Author's response to reviews

Title: Cutaneous metastasis of transitional cell carcinoma of the urinary bladder: 8 years after the primary: a case report

Authors:

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Author's response to reviews: see over
We are appreciative of the reviewers’ comments.

Attached is a revised manuscript with the changes highlighted in yellow.

The manuscript has been revised as per the reviewers’ suggestions:

1. Reviewer Dr Salemis suggested including the laboratory parameters full blood count, biochemical values, urinalysis and tumor markers in the case presentation section. The case report has now been amended to include all of this information on Pages 4 and 5 of the manuscript.
   a. “Laboratory parameters demonstrated a normocytic anaemia with haemoglobin 103g/L (reference range 130-175), stable since at least 2011; and normal platelet and white cell counts. Iron studies were consistent with anaemia of chronic disease with normal ferritin of 78ug/L (reference range, 30-310), reduced iron of 3umol/L (reference range, 11-28) and saturation 6% (reference range 15-50), and transferrin at the lower limit of normal at 2.1g/L (reference range, 2.0-3.6). B12 and folate were normal and thyroid stimulating hormone was reduced at 0.19mU/L (reference range, 0.5-5.5). (No T3 or T4 levels on record). Coagulation profile was normal. Electrolytes were normal however creatinine was elevated at 117umol/L, and estimated glomerular filtration rate was reduced but stable (since at least 2012) at 50mL/min/1.73m2. Liver function tests and adjusted calcium were normal. There was no C-reactive protein, erythrocyte sedimentation rate, prostate specific antigen or other tumour markers on record. Cytology was normal on urinalysis.”

2. The page numbers for references 9 and 16 and the misspelling in the author’s name in reference 15 have been corrected on Pages 10 and 11 (please note that in the revised manuscript these references are now numbered 9, 19, and 18 respectively).

3. Reviewer Dr Swick suggested trying to white balance the immunohistochemical pictures better. I provide a copy of Dr Swick’s article to our pathologist to demonstrate what we would like to achieve. He attempted to do this but unfortunately has been limited in what he could do with the equipment he has. I have attached the revised immunohistochemical pictures (“Figure 3 – revised”)

4. Both reviewers requested additional information regarding histology and staging of the primary tumour. The case report has now been amended to include this information on Page 4 (case presentation) of the manuscript.
   a. “Eight years before this presentation, in 2006, he underwent a cystectomy and ileostomy for high grade transitional cell carcinoma of the bladder. Cystoprostatectomy specimen showed invasive transitional cell carcinoma extending into the inner half of muscularis propria (Stage pT2a) but with a single focus of adventitial intralymphatic tumour, arising in a background of high grade transitional cell carcinoma in-situ mainly involving the left bladder wall. Ureteric and urethral margins were clear and there was no significant prostatic pathology. Histopathology of the resected trigone and lateral bladder wall was graded 2 of 3 in the WHO classification. CT abdomen and pelvis demonstrated no para-aortic or pelvic lymphadenopathy, and no distant metastasis.”
b. As commented by Dr Swick (and now included in the discussion on page 6 of the manuscript, with the addition of 3 new references 11,12 and 13, referenced on Page 10 of the manuscript) “The incidence of metastatic TCC of the bladder is directly related to depth of penetration of the bladder wall, tumour grade and tumour size with depth of tumour penetration being the single most important factor in predicting prognosis in TCC [11,12]. However metastases may be associated with superficially invasive primary disease [13,14].”

Thank you for reviewing our revised manuscript.

With kind regards,

Yours sincerely,

Andrea Lees