Micropapillary carcinoma: usual carcinoma at an unusual site - a case report

S Haroon*, S Hasan

Abstract
Introduction
Urothelial carcinoma has got a tendency for deviating in morphological differentiation from classic transitional cell carcinoma (TCC). The most common variant is squamous and after that glandular. A bladder carcinoma may contain variable proportions of dissimilar histologic patterns. The clinical outcome of some of the variants of urothelial cancer differs a lot from that of a typical one, and different therapeutic approaches may be mandatory. One of the more aggressive variants includes micropapillary urothelial carcinoma (MPUC), and less than 300 cases have been reported in the literature till now. MPUC has been reported to account for 0.7%–6% of tumours of the bladder. There is male predominance, and the patients’ ages range from the fifth to the ninth decade with a mean age of 66 years. The most common presenting symptom is haematuria. Here we report a case of a 58-year-old male who presented with haematuria, and investigations led to the clinical impression of typical TCC. However, biopsy revealed the tumour composed of micropapillary structures. Radical cystectomy was performed, and the recovered lymph nodes were tumour free. Now chemotherapy is being administered.

Case report
A 58-year-old male presented with gross haematuria for the past 3 weeks, but there was not any painful micturition. He had been hypertensive for the past 4 years, and other than this, there was no comorbidity. He was a non-smoker and denied alcohol or any drug abuse. In past, there was no history of bladder stones and no family history of cancer. He was an engineer by profession. His lab investigations showed decreased haemoglobin with Hb 7.2 mg/dl, normal. Liver Function Tests and ultrasound pelvis revealed a hypoechoiec mass in the urinary bladder (Figure 1).

Genital and prostatic examination did not reveal any abnormality. Preoperative CT scan of the abdomen was normal. The biopsy of the bladder tumour was done, which demonstrated poorly differentiated micropapillary TCC with the tumour focally invading the smooth muscle fragments along with a benign surface epithelium in routine haematoxylin and eosin-stained slides after paraffin embedding and alcohol fixation (Figures 2 and 3).

Overall the dominant pattern consisted of delicate filiform processes or infiltrating groups or balls of neoplastic cells, which are present in the form of micropapillary tight clusters with the absence of central vascular cores. Immunohistochemical studies confirmed the clinical impression of tumour of the bladder origin. When the conventional avidin-biotin immunohistochemical technique of formalin-fixed, paraffin-embedded tissue was used, the tumour cells stained positively and strongly with monoclonal antibodies to both the cytokeratins 7 and 20 (1:100 dilution; Dako Corporation, Carpinteria, CA) and also with high molecular weight (34E12) cytokeratin (HMWK; 1:10) and p53 (Figure 4). Positive and negative controls were run concurrently. The
Case report

The MPUC is comparatively recent and a very rare form of urothelial carcinoma that has been reported in the various sites of urinary tract, that is, urinary bladder, ureter and renal pelvis. Our patient’s histopathological diagnosis was done using International Classification of Disease for Oncology, third edition (ICD-O-3) code 8131 (TCC, micropapillary). This variant of TCC shows a strong tendency to invade lymph nodes and vessels leading to poor outcome. Our patient underwent radical cystectomy soon after the diagnosis of MPUC. The main specimen revealed neoplastic cell invasion, into the outer half (deep) muscularis propria along with single regional lymph node invasion. No metastasis was present. His pathological TNM staging was pT2bN1M0. Then the patient received three cycles of chemotherapy with methotrexate/vinblastine/doxorubicin/cisplatin (MVAC) and with 6 months of follow-up till now, he is alive and doing fine.

The first report of MPUC as a distinctive variety of urothelial carcinoma was first described from the University of Texas MD Anderson Cancer Center in 1994, and it consisted of 18 patients with a mean age of 67 years. Males were predominantly involved with a male-to-female ratio of 5:1. More than one-third of patients died of malignancy, despite its deceptive morphological appearance. Size of tumour and gross features vary widely. There are two morphologic patterns of MPUC, invasive and non-invasive, as described by Amin et al.

On histology, the invasive micropapillary component consists of thin

Figure 1: The ultrasound scan of bladder – the scan showed major tumour bulk in the bladder cavity with invasion of muscle layer.

Figure 2: Microscopic picture of micropapillary urothelial carcinoma – the micropapillary component was arranged in small nests or balls of tightly cohesive tumour cells displaying hyperchromatic nuclei and scanty eosinophilic cytoplasm. Overlying benign urothelium is also present (H&E, ×200).
Second is that psammoma bodies, which are frequently associated with other papillary carcinomas, are evidently absent. Third are the lacunae, which are not lined by endothelial cells, containing small aggregates of tumour cells. Smooth muscle invasion is commonly seen, and with the current radiological equipment, deep invasion of bladder cancers cannot be reliably diagnosed, and so pathological findings play a key role in the staging of these tumours.

The micropapillary component is often found in association with non-invasive papillary or invasive typical TCC; however, the total biopsy material examined did not reveal any of these, in our case. Because MUC1 (Mucin 1) is known to be involved in lumen formation and has an inhibitory effect on cell-to-stroma interaction, it may play an important role in the detachment of cells from the stroma, easing the spread of neoplastic cells. The prototype of micropapillary pattern is and delicate filiform processes or tight groups of tumour cells that are present as small papillary foci within lacunae, which are due to retraction artefacts, simulating vascular invasion. These lacunae are negative for endothelial markers. The tumour cells usually show grade 2–3 nuclei; however, our histological slides reveal only focal grade 3 nuclei with predominance of grade 2 nuclei. Mitotic activity is variable, and we observed up to 8 mitoses per 10 high-power fields. Areas of necrosis are frequently seen that were not present in our case. The invasive micropapillary component showed prominent lymphovascular and perineural invasion. In 1982, Hendrickson et al. first described a micropapillary variant of endometrial adenocarcinoma called uterine papillary serous carcinoma, which comprised approximately 8% of endometrial tumours in several series.

Predominantly, three morphologic features of this variant have been described in literature. First, one is the filiform architecture of the tumour cells present on the surface component and tight aggregates of tumour cells in the invasive foci.
papillary serous carcinoma of the ovary, which is characterised clinically by a tendency of aggressive direct spreading along peritoneal surfaces, making laparotomy essential for adequate staging of the disease. This variant is more aggressive than usual TCC.15,16 There have been reports of upstaging of the tumour after radical cystectomy and hence the need of more aggressive chemotherapeutic options being implied so immediate cystectomy is highly recommended after the diagnosis, as was done in our case.17

As these tumours show frequent lymph node involvement, thus extensive sampling of the pelvis is strongly indicated in these tumours. Also these patients, along with local therapy, should be treated with aggressive definitive therapy because despite their low grade features, these tumours behave in a very aggressive manner10,17.

Conclusion

MPUC is an uncommon and distinct variant of bladder carcinoma, most often presenting with a high grade and stage. It is almost always associated with vascular and detrusor muscle invasion, but deviations do occur; as in our patient, no vascular invasion was seen. It is important to report a micropapillary variant of urothelial carcinoma, because of its aggressive behaviour and need for timely radical treatment.

Consent

Written informed consent was obtained from the patient for publication of this report and accompanying images. A copy of this written consent is available for review by the Editor-in-Chief of this journal.

Abbreviations list

TCC: transitional cell carcinoma.

Acknowledgements

We would like to acknowledge Mr Riaz Sirzameen’s (Senior Administrative assistant) contribution towards drafting the manuscript.

References


Licensee OA Publishing London 2013. Creative Commons Attribution License (CC-BY)