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COMMISSIONED REVIEW

Signet ring cell carcinoma of the bladder and urachus

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Summary Primary signet ring cell carcinomas (SRCCs) of the bladder and urachus are extremely rare malignancies with only 28 cases of urachal SRCC recorded and bladder SRCC comprising less than 0.1% of bladder malignancies.

These rare cases of urothelial SRCC occur largely in men and the disease characteristically presents in patients in their 40s for urachal SRCC and 60s for bladder SRCC. Despite the rarity of the diagnosis, a knowledge of the natural history and management of urothelial SRCC may be valuable as the illness has a number of important differences from conventional bladder TCC.

The characteristic pathological findings of sub-mucosal infiltration and spread are often reflected in the clinical presentation and progress of the disease. Bladder SRCC is frequently characterised by a late presentation at an advanced stage, with dysuria the most frequent presenting symptom whilst haematuria is relatively rare. Metastatic spread can occur with retroperitoneal disease that can be difficult to visualise on imaging and can lead to ureteric or small bowel obstruction.

As a result of their rarity there is no structured clinical research in urothelial SRCC and the optimal management of early and advanced cases of this rare tumour is unknown. A number of differing chemotherapy regimens have been reported for advanced disease in various case reports and series with variable responses and generally modest benefits.

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Contents

Incidence and demographics

Signet ring cell carcinoma of the bladder, originally described by Otto Saphir working in Chicago in 1955 [1] is a rare histological variant comprising less than 0.1% of the cases of primary bladder cancer [2]. Since the original publication less than 150 further cases have been reported in the literature and accurate information on the natural history and optimal management of this rare condition remains limited.

There is a considerable male predilection for bladder SRCC, with reports indicating that 72—85% of cases occur in men, with the disease most commonly presenting in patients in their 50s and 60s [3—5].

A further rarer variant of SRCC is signet ring cell cancer arising in the urachus which shares many of the characteristics of bladder SRCC, also occurring predominantly in men and sharing a poor prognosis resulting from early metastasis. A recent review published in 2009 indicated that only 25 cases of urachal SRCC have been recorded in the world literature [6]. In this diagnosis the male to female ratio is also high with 85% of cases occurring in men but at an earlier mean age of presentation of 46 [7].

Presentation and diagnosis

Whilst haematuria is the most common presenting symptom for conventional transitional cell carcinoma of the bladder, up to 40% of cases of bladder SRCC do not present with haematuria, with dysuria or distant symptoms being the most common initial features [4,8]. This differing mode of presentation may relate to the pattern of growth of SRCC which characteristically infiltrates the submucosa without projecting into the lumen of the bladder, and it can present with advanced disease or a linitis plastica like picture despite relatively normal cytsoscopy findings [4,9,10].

In addition to the more common presentations of haematuria, dysuria and other urinary symptoms, bladder SRCC can also present with the effects of distant sub-mucosal and retroperitoneal metastatic spread leading to renal failure as a result of ureteric obstruction [8,11,12]. In contrast, in urachal SRCC the most frequent presenting symptom is haematuria reported to occur in over 80% of cases, with a suprapubic mass or mucus in the urine occurring in the other cases [7].

The diagnosis of these rare malignancies is made histologically, where the sub-mucosal infiltration, mucus production and signet ring cells are characteristic as shown in Fig. 1 [13]. The increasing proportion of signet ring cells has been linked to a poorer prognosis [5].

Primary SRCC of the bladder can be difficult to distinguish histologically from metastases from the more frequently occurring signet ring cell tumours of the gastrointestinal tract. Prior to consideration of cystectomy or other major surgery it is conventional to investigate the gastrointestinal tract to rule out the possibility of the bladder lesion being a metastasis from the GI tract. In this situation the

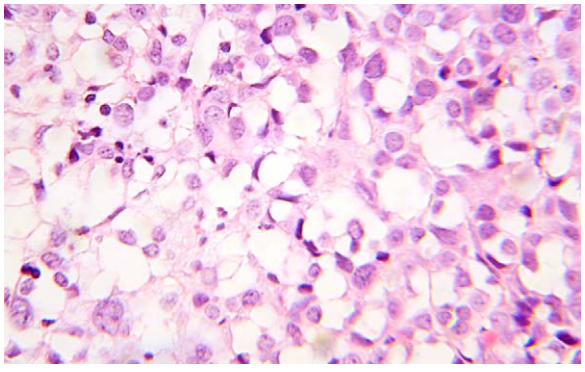

Figure 1 High power image of a signet ring adenocarcinoma of the bladder. A typical signet ring cell is seen in the centre of the image, with a hyperchromatic, compressed nucleus and round pale cytoplasm. The other cells around it are mostly similar tumour cells but not seen so clearly due to the angle of sectioning.