

# EOSINOPHILIC CYSTITIS

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## INTRODUCTION

A clinical manifestation of eosinophilic cystitis may be confused with bladder tumor except for irritative symptoms and the etiology still remains obscure although many authors have speculated this as one of the aspects of an allergic reaction at the bladder level (Frensilli et al. 1972 and Powel et al. 1972)<sup>3,7)</sup>. In addition a histological demonstration of eosinophilic infiltration of vesical muscularis and/or submucosa could be an only method of definite diagnosis.

Up to the present time 16 cases (Brown 1960, Champion 1966, Goldstein 1971, Palubinskas 1960 and Wenzel et al. 1964)<sup>1,2,4,5,8-10)</sup> have been published in English literatures and the treatment of eosinophilic cystitis have been empirical and conservative except for one case in which partial resection was performed for the involved area with parasitic infection (Perlmutter et al. 1968)<sup>6)</sup>.

Two cases of eosinophilic cystitis were herein presented. In the first case colcystoplasty with resection of widely involved bladder segment and in the second only antibiotic therapy was performed both in successful results.

## CASE REPORTS

Case 1. M. T., a 43-year-old woman was admitted to Osaka University Hospital on August 9, 1973 with retention following gross hematuria of one week duration and frequency, urgency and nocturia every hour of several weeks duration. Prior to this, the patient had intermittent irritative symptoms of the lower urinary tract for several years with occasional chill and

fever, and responded to the treatment with nalidixic acid. The past history revealed pyelonephritis at the age of 15, otherwise no contributory illness except for hypersensitivity to the sunlight.

At the time of admission she was afebrile, pulse 80 and blood pressure 128/60. Hemoglobin was 11 gm per cent and the white blood count was 6,800 per cu. mm with 7 per cent peripheral eosinophils. Urinalysis showed numerous red cells and 2 plus proteinuria. Initial urine culture yielded pseudomonas aeruginosa  $10^5$ /ml but negative for tuberculosis. The blood urea nitrogen (BUN) and creatinine were in normal limits with creatinine clearance of 61 ml per minute. The blood coagulation functions were within normal ranges except for slightly increased bleeding time. Serum protein electrophoresis revealed increased alpha 2 globulin. Evaluation for parasite, collagen disorders and allergic reaction test to nalidixic acid were all negative.

An excretory pyelogram demonstrated slightly dilated bilateral ureters without caliectases. A cystogram revealed a thick-walled and irregular surfaced bladder with small capacity and transient mild bilateral vesicoureteral reflux without dilatations (Fig. 1). A cystoscopic examination revealed rather circumscribed lesion over the entire upper dome where the bladder mucosa was extremely edematous, erythematous and proliferative without ulcer formation. The mucosa of the bladder neck to the trigone appeared pale and smooth. A vaginoscopy and pelvic examination were negative. Urine cytology was repeated several occasions but negative for malignant cells. The symptoms such as severe frequency, spasm and hematuria persisted

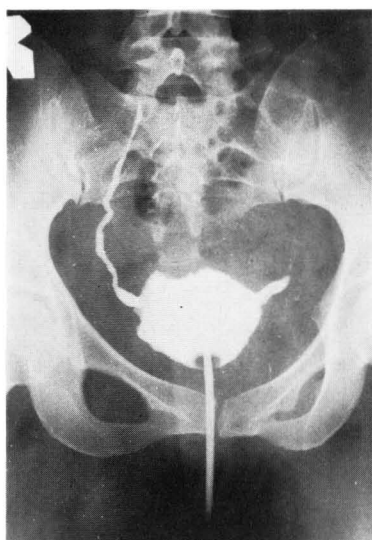


Fig. 1. A cystogram demonstrated bilateral vesicoureteral reflux with contracted bladder.

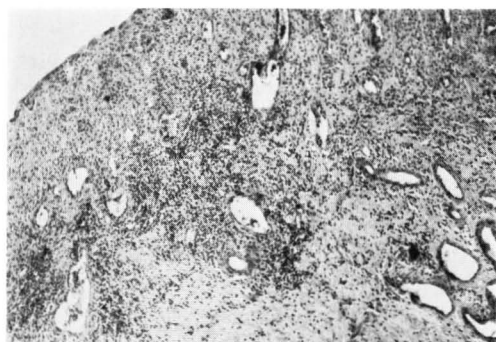


Fig. 2. Resected bladder segment showing marked eosinophilic leucocytic infiltration. H & E, ( $\times 100$ )

in spite of administration of antibiotics, antispasmodic and steroid.

Surgical procedure was therefore performed. At the time of operation the bladder appeared round, thick-walled and there was no perivesical fibrosis or lymphadenopathy. The bladder, the capacity being 130 ml, was injected vigorously resulting massive bleeding. The upper hemisphere of the bladder was excised to perform an anastomosis to the isolated colonic segment for colocystoplasty. The resected specimen was extremely edematous and erythematous with no mucosal ulceration and the muscular layer seemed to be thick with yellowish fibrous appearance. Histological findings were massive eosinophilic infiltra-

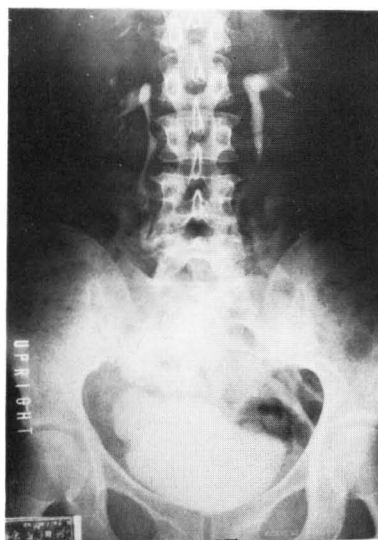


Fig. 3. Postoperative intravenous pyelogram.

tions of the muscular layer and edematous submucosa with lymphocytic infiltrations (Fig. 2).

Postoperative course was uneventful and a cystogram at the 3rd week postoperatively revealed 250 ml bladder capacity with disappearance of right vesicoureteral reflux. Urinary irritative symptoms subsided with nocturia two times. The intravenous pyelogram (Fig. 3) and cystogram at the 12th week postoperatively showed normal upper urinary tract and disappearance of vesicoureteral reflux on left with vesical capacity of 300 ml.

Case 2. S.H., a 59-year-old woman was admitted to Osaka University Hospital on August 18, 1968 because of episode of gross hematuria following irritative bladder symptoms. She had radical hysterectomy due to carcinoma of the cervix 10 years prior to this admission and had been followed in the outpatient clinic in negative findings for recurrence. She stated that she had no allergic history or lost weight.

The physical examination at the time of admission revealed tender suprapubic area. Hemoglobin was 9.9 mg per cent, white blood count 10,700. BUN and creatinine were in normal ranges. Urinalysis included microscopic hematuria, many white cells and one plus proteinuria. Initial urine culture yielded *Klebsiella*  $10^5$ /ml. An intravenous urography on admission showed

normal upper urinary tract with multiple cellulæ of the bladder probably secondary to previous radical hysterectomy. A cystogram revealed no reflux and slightly decreased capacity.

A cystoscopic examination performed on August 20, 1968 revealed the normal bladder neck and urethra and the bladder mucosa with multiple erythematous elevation measuring 1/2 by 1 cm in diameter, varying in size. These lesions did not extend to the trigone with normal appearance of both orifices. Our impression at this time was recurrent cervical carcinoma infiltrating to the bladder or primary bladder tumor.

The transurethral biopsy of the bladder was performed with the histological result of massive eosinophilic infiltration of the subepithelial and muscular layers.

The patient was then treated with administration of antibiotics. The symptoms subsided and the follow-up cystoscopy 4 months later showed marked resolution of the lesions and no longer tumorous elevations of the mucosa.

#### COMMENT AND SUMMARY

A review of literature on eosinophilic cystitis, 18 reported case including our two, suggests that this peculiar phenomenon

Table 1

| case                 | age<br>(sex) | allergic<br>history           | peripheral<br>eosinophilia | u.t.i.* | a.b.**      | a.b.+a.h.***<br>+, or steroid | radiation | operation |
|----------------------|--------------|-------------------------------|----------------------------|---------|-------------|-------------------------------|-----------|-----------|
| Palubinskas 1960     | 31<br>(F)    | (+)                           | 36~80%                     | (-)     |             |                               |           |           |
| Brown 1960           | 50<br>(F)    | (+)                           |                            | (+)     | (+)<br>i.e. | (+)                           | (+)       |           |
| Farber et al. 1963   | 3<br>(F)     |                               | 4~24%                      | (+)     | (+)<br>e.   |                               |           |           |
|                      | 13<br>(F)    |                               |                            |         |             |                               |           |           |
| Wenzel et al. 1964   | 6<br>(M)     | (+)                           | 6~13%                      | (+)     | (+)         |                               |           |           |
| Champion et al. 1966 | 2<br>(F)     | (+)<br>ovarian<br>teratoma    | 12~39%                     | (-)     | (+)<br>i.e. | (+)                           |           |           |
|                      | 12<br>(M)    | (-)                           | 11~22%                     | (-)     | (+)<br>e.   |                               |           |           |
| Perlmutter 1968      | 8<br>(M)     | (+)<br>parasitic<br>infection | 37~51%                     | (-)     |             |                               |           |           |
| Goldstein 1971       | 49<br>(F)    | (-)                           | 5%                         | (-)     | (+)<br>e.   |                               |           | (+)       |
|                      | 48<br>(M)    | (-)                           | 12~20%                     | (+)     | (+)<br>i.e. | (+)                           |           |           |
|                      | 53<br>(M)    | (+)<br>Couma-<br>dine         |                            | (-)     | (+)<br>i.e. | (+)                           |           |           |
| Frensilli 1971       | 19<br>(F)    | (+)                           | 12%                        | (-)     | (+)<br>i.e. | (+)                           |           |           |
|                      | 29<br>(F)    | (+)                           | 29%                        | (-)     | (+)<br>i.e. | (+)                           |           |           |
| Marshall et al. 1974 | 40<br>(M)    | (-)                           | 3%                         | (-)     |             |                               |           |           |
|                      | 75<br>(M)    | (-)                           | 2~11%                      |         |             |                               |           |           |
| Rubin et al. 1974    | 60<br>(M)    | (+)                           | 7%                         | (-)     |             |                               |           |           |
| present cases 1974   | 43<br>(F)    | (+)                           | 7%                         | (+)     | (+)<br>i.e. | (+)                           |           | (+)       |
|                      | 59<br>(F)    | (-)                           |                            | (+)     | (+)<br>e.   |                               |           |           |

\*: urinary tract infection, \*\*: antibiotics, \*\*\*: antihistamine.

could be an acute allergic response at the bladder level and severity of clinical symptoms are not related to the degree of peripheral eosinophilia. Various antigens causing this allergic reaction have been speculated such as foods, drugs, foreign tissue protein of ovarian teratoma or parasite. As shown in Table 1, 10 cases out of 18 demonstrated previous allergic history; 6 asthma, 1 ovarian teratoma, 1 parasite, 1 Coumadine and 1 hypersensitivity to sunlight. However no particular antigen causing eosinophilic cystitis has been found so that any antigen might have possibility in pathogenesis of this disease.

As to treatment of 18 cases as shown in Table 1, 5 cases were administered antibiotics only, 7 antibiotics plus antihistamine and/or steroid, one received additional radiation and one proved parasitic infection had partial resection of the involved bladder area resulting no further recurrence.

Analysis of these documented treatments suggests that antibiotic therapy could be useful in cases having no previous allergic history. On the other hand, without antihistamine or steroid administration no successful result could be obtained in cases having allergic history. As long as eosinophilic cystitis is based on an allergic reaction, a conservative therapy should be indicated together with detection and elimination of antigen. In cases of failure in conservative treatments, however, partial resection with or without cystoplastic procedure may be indicated if the lesion is localized.

The authors presented 2 cases of eosino-

philic cystitis. One case was successfully treated with antibiotics only. Another case was treated by cystoplastic surgery with resection of the involved bladder segment after failure in conservative therapy. The previously documented cases were reviewed and a discussion was made with emphasis on etiology and therapy.

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## 和文抄録

## 好 酸 球 性 膀 胱 炎

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好酸球性膀胱炎はまれな疾患であり、1960年に第1例目が報告されているが、欧米の文献では現在まで16例が報告されているにすぎない。その原因にかんし各症例ごとに種々の検索がなされており、現在のところアレルギー説が大勢を占め、膀胱レベルでの急性アレルギー反応と考えられている。しかしながら卵巣奇形腫、寄生虫、薬剤、喘息などがアレルゲンとして考えられているものの、まったくこれらの既往のないものもありいぜんとしてその原因は不明である。

診断にかんしてはほとんどの症例で経尿道的膀胱生検により確定診断がなされており、治療は1例の膀胱部分切除を施行されたものをのぞき、抗生物質、抗ヒスタミン剤、ステロイド剤などを用いた保存的療法が主である。

今回われわれは2例の好酸球性膀胱炎を経験し、1例は保存的に、他の1例は手術的に治療したのでその臨床経過を述べるとともに、おもに好酸球性膀胱炎の治療にかんして文献的考察を加えた。