CASE REPORT

Keratinising squamous cell metaplasia: when is it safe to stop looking?

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SUMMARY

Keratinising squamous cell metaplasia (KSCM) is an uncommon diagnosis in the West. Patients typically present with lower urinary tract symptoms: haematuria (visible and non-visible), dysuria, urgency and frequency. Investigation is rigid cystoscopy. Abnormal bladder wall tissue should be resected and biopsies sent for histopathology to confirm KSCM. This is a preneoplastic condition with strong associations with squamous cell carcinoma. Due to a significant lag time, annual cystoscopy with multiple biopsies is recommended.

BACKGROUND

Keratinising squamous cell metaplasia (KSCM) has been reported in 1:10 000 hospital admissions,¹ though the incidence may be more common.^{1 2} There is limited guidance on follow-up for patients presenting with this condition. We report this case to increase understanding of this diagnosis and to encourage further research into appropriate follow-up.

CASE PRESENTATION

An 83-year-old male patient was referred by his general practitioner (GP) to the urology unit with two episodes of nocturia and one confirmed episode of non-visible haematuria (2+ blood on urine dipstick at GP surgery). He denied dysuria, changes in volume or flow or any incontinence outside of the two episodes of nocturia.

The patient's medical history included a transurethral resection of prostate in 2002 for benign prostatic hypertrophy, an aneurysm repair in 2011, stage 3 chronic kidney disease, hypertension and deafness. He was an ex-smoker, who rarely drank alcohol. Previously, he had been a postman, now retired. There was no family history of note.

INVESTIGATIONS

A urine dipstick in clinic showed 3+ blood but was otherwise unremarkable. An ultrasound of the urinary tract found no abnormalities. A flexible cystoscopy showed large white outgrowths of debris which appeared to float on the right lateral wall of the bladder with associated inflamed mucosa in a clearly demarcated area. A CT intravenous urogram (IVU) showed an irregularity of the bladder wall only and recommended correlation with cystoscopy findings. A rigid cystoscopy found the same large white outgrowths as found with the flexible cystoscopy. It was felt that they were not typical

of transitional cell carcinoma. An urgent transurethral biopsy of bladder tumour was performed and samples sent for histology. Histology confirmed KSCM of the urinary bladder.

DIFFERENTIAL DIAGNOSIS

1. KSCM
2. Non-KSCM
3. Squamous cell carcinoma (SCC)

TREATMENT

The abnormal tissue was resected and biopsies were taken for analysis. No further treatment was indicated. Annual follow-up is advised for KSCM.

OUTCOME AND FOLLOW-UP

The patient was discharged home with annual cystoscopy arranged as follow-up.

DISCUSSION

Squamous cell metaplasia of the bladder comes in two forms, non-keratinising and keratinising. Non-KSCM is a benign squamous metaplasia detected in the trigonum of the female bladder only. It is a natural variant and does not require treatment.³

By contrast, KSCM is an abnormality of the urothelium in which urothelium transforms into squamous cell epithelium beneath a layer of keratin (see figure 1). The affected area has the appearance of pearl-coloured plaques floating above the bladder wall surface. The plaques may be distinctly demarcated or may indistinctly blend with the surrounding tissue. When the plaques are instrumented, the underlying tissue is papillary in appearance and bleeds easily.^{2 4 5} The plaques can be found anywhere in the bladder though the ureteric orifices are usually spared.^{2 4}

The extent of bladder wall affected by KSCM on first detection has been closely linked to prognosis.^{2 3 6} In Khan *et al*, a distinction was drawn between patients who had greater than 50% (group A) involvement of their mucosal surface and those who had less than 50% involvement (group B). In group A, 55% (6/11) developed SCC compared with 12.5% (2/16) of those in group B.²

A review article from the Committee no. 2 at the International Consultation on the Diagnosis of Non-Invasive Urothelial Neoplasms defines KSCM as a preneoplastic condition.⁷ Among the papers reviewed, the likelihood of KSCM progressing to SCC has been reported as

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Figure 1 Keratinised squamous metaplasia of hyperplastic urothelium.

20%–55%.^{1–3 5 6} The lag time for this progression is reported as 4–28 years.^{2 4}

The figure for incidence of SCM is 1:10 000 hospital admissions.¹ This is based on data from one centre and it is posited that this figure is under-representative.^{1 2 4}

The aetiology of KSCM is unclear though the underlying pathology is hypothesised to be inflammatory changes in response to inflammatory stimulus leading to metaplasia and subsequently dysplasia. Stimulus is grouped into two sources: urinary tract infections and urinary tract irritants. Urinary tract infections were reported as causative with *Escherichia coli*, proteus and *Streptococcus faecalis* as the primary pathogens in the West.^{2–6} Elsewhere, schistosomiasis and tuberculosis are the primary pathogens. Urinary tract irritants were also a driver of inflammatory changes including bladder calculi, urinary outflow obstruction, fistula, tumours, bladder extrophy, neurogenic bladder, previous bladder surgery and vitamin A deficiency.^{2–6}

There was a single a case report of three patients in the same family who developed KSCM with no predisposing factors leading the author to suspect a genetic component. However, there is no further supportive data published at present.⁸

In keeping with the inflammatory aetiology, patients present with irritative lower urinary tract symptoms: haematuria, dysuria, urgency, frequency.^{2–4} One literature review reported that 80% of male patients presented with haematuria⁵ and another described a patient who presented after passing white flakes in his urine.²

Treatment is complete conservative resection of the affected mucosa.^{2–6} Khan *et al* recommend cystectomy and ileal conduit diversion if the patient has extensive KSCM (>50% mucosal surface involvement) and a life expectancy of greater than 10 years.² Clouston *et al* state that cystectomy should be considered for such a patient group but stop short of recommending it.⁵ Ahmad *et al* feel there is insufficient evidence to support cystectomy as the treatment of choice,⁴ while cystectomy is not discussed in the recommendations of the other papers reviewed. Özbey *et al* describe one patient whose KSCM progressed to transitional cell carcinoma and who was treated with cystectomy and ileal conduit formation. The patient was alive with no recurrence of disease at 2 years. No further follow-up was reported.⁶

Follow-up is recommended in all patients who present with KSCM. Annual cystoscopy with biopsies is recommended by all authors, with several recommending biopsies even in the absence of macroscopic changes.^{2–4} This is supported by Kahn *et al*'s evidence of a lag time of 4–28 years.² In practice, this requires that follow-up is lifelong. Kahn *et al* also recommend annual upper tract imaging to observe for complications of bladder keratinisation.²

Here, we report a rare diagnosis with significant implications for life expectancy. This diagnosis should be considered in any patients with lower urinary tract symptoms and confirmed with cystoscopy. The literature recommends resection of abnormal urothelium and annual, lifelong follow-up with cystoscopy and biopsies regardless of macroscopic appearance. Annual upper tract imaging can be considered in these patients also.

Learning points

- ▶ Keratinizing squamous cell metaplasia is an uncommon pre-neoplastic condition. The pathophysiology is not understood. More research is needed into understanding the underlying process.
- ▶ Optimal treatment is conservative resection. Though cystectomy should be considered for patients with more than 10 years life expectancy and with greater than 50% mucosal involvement at diagnosis.
- ▶ Given the long-term risk of progression to malignancy follow-up cystoscopy is required annually for life.

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