Figure 1 Photomicrographs of colonic mucosal biopsy specimens from children with epidermolysis bullosa, showing non-specific inflammatory changes, including eosinophils (A), focal mucosal haemosiderin laden macrophages (Perls stain; B), and prominent subepithelial lamina propria karyorrhectic debris and macrophages (C and D).

suggestive of the diagnosis if confirmed in larger series.

Significant gastrointestinal problems are common in EB, with most studies showing up to 50% or more of the patients being affected.⁵ Constipation is the most common complaint, affecting about one third of patients; this frequent clinical problem is often due to the combination of recurrent anal fissuring together with a low fibre diet and poor fluid intake. Treatment in this group largely centres on polyethylene glycol products, such as low dose Movicol (1–2 sachets a day). Gastro-oesophageal reflux is common in patients with dystrophic EB types and is the second most common gastrointestinal problem, being present in up to a third of all children with EB. Dysphagia, partly due to structuring, leads to great deal of morbidity in these children; recurrent dilatation, usually of the proximal oesophagus, is required, with most such cases of oesophageal strictures treated by balloon dilatation of the oesophagus under general anaesthesia.⁷

Those cases with colonic lamina propria karyorrhectic debris and inflammatory changes in their gastrointestinal biopsy specimens appear to represent a sub-group of children primarily with recessive dystrophic EB. Diarrhoea is the most prominent lower gastrointestinal problem affecting 10% of these children, causing significant morbidity. Following demonstration of histological evidence of the presence of inflammation, as provided in this series, both anti-inflammatory and immunosuppressive therapies, including sulphasalazine and slow weaning courses of prednisolone, have been used with significant subjective clinical improvement in symptoms.

We have reported the gastrointestinal mucosal biopsy findings in patients with EB, and shown that they may exhibit inflammatory

changes, iron-laden macrophages and a florid increase in colonic mucosal lamina propria karyorrhectic debris, predominantly in cases of recessive dystrophic EB. The mechanism underlying these changes remains to be elucidated but we hypothesise that the defective cell adhesion in this condition results in both altered epithelial cell turnover and abnormal mucosal permeability.

N Shah, E Freeman

Department of Paediatric Gastroenterology, Great Ormond Street Hospital, London, UK

A Martinez, J Mellerio

Department of Paediatric Dermatology, Great Ormond Street Hospital, London, UK

V V Smith

Department of Histopathology, Great Ormond Street Hospital, London, UK

K J Lindley

Department of Paediatric Gastroenterology, Great Ormond Street Hospital, London, UK

N J Sebire

Department of Histopathology, Great Ormond Street Hospital, London, UK

Correspondence to: Dr N Shah, Consultant Paediatric Gastroenterologist, Great Ormond Street Hospital, Great Ormond Street, London WC1N 3JH; ShahN@gosh.nhs.uk

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Urinary bladder xanthoma: a report of 2 rare cases highlighted with anti-CD68 antibody

Xanthomata are non-neoplastic, reactive tumour like processes, usually arising in response to lipid profile disturbances. They represent a localised collection of tissue histiocytes containing lipid (foamy macrophages).¹ Xanthomata occur more frequently in the skin, tendons, subcutaneous tissue and gastrointestinal tract, but, unlike them, urinary bladder xanthoma (UBX) appears to be a rare condition, with only 12 cases (including our two cases) reported in the Japanese and English literature.^{2–4} It is believed that xanthomata are reactive proliferations of histiocytes secondary to alterations in the lipid serum. Because xanthoma is one of the presentations of hyperlipidaemia, all patients, irrespective of the site, should be investigated for an underlying lipid disorder.¹ However, only 50% of patients with UBX have hyperlipidaemia. Xanthoma may occur in either primary hyperlipidaemia, or secondary hyperlipidaemia, such as in diabetes mellitus. Occasionally, xanthomata occur in normolipidaemic states. Interestingly, xanthomata can occur as part of many tumour or inflammatory processes, and be related to trauma or surgery, as has been hypothesised for stomach xanthoma.⁵ The latter was probably due to disturbances in lipid metabolism in the mucosa which might explain their development. In contrast, it has been suggested that stromal, histiocytic, endothelial or even epithelial cells may have transformed into xanthoma cells. It is interesting to note that 6 of the 12 cases (50%) were reported in the Japanese literature.

Case reports

Case 1: A 74-year-old woman was referred to the urology department with urinary frequency and incidental finding of microscopic haematuria. There were no other significant lower urinary tract symptoms. Physical examination was unremarkable and vaginal examination showed atrophic vaginitis. Urinary cytology showed no malignant cells and culture failed to grow any organisms. Ultrasound scan of the kidneys was normal. Flexible cystoscopic examination revealed a yellow patch on the dome of the bladder.

Case 2: A 53-year-old man presented with microscopic haematuria. Physical examination was unremarkable with no lymphadenopathy or organomegaly. A transurethral resection of the prostate scan and biopsies were negative

Figure 1 (A) Sections stained with H&E showing urinary bladder xanthoma from patient 1 (note macrophages in the submuco) (original magnification $\times 20$). Note the denuded urothelium. (B) H&E stained sections showing foamy macrophages with abundant vacuolated cytoplasm and dense round nuclei (original magnification $\times 40$).

for malignancy. There were no other significant lower urinary tract symptoms. Urinary cytology showed no malignant cells and culture failed to grow any organisms. Renal ultrasound scan was normal. Flexible cystoscopy examination revealed a brown solitary plaque up to 10 mm in maximum diameter on the dome of the bladder.

Blood counts, lipid profile and other haematological and biochemical investigations for both patients were, otherwise, within limits.

Histological examination of both lesions showed macrophages with abundant vacuolated cytoplasm and dense round nuclei in the lamina propria, focally and in clusters (fig 1). These cells were negative for both periodic acid-Schiff reaction and Alcian blue, but showed strong immunoreactivity with CD68 (KP1) antibody (fig 2). This profile confirmed the diagnosis of UBX; all special stains excluded infections.

Treatment of both cases consisted of local excision. Both cases had two follow-up cystoscopies (at 6 month intervals) which were normal.

Discussion

The differential diagnoses on gross appearance includes malakoplakia, which can only be excluded by histological examination.² The differences between xanthoma and xanthogranulomatous cystitis is that the latter consists of xanthoma cells with multinucleated giant cells and chronic inflammatory cells, while the former comprises neither chronic inflammatory cells nor giant cells.⁶

It can be speculated that the submucosal location in our two cases might explain the presence of gross lesions during the cystoscopy.

From the literature review, including our two cases, it seems that UBX is slightly more common in women than in men. The main clinical symptoms are haematuria, abdominal pain or urinary retention.^{2 5 7 8}

Xanthoma of the urinary bladder has been found as an incidental finding in all the 12 cases (including our two cases) during the course of a procedure or investigations on the lower urinary tract, and the link between the presenting symptoms and the histological findings is "circumstantial".

The coexistence of xanthoma and carcinoma in a bladder diverticulum has been documented,⁴ as has bladder xanthoma developing adjacent to urothelial cell carcinoma.⁹ However, the pathogenesis of peritumoral xanthoma has not yet been established.

Treatment in the presence of symptoms and no other lesion to account for them, may require complete transurethral resection.² On the other hand, because it is unlikely that UBX accounts for the presenting symptoms of haematuria or urinary tract infection, and after checking the lipid profile, long-term follow-up is not mandatory, as UBX has no malignant potential.⁸

In summary, UBX is a distinctive, rare clinical entity that should be considered. CD68 is a helpful marker for identifying macrophage collections and confirming the diagnosis. The addition of our two cases to the literature offers new clinicopathological data, useful for better defining the diagnosis of this rare entity. Furthermore, and to the best of our knowledge, the positivity of xanthoma cells for CD68 is used for the first time as a helpful immunohistochemical marker that may aid the diagnosis.

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W I Al-Daraji

Department of Histopathology, Darent Valley Hospital, Dartford, UK

M Varghese

Department of Histopathology, Sheffield University Teaching Hospitals NHS Foundation Trust, Sheffield, UK

E A Husain

Department of Pathology, Harold Wood Hospital, London, UK

A Abellaoui

Department of Surgery, Darent Valley Hospital, Dartford, UK

V Kumar

Department of Urology, Sheffield University Teaching Hospitals NHS Foundation Trust, Sheffield, UK

Correspondence to: Dr W I Al-Daraji, Histopathology Department, Darent Valley Hospital, Dartford, Kent DA2 8DA, UK; waldaraji@aol.com

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Figure 2 (A) Sections stained with H&E showing urinary bladder xanthoma from patient 2 (note foamy macrophages in the submuco, short black arrows) (original magnification $\times 10$). (B) Immunohistochemical staining macrophages for CD68 (original magnification $\times 63$).