Oncology

Metastatic urothelial carcinoma of the bladder with sarcomatoid differentiation showing large cell neuroendocrine transformation in the liver; an unusual behaviour of a rare disease

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A B S T R A C T

Metastatic urothelial carcinoma of the bladder is generally considered to be an aggressive disease with many recognised variants, however what is unique about our patient is the metastatic transformation from a urothelial primary malignancy with sarcomatoid variation to a neuroendocrine deposit within the liver. From what we have identified, this pattern of pathological transformation has not been reported for a urothelial malignancy in the literature. We present a 64 year old male who we believe is the first reported case of a primary urothelial malignancy presenting de-novo with metastatic liver deposits showing neuro-endocrine transformation.

Introduction

Metastatic urothelial carcinoma of the bladder is generally considered to be an aggressive disease.1 It usually occurs in the context of primary urothelial bladder cancer which has the potential to metastasise to lymph nodes, bones, lung, liver, and peritoneum. Tumours in a more advanced T category and those with atypical histologic features metastasise earlier. Tumours with atypical histologic features also have a higher frequency of peritoneal metastasis. It is recognised that even with contemporary systemic multi-agent chemotherapy regimens, the five year survival of metastatic urothelial carcinoma is approximately 15%.2

Although urothelial carcinoma of the bladder is the most commonly encountered pathologic subtype in regions where Schistosomiasis is not endemic, there are many recognised variants as well as non-urothelial malignancies of the bladder.3 Generally speaking, non-urothelial malignancies of the bladder behave in a more aggressive manner than urothelial malignancies, but their rarity precludes any predictable known patterns of behaviour. If a bladder malignancy presents at a metastatic stage, the management of such disease is primarily palliative. Defined treatment protocols in this cohort of patients are yet to be established but our local protocols for typical treatment for a metastatic non-urothelial bladder cancer follow that of metastatic urothelial bladder cancer.

Urothelial carcinoma with sarcomatoid differentiation is a relatively rare phenomenon with approximately 100 reported cases in the literature.3 It has previously been a controversial pathologic entity with pathologists often having trouble distinguishing primary epithelial histology versus primary sarcomatoid histology.4

Neuro-endocrine transformation of metastatic deposits is an extremely rare phenomenon and not one that has been reported in the literature for urothelial malignancy. It has been reported in the context of primary lung and gastro-intestinal malignancies5 but we believe this is the first reported case of a primary urothelial malignancy presenting de-novo with metastatic liver deposits showing neuro-endocrine differentiation.

Case report

A 64 year old man with a heavy smoking background was referred to our urology clinic with macroscopic haematuria. Initial workup comprised a CT intravenous pyelogram which demonstrated a large filling defect in the right posterolateral wall of the bladder but no upper tract abnormalities (Fig. 1).

The patient proceeded to undergo a cystoscopy where transurethral resection of a large right sided bladder tumour was undertaken. There was also an adjacent satellite tumour on the left lateral wall of the bladder. Ureteric orifices were uninvolved but endoscopically the tumour appeared aggressive with macroscopic evidence of calcified and necrotic areas. Due to several areas of dense calcification, resection was difficult but macroscopically all visibly abnormal areas were resected to completion. Random biopsies of the bladder were not taken as the tumour was obviously muscle invasive bladder cancer and patient was

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not a candidate for partial cystectomy. Post-procedure recovery was uneventful but due to the endoscopic appearance of the lesion he was sent for a staging CT Chest, abdomen and pelvis (CAP) and whole body bone scan.

Upon review in clinic, the histology demonstrated invasive urothelial malignancy with sarcomatoid differentiation including osteoid components. Unfortunately, the staging CT scan showed numerous metastatic deposits in the liver which presented a slightly atypical appearance. There were also isolated bony deposits in the rib cage (Fig. 2).

The patient proceeded to have an image guided biopsy of the liver lesion which demonstrated large cell neuroendocrine malignancy, with an immunohistochemical profile supporting a bladder origin as seen in pathology slides in Fig. 3A–F.

The patient was counselled on the severity of the diagnosis, which was essentially a metastatic variant urothelial carcinoma with neuroendocrine transformation of a liver deposit. His performance status declined rapidly and progressed to WHO Grade 3. He was thus considered unsuitable for palliative chemotherapy. Progression from diagnosis to metastatic spread was rapid and unfortunately the patient died without commencement of systemic therapy, approximately 3 months from the time of the initial CT scan performed to investigate the macroscopic haematuria.

Discussion

Our patient presented with a high grade aggressive bladder tumour that was likely metastatic at presentation. Although metastatic bladder cancer is a known aggressive pathology, what is unique about our patient is the metastatic transformation from a urothelial primary malignancy with sarcomatoid variation to a neuroendocrine deposit within the liver. From what we have identified, this pattern of pathological transformation to neuroendocrine variant has not been reported for a urothelial malignancy. It has been seen in other malignancies, theorised to be a result of acquired mutations to certain chemotherapeutic agents. In our particular case, the patient had not had any exposure to chemotherapy and thus demonstrates a de novo metastatic transformation.

The primary oncological risk factors applicable to our patient are a lifelong smoking history as well as a history of significant peripheral vascular disease. The latter diagnosis has meant the patient had undergone numerous radiologic and angiographic exposures to potentially oncogenic ionising radiation. Beyond these two factors, we do not have any other explanation underpinning this highly aggressive presentation.

Although not applicable in our case, patients who present with variant histology urothelial malignancy with a rapid and unusual pattern of metastatic disease should have consideration for biopsy of the metastatic sites in order to potentially inform further treatment decisions as well to help develop treatment protocols for uncommon urothelial malignancies.

Conclusion

Our patient presented with a rare, rapidly progressive urothelial malignancy, as evidenced by the short time frame between symptoms and death. The case discussion herein demonstrates the utility of accurate histologic diagnosis in metastatic urothelial cancer as well as the importance of counselling patients with highly aggressive lesions.

Consent

Written informed consent was obtained from patient’s next of kin for
publication of this case report and accompanying images.

Financial conflict of interest

None.

Declarations of competing interest

None.

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