Author’s response to reviews

Title: Composite hemangioendothelioma of the forehead and right eye: A case report

Authors:

Mohamad Goldust (Mohamadgoldustj@gmail.com)
Ghasem Rahmatpour Rokni (Dr.rokni@yahoo.com)
Fatemeh Montazer (Saa_montazer@yahoo.com)
Mahnaz Sharifian (Drsharif_m@yahoo.com)

Version: 2 Date: 17 Oct 2017

Author’s response to reviews:

Reviewer reports:

Sherina Laskar (Reviewer 1): This is a very interesting case with an unusual presentation as well. A few points were not clear or need revision:

1. The definition of a composite hemangioendothelioma needs to be more clear and not repetitive of the same ideas as has been presented in the first paragraph of the introduction. A CHE is generally regarded as a low grade malignant neoplasm and is a mix of different histological patterns which range from benign to malignant.
   - I have modified the definition of composite hemangioendothelioma in the discussion section

2. Regarding the investigations, why was an MRI followed by CT scan and then ultrasound? Also, it is not clear what is meant by 'superficial vessels were detailed in the radiation therapy'.
   - Since the lesion was progressive and it was not properly diagnosed before histopathology, different radiologic modalities were conducted to diagnose the lesion.
   - 'superficial vessels were detailed in the radiation therapy'.
   - I have removed this section.
3. It has been mentioned that there was no history of the patient having undergone radiotherapy, but later it is said that tissue edema was more pronounced on the radiotherapy site. Please do clarify/rectify.

- Before beginning the surface lesion, there were no history of radiotherapy but after beginning lesion, the patient underwent radiotherapy.

Also, the medications taken by the patient seem to be for associated coronary artery disease; therefore why was the tumor expected to improve with these?

- Exactly not. I have modified this section.

4. 'Cellulite' is probably a typographical error for 'cellulitis'.

- I have corrected the error.

5. It is not clear from the described biopsy findings why a diagnosis of CHE was considered rather than retiform hemangioendothelioma (apart from an infiltrative growth pattern and mitotic figures which are not seen on Fig 2). Papillary intravascular structures are also seen in the latter. IHC cannot differentiate between the two, unless a lymphatic marker, D240/podoplanin is done to rule out presence of lymphatic channels in CHE compared to RHE. The site of lesion is not typical for either.

- Since in our biopsy there were three form of vascular tumors including epithelioid hemangioendothelioma, angiosarcoma and retiform hemangioendothelioma the diagnosis of CHE was made.

6. The patient was recommended to undergo full excision, but only a partial was done, but it is not explained why. It is mentioned that the tutor only regressed partially with post-op thalidomide; no mention of additional treatment or recurrence has been made.

- Since the lesion was too big that a total excision could not be done, so we decided to do partial excision and post-op thalidomide. With this protocol the patient could opened her eyes and the lesion regressed incompletely and no recurrence was observed in following up the patient.
7. Individual histopathology images of the different magnifications could be provided, rather than a collage. The subcutis is not visualised in the low power image and no mention of the respective magnifications is present in Fig 2.

- I have added another figure and modified the legend of figure 2.

Gopikrishnan Anjaneyan (Reviewer 2):

line 63 -may be edited and references added..

According to previous studies, there is an association between the CHE and some tumors (such as vascular tumors) and hemangioma.

- I have modified this section and added reference.

lines 83-89 -kindly rearrange - MRI 'examination' and 'findings' has a 'chief complaint' sentence sandwiched in-between.

A soft tissue with a slightly lobulated surface was observed using magnetic resonance imaging (MRI). The chief complaint of the patient was ....... undergoing radiotherapy or chemotherapy. The result of the brain MRI in May 2015 demonstrated a mucosal thickening in the right maxillary sinus.

- I have rearranged this section

line 115- kindly mention the details of the biopsy taken, type of biopsy, site margins etc.

Five months later, the microscopic examination revealed a malignant vascular neoplasm composed of a…

- I have mentioned these points in the article.

line 123 kindly edit these 2 line and merge if required (eg ...neoplastic tissue...therefore IHC was performed)
The biopsy examination demonstrated a neoplastic tissue composed of a papillary structure and an alveolar pattern. Therefore, the patient was referred to undergo the immunohistochemistry (IHC) test

- I have modified this section.

line 128 change CHT=CHE

Based on the combination of histopathological findings and IHC results, the patient was diagnosed with CHT;

- I have modified this section.

line 147 - may be edited and references added..

So far, about 40 cases with CHE have been reported in previous studies; these were mainly located at the cutaneous level

- I have removed this section

156 line- eye examination..

however, the patient's eye exam was normal.

- I have modified this section

line 170- kindly elaborate

Therefore, the dentition of pure components of CHE is difficult.

- I have removed this section since, the definition of CHE was mentioned in other parts of the article.

line 202 ,212 kindly edit & rearrange

Thalidomide and was first used as an antiemetic, but, sadly, soon linked to phocomelia birth defects.
thalidomide led to reducing in periorbital edema and eliminating the lesion pressure effect the tumor did not regress completely.

- I have modified this section.

line 215 -kindly edit & rearrange

The evidence of the coexistence of variable components of the CHE was suggested in our study, indicating that the CHE has a distinctive morphology and biology.

- I have modified this section

figure 2 histopathology image- the magnification can be mentioned in the collage top corner of each box.

- I have mentioned the magnification.

also please go through the case presentation part and rearrange the events in a continuous flow of events: the past & present history of presentation and investigations done.

- I have modified this section.