 12 women with BPS were found to have bladder ulcers by cystoscopy without anesthesia. Previous therapy results for these patients had been limited. All patients received a bladder ulcer biopsy and cystoscopic electrocauterization in our hospital as treatment for the bladder ulcers. Patient demographics, patient clinical history, the characteristics of the cystoscopic findings, and treatment outcomes were recorded.

Results: The cystoscopy characteristics of the bladder ulcers were central hyperemic patches with peripheral scarring and increased vascularity. Several subtypes of cystoscopic finding were also identified. The pathology findings of these patients included chronic cystitis with ulceration or eosinophilic cystitis. Mast cells and macrophages were also found in the bladder mucosa by immunohistochemical staining for c-kit and CD68. Nine of the 12 patients were immediately pain-free after electrocauterization, and the other three also showed a marked improvement. The patients' mean Visual Analogue Score before the operation was 9.64 ± 0.81, and their mean Visual Analogue Score after electrocauterization showed significant improvement (2.95 ± 1.85, p < 0.001). Bladder pain relapse occurred at 2–4 months after the procedure in six patients.

Conclusion: Patients with BPS who show a poor response to conventional intravesical treatments should receive cystoscopy to identify ulcer type BPS. Treatment of patients by transurethral electrocauterization when they have ulcer type BPS is able to provide pain relief.

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1. Introduction

Patients who suffer from bladder pain without infection, urothelial tumor, urolithiasis, or other organic diseases affecting the genitourinary tract are often diagnosed as suffering from interstitial cystitis (IC). Current consensus suggests that the term IC is misleading and should be replaced by “bladder pain syndrome” (BPS).1 IC/BPS can be subdivided into two types, ulcerative and nonulcerative, as determined by cystoscopic findings indicating either bladder ulcers or glomerulations on the bladder wall without ulceration. Bladder ulcerations was used to be known as Hunner’s ulcer in the past decades, and in recent years, the European Urology Association guideline opted to use the term Hunner’s lesion instead of Hunner’s ulcer, and this is gradually being adopted worldwide.

Hunner’s lesions are found in about 10% to 20% of patients with IC/BPS.2 Some studies have asserted that patients with Hunner’s lesions tend to be older, to have a smaller bladder capacity, and to have a higher urinary frequency than patients without Hunner’s lesions.3,4 However, another study did not agree with this conclusion.5 In our experience, patients with IC/BPS and bladder ulceration often suffer from intractable lower abdominal pain, and this pain usually does not respond to medical treatment.

Although numerous studies have focused on the pathophysiology of IC/BPS, the actual etiology, pathogenesis, and diagnostic criteria of bladder ulcers remain unclear, and there is also no definitive treatment method. In clinical practice, we observed 12

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patients who had Hunner’s lesions and who were refractory to any treatment. In this study, we try to characterize the cystoscopic findings related to Hunner’s lesions and propose a new method for the diagnosis and treatment of Hunner’s lesions in patients with IC/BPS.

2. Materials and methods

This is a retrospective longitudinal study. From 2005 to 2011, among 95 patients diagnosed to have IC/BPS, 12 women (12.6%) were found to have Hunner’s lesions. The lesions were defined as a circumscript, reddened mucosal area with small vessels radiating toward a central scar, or a discontinuity or break lesion or patch of bladder mucosa. These patients had suffered from severe bladder pain and urinary frequency for several years, and all of these patients were found to have bladder ulcers by cystoscopy without anesthesia. The patient demographics, clinical history, treatment, and cystoscopic findings are reported. The Visual Analogue Score (VAS) of pain was also recorded before and after the operation. This study was approved by Buddhist Tzu Chi General Hospital Research Ethics Committee, and written informed consent was obtained from each patient.

3. Results

Since August 2011, we have attempted to discover possible bladder lesions in the patients who have failed to respond successfully to intravesical treatment. Cystoscopy without anesthesia was performed on patients who had intractable bladder pain when the bladder was nondistended, and those who had frequency, urgency, and had shown abnormally increased vascularity and hyperemic patches during previous cystoscopic hydrodistention investigations. Among patients receiving cystoscopic examination, 12 were found to have definite bladder lesions. The demographics of these patients are listed in Table 1. Their ages ranged from 45 to 73 years, and the duration of treatment for IC/BPS ranged from 1 to 13 years. All patients had been previously diagnosed to have IC/BPS by cystoscopic hydrodistention under general anesthesia.

These patients had previously received various types of medication such as anticholinergic drugs, nonsteroid anti-inflammatory drugs (NSAIDs), analgesics, and oral pentosanpolysulfate (Elmiron), but the therapeutic effect of these treatments had usually been disappointing. The patients had also undergone multiple intravesical procedures including cystoscopic hydrodistention, intravesical hyaluronic acid installation, and intravesical botulinum toxin-A injections. The effects of these intravesical treatments had also been limited or unsatisfactory. Intractable bladder pain and frequent urination continued to afflict these patients. All 12 patients had severely reduced quality of life. They could hardly leave their home for a trip or for leisure. Four patients had been treated with long-term antibiotics for pyuria with a negative urine culture result, but bladder pain and frequent urination remained. Urodynamic studies universally revealed a small cystometric bladder capacity and a strongly positive potassium chloride test.

During the cystoscopic procedure, the bladder was not distended to more than 100 mL, and it was then that the ulcers were seen. The ulcers were either single or multiple and were mainly located on the posterior or lateral wall. No ulcer was found in the trigone. The characteristics of the bladder ulcers were as follows: (1) hemorrhagic patches without definite scarring or urethral erosion, (2) central hyperemic patches with peripheral scarring, (3) increased vascularity with a centralized distribution of vessels, (4) severe scarring with a central scar and hyperemic patch, (5) localized erythema as well as edematous and erosive mucosa, (6) easy bleeding from the bladder ulcer and a mucosal fissure that appeared during bladder filling (Fig. 1A–F). The ulcers were different from classic ulcers, which have an oval defect or volcano appearance. Glomerulations of the bladder mucosa at the other sites may or may not be present when the bladder was further distended with anesthesia.

Cystoscopic electrocauterization to treat the bladder ulcers was performed on all patients before bladder hydrodistention. We used a roller electrode to cauterize the ulcer base and the margin of the surrounding mucosa as shown in Fig. 2. Bladder biopsy of the ulcers was performed before electrocauterization. After electrocauterization, no bleeding was seen to occur from the ulcer. A three-way Foley catheter was inserted to allow normal saline continuous irrigation for 2 days. Prophylactic antibiotics and oral NSAIDs were also used to provide symptomatic treatment for these patients. Follow-up cystoscopy was performed at 3 months after the procedure if patients still had bladder pain symptoms.

A minor bladder perforation during the procedure was noted in one patient who received extensive cauterization for multiple bladder ulcers, and with this patient we retained the urethral catheterization for 1 week (grade I complication of Clavien Classification). All patients became pain-free or had reduced pain immediately after electrocauterization, and the symptoms remained improved after removal of the catheter. The patients’ mean VAS before the operation was 9.64 ± 0.81, and their mean VAS after electrocauterization showed significant improvement (2.95 ± 1.85, p < 0.001). The patients with hemorrhagic patches, increased vascularity, and centralized distribution of vessels in the

<table>
<thead>
<tr>
<th>No.</th>
<th>Age (y)</th>
<th>Disease history (y)</th>
<th>Location of ulcer</th>
<th>Maximum bladder capacity (mL)</th>
<th>Therapeutic duration of electrocauterization</th>
<th>Biopsy results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64</td>
<td>1</td>
<td>Left posterior wall</td>
<td>300</td>
<td>2 and 9 mo not recurred yet</td>
<td>Chronic cystitis with edema</td>
</tr>
<tr>
<td>2</td>
<td>61</td>
<td>5</td>
<td>Right and left posterior wall</td>
<td>450</td>
<td>3 and 5 mo not recurred yet</td>
<td>Chronic ulcer with granulation tissue</td>
</tr>
<tr>
<td>3</td>
<td>66</td>
<td>9</td>
<td>Posterior wall</td>
<td>550</td>
<td>3 and 4 mo not recurred yet</td>
<td>Chronic ulcer with granulation tissue</td>
</tr>
<tr>
<td>4</td>
<td>70</td>
<td>4</td>
<td>Left posterior wall</td>
<td>200</td>
<td>2 and 6 mo not recurred yet</td>
<td>Chronic ulcer with granulation tissue</td>
</tr>
<tr>
<td>5</td>
<td>56</td>
<td>10</td>
<td>Small ulcer over right and left posterior wall</td>
<td>350</td>
<td>Mixed acute and chronic inflammatory cells infiltration</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>45</td>
<td>13</td>
<td>Right posterior wall</td>
<td>400</td>
<td>&gt;3 mo</td>
<td>Eosinophilic cystitis</td>
</tr>
<tr>
<td>7</td>
<td>55</td>
<td>6</td>
<td>Right posterior wall</td>
<td>450</td>
<td>&gt;12 mo</td>
<td>Chronic cystitis</td>
</tr>
<tr>
<td>8</td>
<td>54</td>
<td>10</td>
<td>Right posterior wall</td>
<td>350</td>
<td>2 and 4 mo not recurred yet</td>
<td>Chronic inflammatory with foreign body giant cells</td>
</tr>
<tr>
<td>9</td>
<td>73</td>
<td>5</td>
<td>Right posterior wall</td>
<td>300</td>
<td>&gt;4 mo</td>
<td>Chronic cystitis</td>
</tr>
<tr>
<td>10</td>
<td>65</td>
<td>2</td>
<td>Left lateral wall</td>
<td>300</td>
<td>&gt;6 mo</td>
<td>Chronic cystitis</td>
</tr>
<tr>
<td>11</td>
<td>55</td>
<td>3</td>
<td>Right and left posterior wall</td>
<td>500</td>
<td>&gt;4 mo</td>
<td>Chronic cystitis</td>
</tr>
<tr>
<td>12</td>
<td>63</td>
<td>2</td>
<td>Multiple ulcers in posterior wall</td>
<td>550</td>
<td>&gt;3 mo</td>
<td>Eosinophilic cystitis</td>
</tr>
</tbody>
</table>

IC/BPS — interstitial cystitis/bladder pain syndrome.
bladder had better therapeutic results after electrocauterization. The improvement in patients with only hyperemic patches was not as good as that of the other patients. Among the 12 patients, six had recurrent bladder pain 2 to 3 months after the first procedure; the therapeutic duration of electrocauterization is listed in Table 1. Cystoscopy revealed that new bladder ulcers had formed near the scars of the previous ulcers, and a second electrocauterization was performed that gave a similar improvement after the procedure. The therapeutic duration of electrocauterization has a tendency to last longer after repeat procedure.

The pathology reports on the bladder biopsies of these patients revealed lymphocyte infiltration with chronic ulceration and the presence of granulation tissue (Fig. 3A), whereas three of the biopsy reports showed eosinophilic cystitis (Fig. 3B). Mast cells and macrophages were identified in the bladder mucosa by immunohistochemical staining for c-kit and CD 68, respectively (Fig. 3C and D).

4. Discussion

Fenwick\textsuperscript{6} first described nonmalignant bladder ulcers in 1896. In his case series, many patients had multiple bladder ulcerations that involved the trigone. Hunner\textsuperscript{7} presented the first report of eight cases of bladder ulcers in women. Peterson and Hager\textsuperscript{8} reported a case series including patients with urinary frequency, suprapubic pain, and cystoscopic bladder Hunner’s lesions; they chose to call the disease “interstitial cystitis,” as Skene first used this term in his textbook in 1887. Currently, IC/BPS can be subdivided into

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**Fig. 1.** Characteristics of the Hunner’s lesion: (A) hemorrhagic patches without definite scarring or urothelial erosion, (B) central hyperemic patches with peripheral scarring, (C) increased vascularity with centralized distribution of vessels, (D) severe scarring with a central scar and hyperemic patch, (E) localized erythema and edematous and erosive mucosa, and (F) the bladder ulcer easily bled and a mucosal fissure appeared during bladder filling.

**Fig. 2.** Using transurethral roller electrode to cauterize the ulcer base and the margin of the surrounding mucosa.
ulcerative and nonulcerative types based on cystoscopic findings. The study of Peters et al. found that ulcerative type IC was associated with more severe lower urinary tract symptoms and less coexisting illnesses. He proposed that ulcerative and nonulcerative IC are two distinct diseases.

In this study, we found that the appearance of bladder ulcers in IC/BPS patients was not uniform. There was no typical ulcer base or crater margin; rather, the typical ulcer was formed as a dense central scarring with eroded mucosa and increased vascularity radiating from the center to the periphery. The characteristic cystoscopic findings related to bladder ulcers indicate the presence of localized bladder inflammation with an unhealthy mucosa. Unless the chronic inflammatory lesions are ablated, it seems likely that it will be almost impossible to eradicate bladder pain.

Johansson and Fall collected specimens by transurethral resection of the bladder wall from patients with ulcerative and nonulcerative IC. Patients with ulcerative IC showed mucosal ulceration and hemorrhage, tissue granulation, intense inflammatory infiltration, elevated mast cell counts, and perineural infiltrates. Patients with nonulcer IC, despite displaying the same severe symptoms, had relatively unaltered mucosa with a sparse inflammatory response. In the present study, bladder biopsy from patients with Hunner’s lesion showed bladder mucosa ulceration, lymphocyte infiltration, and tissue granulation. Eosinophilic cystitis was also detected in three of the 12 patients. The patients with eosinophilic cystitis might be treated with steroid or montelukast sodium if bladder pain persisted after current therapy. Further immunochemical stain revealed mast cell and macrophage accumulation in the bladder submucosa. Because the presence of macrophage implies chronic inflammation and mast cells imply an allergic reaction, the underlying pathophysiology of Hunner’s lesion might be attributed to allergic reaction and chronic inflammation.

Zhang et al. investigated biomarkers such as antiproliferative factor, heparin-binding epidermal growth factor (EGF), and EGF in patients with IC/PBS and found that EGF levels were significantly higher in patients with nonulcerative IC than those with ulcerative IC. The clinical characteristics of patients with ulcer type IC/BPS in our series are intractable bladder pain that is not related to bladder distention as well as manifestation of symptoms such as frequency, urgency, and nocturia. Therefore, for a patient who has been diagnosed to have IC/BPS but has bladder pain that persists despite multiple types of medications and/or intravesical treatment, cystoscopy without anesthesia should be performed to try and detect the presence of bladder ulcers.

Many different specialized treatments have been used to treat ulcer type IC/PBS. Since the early 20th century, segmental resection of the part of the bladder wall with ulcers has been performed on patients with ulcer type IC. However, this approach has produced unsatisfactory results and a great tendency for the ulcers to recur.
after the surgery. Rössberger et al reported the long-term results of cystectomy or partial cystectomy with reconstructive surgery for patients with ulcerative IC/PBS; in this series, 28 of the 34 patients had complete symptom resolution after this surgical procedure. Rofeim et al used cystoscopic YAG laser to ablate Hunner's lesion, and it was found that both pain and lower urinary tract symptoms were greatly improved after this procedure; however, some patients needed to undergo a repeat procedure. Soucy reported his experience using steroids to treat 14 patients with ulcerative IC/PBS. Nine of these patients showed a response to this therapy, whereas the others did not. Cox et al used a submucosal injection of triamcinolone to treat Hunner's lesion subtype IC, and as a result the mean International Prostate Symptom Score improved after the procedure without any complications. Hyperbaric oxygen therapy has also been used to treat IC/PBS with Hunner's lesion, and after a course involving 20 sessions of hyperbaric oxygen therapy, Hunner's lesion seemed to disappear.

Although many different methods have been used to treat patients with ulcer type IC/PBS, none seem to be definitely cure this disease. The American Urological Association guidelines recommend the fulguration (with laser or electrocautery) and/or injection of triamcinolone if Hunner's lesions are present. In this study, we tried simple electrocauterization using an ordinary transurethral resectoscope and roller to cauterize the bladder ulcers. The results in terms of immediate pain relief were excellent. Although the IC symptoms did relapse in some patients, a repeat procedure remained effective.

All 12 patients with ulcer type IC/PBS in this study had failed to improve when treated previously with oral medication and intravesical treatments including hyaluronic acid instillations and botulinum toxin A injections. Only electrocautery was able to provide relief from their bladder pain symptoms and allow the patients to attain a better quality of life. We suggest that urologists use different treatments for patient with ulcerative and non-ulcerative type IC/PBS. Bladder biopsy of the bladder ulcers should be performed to identify the underlying pathology, such as eosinophilic cystitis, and the resulting pathological report may have an impact on the choice of therapy strategy. The limitations of this study were the small case number and the retrospective study design. However, Hunner's lesions are only found in about 10% of the patients with IC/PBS. We considered the improvement in VAS as significant, despite the small case number used in this study. Further prospective study involving a control group should be considered.

5. Conclusions

Patients with ulcer type IC/PBS should be treated as having a different disease from patients with nonulcer type IC/PBS. Once a patient is found to be refractory to conventional intravesical treatment for IC/PBS and intractable bladder pain persists, cystoscopy should be performed as early as possible in order to detect ulcer type IC/PBS. Transurethral electrocauterization of the bladder ulcers is a simple and effective procedure that brings pain relief very quickly. Although symptom relapse may occur, a repeat of the procedure is usually effective.

Conflicts of interest statement

The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in the manuscript.

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