Author's response to reviews

Title: A distinctive colour associated with high iodine content in malignant pleural effusion from metastatic papillary thyroid cancer: A case report

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Author's response to reviews: see over
Dearest Editor,

Re: Manuscript ID 1286094938899077 - "A distinctive colour associated with high iodine content in malignant pleural effusion from metastatic papillary thyroid cancer: A case report".

Thank you for your letter of February 27, 2013 and for considering our manuscript for publication in the Journal of Medical Case Reports. Thank you in particular for the constructive comments from the reviewers. We believe that the manuscript is significantly improved with these changes and will be of sufficient standard for publication.

Our specific responses to the reviewers' comments are listed below. Should there be any further queries please do not hesitate to contact the undersigned via email or fax. Thank you once again for the opportunity to resubmit our manuscript.

Yours sincerely

Andrew Rosenstengel MBBS FRACP FCCP
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Response to editorial comments:

Manuscript ID 1286094938899077 - "A distinctive colour associated with high iodine content in malignant pleural effusion from metastatic papillary thyroid cancer: A case report".

We like to thank the reviewers for reviewing our article and for the constructive comments which we have incorporated in the revised paper. We are delighted that both reviewers found our paper ‘very interesting’ and ‘nicely written’.

We believe that the manuscript is significantly improved with these changes and will reach the standard for publication in the Journal of Medical Case Reports.

Reviewer 1:

We thank the reviewer for the helpful comments.

Comment 1 a) A comprehensive table of pleural fluid characteristics from all case reports, including pleural to serum ratios of thyroglobulin levels, would be very useful, and perhaps strengthen the case for its testing as a diagnostic tool.

Response 1a: We agree that collection of such data in the future would be useful. Unfortunately the published data in the literature to date are poorly reported, with too many characteristics missing from the case studies to
generate a useful table. We have added in the reference that the reviewer suggested.

Comment 1 b). the diagnosis of the malignant effusion: ‘was the cytology positive?’

Response 1b: The pleural fluid pH and glucose values were indeed low. Cytological and immunohistological features were reported by our pathologists as being consistent with adenocarcinoma, with positive TTF1 and PAX8 suggesting metastatic thyroid carcinoma. However thyroglobulin staining was negative, making an unequivocal diagnosis difficult. This point has been added to the text.

Comment 2. ‘description of CT finding’

Response 2: The visceral and parietal pleura on CT were thickened, with nodularity and irregularity. The lung was trapped, and this was clearly evident after drainage of the effusion. There were no CT features like those expected in amiodarone lung diseases.

Comment 3. Needing further details on thyroid cancer status: ‘Why panzopanib was started?’ ‘Was mutation testing performed?’

Response 3. Patient has iodine-refractory disease and was given pazopanib on a clinical trial. He had not received chemotherapy previously. Mutation
analysis was not performed. These details have now been incorporated in the text.

Comment 4. ‘surprised that he had avid FDG uptake on PET as lung metastases were often miliary’

Response 4. PET/CT is not routinely used to assess for the presence of metastatic PTC. In this case it had been requested by the treating medical oncologist five years prior to the time of initial pleural intervention. It was not repeated, and the patient was followed biochemically and via CT and CXR. We agree with the reviewer makes a good point about disease perhaps being difficult to define with PET, and we are not advocating it as a screening/diagnostic tool in this setting.

Comment 5. ‘other causes of brown fluid’ should be included

Response 5. We agree with the reviewer that a brownish pigment can be seen in other effusions, for example long standing hemothoraces due to hemoglobin breakdown, anaerobic empyema, and parasitic effusions. The color in isolation is not enough to diagnose the condition described in the case report, however its appearance in the appropriate clinical scenario should inform the clinician to consider metastatic papillary thyroid cancer as a possibility for a malignant effusion. The comment has been addressed in the Discussion section, and a further image of the fluid included pre centrifugation and post centrifugation analysis more clearly demonstrating the distinctive brown pigmentation subsequently shown to be due to a high iodine content.
Comment 6. ‘pleuroscopy revealed trapped lung’… and subsequent malignant fluid management.

Response 6. The visceral and parietal pleura were thickened on pleuroscopy. There was a post procedural CXR, and the lung remained trapped. The patient went on to have an indwelling pleural catheter placed which provided effective drainage and good symptomatic benefit.

Comment 7. ‘pleural fluid iodine…. Intracellular or extracellular’

Response 7. We have confirmed with our biochemistry laboratory that the pleural fluid iodine is extracellular as was the pleural fluid thyroglobulin concentration. This response has been incorporated in the text.

Comment 8. ‘histology slide to show papillary carcinoma’

Response 8. We agree that a slide showing histological/cytological features of metastatic papillary thyroid cancer would be interesting. However such slides are readily available from standard histology texts. In view of the limitation on the length and figure numbers we felt that a histology slide is not of the priority as the other figures used. This is because the main point of the case study is the pigmentation of the fluid and high iodine content aiding
diagnosis of the effusions cause. The proposed image is readily available elsewhere and would not clearly add to the case in its present form.

Reviewer 2:
We thank the reviewer for the comments. We are glad the reviewer found our case report interesting.

Comment 1. ‘regarding the color of the fluid… brownish fluid is common in our clinical practice.’ ‘However considering the clinical scenario the thyroglobulin level and pleural biopsy are diagnostic.’

Response 1. We agree with the reviewer that a brownish pigment can be seen in other effusions. The color in isolation is not enough to diagnose the condition described in the case report, however its appearance in the appropriate clinical scenario should inform the clinician to consider metastatic papillary thyroid cancer as a possibility for a malignant effusion. The comment has been highlighted in the case report discussion.

The above comments and changes have been incorporated in the text as appropriate. Thank you again for reviewing our manuscript.