



## Original Article

# Urinary bladder biopsies in spinal cord injured patients

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**Study design:** A series of 94 urinary bladder biopsies in spinal cord injured (SCI) patients were histopathologically and statistically analysed.

**Objectives:** The following hypotheses were examined: (1) The number of clinical bladder infections per year in each patient does not influence the histopathological type of inflammation of the urinary bladder; (2) The duration of the spinal cord lesion does not have a strong effect on the type of inflammation; (3) The different neurological levels (upper and lower motor neuron lesions) do not relate to a specific histopathology.

**Settings:** All patients received their treatment at the Swiss Paraplegic Centre in Nottwil, near Lucerne (Switzerland).

**Methods:** The samples were taken from the bladder fundus during endoscopic urologic operations. Histopathological standard procedures were carried out. Statistical analysis including Kruskal–Wallis and Chi-square tests were performed.

**Results:** Histopathological analysis showed abnormal alterations of the urinary bladder mucosa in 86 SCI-patients: (91.5%). 63 cases (67.0%) showed a chronic type and 23 cases (24.5%) showed a subacute type of inflammation. A normal urinary bladder was found in eight cases (8.5%). The three hypotheses were statistically not rejected.

**Conclusion:** Results demonstrated no correlation between the number of bladder infections per year, the period since injury, the neurologic level of the spinal cord lesion and the histopathology of the urinary bladder mucosa.

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**Keywords:** spinal cord injured patients; urinary bladder biopsies

## Introduction

The physiological mechanisms of filling and emptying the urinary bladder are disturbed in spinal cord injured (SCI) patients resulting in a reduction of the bladder's wash-out mechanism.<sup>1</sup> This enables microorganisms to multiply within the bladder and cause infections with clinical symptoms. Normally the urothelium is resistant to bacterial infections. High spastic pressure supports a vesicoureteric reflux of infected urine resulting in pyelonephritis.

In 1995 we reported the first results of urinary bladder biopsies in a small series at the Swiss Paraplegic Centre.<sup>2</sup> The aim of the present study (94 patients) is to examine the following hypotheses: (1) The number of clinical bladder infections per year in each patient does not influence the histopathological type of inflammation of the urinary bladder; (2) The

period of the spinal cord lesion does not have a strong effect on the type of inflammation; (3) The different neurological levels (upper or lower motor neuron lesions) do not relate to a specific histopathology.

## Methods

The study group consisted of 94 SCI patients receiving treatment at the Swiss Paraplegic Centre in Nottwil (near Lucerne). This specialized hospital, founded by GA Zäch in 1990, coordinates both acute care and rehabilitation of para- and tetraplegics.

All patients were free of clinical signs of bladder infections. For each individual, urinary bladder biopsies were taken from the bladder fundus during endoscopic urologic operations. Urine specimens obtained during the study of each individual were sterile and there were no complications during the intra- and/or the postoperative phase.

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The fresh samples, measuring between 2 and 4 mm in diameter, were immediately fixed in 4% formalin solution. Standard procedures were carried out after paraffin blocking; 4–6 micrometer thick sections were stained with hematoxylin-eosin technique.

Statistical analysis of the hypotheses was performed using Kruskal–Wallis and Chi-square tests.

## Results

### *Clinical and histopathological results*

The average age of the study group was 40.6 years (ranging from 17 to 78 years) and the male : female ratio was 89:5. Each patient showed a traumatic lesion of the spinal cord as the cause of para- or tetraplegia. None of the patients had an indwelling bladder catheter. The following histopathological observations were made after microscopic examination of the samples obtained: (a) 86 SCI patients (91.5%) presented alterations of the urinary bladder. Normal bladder mucosa was found in eight cases (8.5%). The uroepithelium showed minimal alterations in nuclear polarity but no dysplasia was found. The cells of basal and intermediate layers were compact and cuboidal in form. The surface cells were more polygonal with large round nuclei. Three to seven cell layers in the uroepithelium were observed. (b) 63 SCI patients (67.0%) showed a chronic type of inflammation. The inflammatory infiltrate consisted of B- and T-lymphocytes and plasma cells, was localized in the lamina propria (Figure 1). (c) 23 SCI patients (24.5%) showed a subacute type of infection. The infiltrate was composed of lymphocytes/plasma cells and rare polymorph granulocytes. (d) Further histopathological observations revealed the presence of a diffuse fibrosis in 37 cases (39.4%), edema in 10 cases (10.6%) and



**Figure 1** Urinary bladder biopsy showing chronic cystitis with rare mononuclear inflammatory infiltrates in the lamina propria (arrows) (Hematoxylin and eosin-stain,  $\times 150$ ; 71-year-old male patient; paraplegia level T8; 35 months after the injury)

lymphoid hyperplasia (follicular cystitis) in three cases (3.2%) (Figure 2). Five cases (5.3%) revealed an association of these microscopic findings which were localized exclusively in the lamina propria. In 39 cases (41.5%) the lamina propria was normal. In 31 cases (32.97%) the muscularis presented a leiomyomatous-like hyperplasia. Neither urothelial proliferations (papillomas, transitional cell carcinomas) nor interstitial cystitis were diagnosed.

### *Statistical analysis*

**Hypothesis 1:** The number of clinical bladder infections per year in each patient does not influence the histopathological type of inflammation of the urinary bladder.

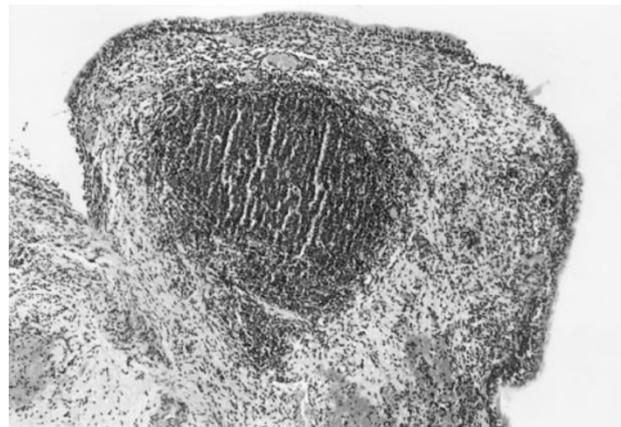
Clinical bladder infections occurred in each patient ranging from one to 12 times per year (median 3). For this analysis the Kruskal–Wallis-test demonstrated a value  $P=0.0830$ . This hypothesis was not rejected, it means that the number of clinical bladder infections per year in each patient does not influence the histopathology.

**Hypothesis 2:** The period of the spinal cord lesion does not have a strong effect on type of inflammation.

The median period since the injury was 65 months (range 4 to 528 months). Also for this analysis the Kruskal–Wallis-test was used ( $P=0.2930$ ). This hypothesis was not rejected, it means that the period of the spinal cord lesion does not have a strong effect on the type of inflammation.

**Hypothesis 3:** The different neurological levels (upper and lower motor neuron lesions) do not relate to a specific histopathology.

The neurologic level of the spinal cord lesion varied within the group such that 85 patients (90.4%) had upper motor neuron lesions and nine patients (9.6%) had lower motor neuron lesions of the spinal cord.



**Figure 2** Lymphoid hyperplasia in the lamina propria as a result of persistent chronic cystitis (follicular cystitis) (Hematoxylin and eosin-stain,  $\times 100$ ; 37-year-old female patient; paraplegia level L 1; 19 months after the injury)

This hypothesis was not rejected (Chi-square test;  $P=0.5580$ ), it means that the different neurologic level of spinal cord lesion does not relate to a specific histopathology.

## Discussion

To our knowledge, this study involved the largest series or urinary bladder biopsies of SCI patients. The aim of long-term bladder rehabilitation of SCI patients, including yearly cytology and biopsies, is the prevention of bladder infections and avoidance of urinary complications.<sup>3</sup> In our series there was no significant statistical difference between the number of infections, the period since the injury, the neurologic level of the spinal cord lesion and the histopathology. These results show that none of these variables have affected the histopathological inflammation type. The inflammatory infiltrate has been shown to be located solely in the lamina propria. The increase in the number of cell layers of the urothelium and fibrosis of the lamina propria can be accounted for by the repair processes in the pathogenesis of chronic inflammation.<sup>4–6</sup> The fibrosis most likely plays an important role in the etiology of the low compliance bladder.<sup>7</sup> This study reveals a discrepancy between clinical symptoms and histopathological findings: 91.5% of the examined patients showed pathologic alterations to their bladder wall, yet there was an absence of clinical symptoms at the time of biopsy. According to this discordance, Nochomovitz has reported the low level morphological changes of the urinary bladder mucosa and has contrasted this with the symptoms of bladder infection such as a severe bacteriuria and high fever.<sup>8</sup>

Our findings prove that only microscopical examinations permit the recognition of the whole range of mucosal lesions of the urinary bladder. In the future more histopathological examinations of biopsies are indicated in order to achieve a greater comprehension of the morphological changes of the urinary bladder in SCI patients.

## Conclusions

The histopathological analysis of urinary bladder biopsies of 94 SCI patients revealed that in 63 cases

(67%) the inflammatory infiltrate in the lamina propria was chronic and in 23 cases (24.5%) it was subacute. In eight cases (8.5%) there were no pathological alterations. Statistically no significant difference was proven between the clinical number of bladder infections per year, the period since injury, the neurologic level of the spinal cord lesion and the histopathology of the urinary bladder mucosa.

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