Eosinophilic cystitis

P C M S Verhagen, P G J Nikkels, T P V M de Jong

Abstract
We describe four cases of eosinophilic cystitis in whom no specific cause could be found, and review the literature. Complaints at presentation included urgency, frequency, abdominal pain, and haematuria. In three patients the symptoms and ultrasound pictures suggested a bladder tumour. One patient was treated with anticholinergics and corticosteroids without relief of symptoms; a localised eosinophilic tumour was excised in one patient who remained symptom free; and two patients were managed conservatively with spontaneous resolution of bladder pathology and symptoms. One case was identified by random bladder biopsy in 150 consecutive patients with unexplained irritative micturition complaints. Eosinophilic cystitis is rare in children. After biopsy, we consider a wait and see policy justified as symptoms tend to disappear spontaneously. Routine bladder biopsies in children with unexplained bladder symptoms is not justifiable.

Keywords: eosinophilic cystitis; bladder biopsy

Table 1 Literature review

<table>
<thead>
<tr>
<th>First author</th>
<th>Year of publication</th>
<th>Sex</th>
<th>Age (y)</th>
<th>Tumour</th>
<th>Therapy</th>
<th>Time for symptoms to subside (wk)</th>
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<tbody>
<tr>
<td>Farber</td>
<td>63</td>
<td>F</td>
<td>3 +</td>
<td>Staphylococcus</td>
<td>Antibiotics</td>
<td>Exacerbations &gt; 8 months</td>
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<tr>
<td>Wenzel</td>
<td>64</td>
<td>F</td>
<td>6 -</td>
<td>Antibiotics</td>
<td></td>
<td>Uneventful recovery</td>
</tr>
<tr>
<td>Champion</td>
<td>66</td>
<td>M</td>
<td>12 +</td>
<td>Antibiotics</td>
<td></td>
<td>Uneventful recovery</td>
</tr>
<tr>
<td>Permutten</td>
<td>68</td>
<td>M</td>
<td>8 +</td>
<td>Resection</td>
<td></td>
<td>Uneventful recovery</td>
</tr>
<tr>
<td>Kessler</td>
<td>75</td>
<td>M</td>
<td>0* +</td>
<td>Steroids</td>
<td></td>
<td>Uneventful recovery</td>
</tr>
<tr>
<td>Tauscher</td>
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<td>M</td>
<td>3 +</td>
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<td></td>
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<tr>
<td>Aubert</td>
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<td>M</td>
<td>17 -</td>
<td>Imuran</td>
<td></td>
<td>Uneventful recovery</td>
</tr>
<tr>
<td>Snow</td>
<td>84</td>
<td>M</td>
<td>4 +</td>
<td>Steroids</td>
<td></td>
<td>Uneventful recovery</td>
</tr>
<tr>
<td>Suphin</td>
<td>84</td>
<td>M</td>
<td>7 +</td>
<td>None</td>
<td></td>
<td>Uneventful recovery</td>
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<tr>
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<td></td>
<td>Uneventful recovery</td>
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<tr>
<td>Axelrod</td>
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<td>M</td>
<td>7 +</td>
<td>Steroids</td>
<td></td>
<td>Uneventful recovery</td>
</tr>
<tr>
<td>Bauer</td>
<td>91</td>
<td>M</td>
<td>2 +</td>
<td>Antibiotics</td>
<td></td>
<td>Uneventful recovery</td>
</tr>
<tr>
<td>Suika</td>
<td>92</td>
<td>M</td>
<td>14 -</td>
<td>Antibiotics</td>
<td></td>
<td>Granulomatous infiltration lung</td>
</tr>
<tr>
<td>Spark</td>
<td>91</td>
<td>M</td>
<td>3 -</td>
<td>Resection</td>
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<td>Ureteritis; uneventful recovery</td>
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<tr>
<td>Gerharz</td>
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<td>M</td>
<td>11 +</td>
<td>Steroids</td>
<td></td>
<td>Uneventful recovery</td>
</tr>
<tr>
<td>Vetter</td>
<td>95</td>
<td>F</td>
<td>2 +</td>
<td>Resection</td>
<td></td>
<td>Uneventful recovery</td>
</tr>
<tr>
<td>Ladosci</td>
<td>95</td>
<td>M</td>
<td>4 +</td>
<td>Steroids</td>
<td></td>
<td>Uneventful recovery</td>
</tr>
<tr>
<td>Scully</td>
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<td>F</td>
<td>10 +</td>
<td>Steroids</td>
<td></td>
<td>Intermittent symptoms &gt; 1 year</td>
</tr>
<tr>
<td>Netto</td>
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<td>M</td>
<td>11 +</td>
<td>TUR</td>
<td></td>
<td>Uneventful recovery</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F</td>
<td>2 +</td>
<td>Drainage</td>
<td></td>
<td>Uneventful recovery</td>
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*Five days.
TUR, transurethral resection.

The aetiology and treatment of eosinophilic cystitis remain poorly understood in spite of many case reports. Brown is often quoted as the first to publish on eosinophilic cystitis owing to his description of eosinophilic granulomas of the bladder wall.1 In 1949 Kindall and Nickels identified eosinophilic leucocytes in the urine and in the bladder wall of patients with micturition complaints. These patients improved after eliminating suspected food allergens from their diet.2

The pertinent characteristic of the disease is eosinophilic infiltration as observed in bladder wall biopsy specimens. The symptoms often mimic those of urinary tract infection. The bladder lesions seen by ultrasound and cystoscopy may be initially interpreted as malignant.

Several drugs have been reported to induce eosinophilic cystitis in adults: cyclophosphamide,3 coumadine,4 tranilast (an antiallergic drug),5 penicillin, and clometacin.6 Intravesical instillations with mitomycin and thiotapecan cause eosinophilic infiltration of the bladder wall.7 Goble et al found urethral eosinophilic infiltration in response to catheterisation.8 Engler et al reported eosinophilic cystitis at the site of chromic catgut sutures.9

Treatment is empirical.11 It consists of removal of any suspected allergen. Corticosteroids, anticholinergic drugs, and antiallergic drugs have been reported to relieve symptoms. Partial cystectomy has been performed in cases of circumscribed lesions that show no tendency to disappear spontaneously.12 Many reports mention the self limiting course of the disease.13–28 Our search of the literature produced 24 patients under the age of 18 (table 1). Seventeen presented with a tumour in the bladder. The symptoms subsided spontaneously or during corticosteroid therapy in 20, including 15 with a bladder mass.

Our study comprises four children with eosinophilic cystitis. Three were suspected of having bladder tumours. One was identified by our previous policy to perform bladder biopsies in children with severe unexplained micturition complaints. We assessed retrospectively how often eosinophilic cystitis was found in this group of 150 consecutive patients.

Patients and results
One patient (patient A) was identified on routine bladder biopsies in patients with unexplained micturition complaints. No specific pathological diagnosis was established in the 149 other patients biopsied. The symptoms of
Patient A were not remarkably different from the other biopsied patients. Our other three patients (B, C, and D) were referred because of pain and/or haematuria. The clinical suspicion of a bladder tumour leads to the diagnosis.

Patient A, a boy, became continent night and day at 3.5 years of age. At 4 he started wetting day and night, for which he was evaluated elsewhere. Both parents had suffered nocturnal enuresis until the age of 14. At 9 years of age he became dry during the day, taking oxyphenonium bromide 5 mg three times daily and imipramine chloride 25 mg twice daily. Physical examination and laboratory results were normal except for a modest blood eosinophilia (0.5 × 10^9/l). A grade 2 reflux was found at the right hand side on the micturition cystogram. Intravenous urography was normal. He presented to our department at the age of 11 because of persistent nocturnal enuresis and frequency. He was of normal height and weight. Blood pressure was 90/60 mm Hg. White blood cell count (WBC) showed 8.1 × 10^9/l with 1.5 × 10^9 eosinophils/l.

Repetitive urine sediments and cultures were normal. Analysis of stools revealed no cysts or worm eggs. Allergic tests were positive for dust, pet dander, pollen, canary, parrot, and parakeet. Worm eggs. An abdominal ultrasound showed an irregular mass, suspected to be malignant. Cystoscopy showed severe oedema of the bladder wall. Biopsy specimens showed severe infiltration with eosinophilic leucocytes. The tumour was removed by laparotomy and partial cystectomy. The sigmoid colon was adherent to the tumour. Histological analysis showed homogeneous eosinophilic infiltration throughout the swelling. The patient was free of urological symptoms after this procedure and has remained so for 10 years.

Patient B, a 17 year old girl, was referred to our department because of terminal haematuria and pain during micturition. His voiding frequency had increased from four to eight times daily. On physical examination he was of normal height with weight for height according to the 75th centile. His blood pressure was 113/58 mm Hg. Abdominal investigation revealed a slight suprapubic pain. Results of laboratory investigations were as follows: ESR 3 mm/h; haemoglobin 9.2 mmol/l; WBC 9.5 × 10^9/l; eosinophilic leucocytes were within normal range. Urine sediment contained one to five leucocytes per high power field. Urine cultures were repeatedly negative (24 hour urine: volume 2.1 l; Na 77 mmol/l; K 15 mmol/l; urea 67 mmol/l; creatinine 3.2 mmol/l). Amino acid excretion was high for branched amino acids, iminoacids, citrulline, and arginine (Fanconi syndrome). Abdominal ultrasound showed a 45 mm tumour which was continuous with the bladder wall. At cystoscopy, this was seen protruding into the bladder. Biopsy specimens showed severe infiltration with eosinophilic leucocytes. The tumour was removed by laparotomy and partial cystectomy. The sigmoid colon was adherent to the tumour. Histological analysis showed homogeneous eosinophilic infiltration throughout the swelling. The patient was free of urological symptoms after this procedure and has remained so for 10 years.

Patient C, an 11 year old boy, was referred to our department because of terminal haematuria and pain during micturition. His voiding frequency had increased from four to eight times daily. On physical examination he was of normal height with weight for height according to the 75th centile. His blood pressure was 113/58 mm Hg. Abdominal investigation revealed a slight suprapubic pain. Results of laboratory investigations were as follows: ESR 3 mm/h; haemoglobin 9.2 mmol/l; WBC 9.5 × 10^9/l; eosinophilic leucocytes were within normal range. Urine sediment contained one to five leucocytes per high power field. Urine cultures were negative. Stools showed no cysts or worm eggs. An abdominal ultrasound showed normal kidneys. The bladder contained an irregular mass, suspected to be malignant. Cystoscopy showed severe oedema of the bladder neck. Biopsy specimens taken from the oedematous area showed submucosal eosinophilic infiltration. Symptoms resolved spontaneously over several days.

Patient D, an 11 year old girl, was referred because of urgency and haematuria. She was allergic to pollen and used ketotifen, discontinued shortly before referral. Rectal examination revealed a mobile 3 cm diameter pelvic mass. Results of laboratory investigations were as follows: WBC 7.3 × 10^9/l; eosinophilic leucocytes 0.07 × 10^9/l, serum IgE 73 IU/ml (normal). Abdominal ultrasound showed an irregular tumour in the bladder. Transurethral bladder...
biopsy specimens of the tumour showed infiltration of the bladder wall by eosinophils (fig 1). Spontaneous resolution of symptoms occurred over several days. After three months the tumour had disappeared.

Discussion

Eosinophilic cystitis has a variable presentation and outcome. Two of our four patients were known to have allergies, an association also reported in the literature (five of 24 reported paediatric patients had allergies). However, we could not identify a cause of the disease in our patients. Patient D had used ketotifen which could not identify a cause of the disease in our literature (five of 24 reported patients). Patient A is our only patient whose symptoms did not resolve spontaneously, possibly due to limited follow up. In retrospect, it is possible that resolution in patient B might have also been accomplished by more conservative management.

In children with unexplained micturition complaints, eosinophilic cystitis is rarely found. In our patients no other explanation for the micturition complaints was revealed by the bladder biopsies. We conclude that routine bladder biopsy in children with unexplained urgency is not justifiable.

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