Author’s response to reviews

Title: Metachronous extraskeletal (soft tissue) epithelioid osteogenic sarcoma: A rare case report

Authors:
Gireesha Rawal (gireesharawal@yahoo.in)
Charajneet Ahluwalia (charanjeet.ahluwalia@rediffmail.com)
Amit Yadav (——@gmail.com)
Rashmi Arora (——@gmail.com)

Version: 1 Date: 25 Mar 2019

Author’s response to reviews:

Response to reviewers:

Reviewer #1:

1. Do you believe the case report is authentic?

Yes

2. Do you have any ethical concerns? Please consider if local Institutional Review Board approval or ethical approval was obtained (if appropriate) and if the patient (or their parent or guardian in the case of children under 18) gave written, informed consent to publish this case and any accompanying images. A statement to this effect should appear in the manuscript.

Comments:

No ethical concerns. Written informed consent obtained from patient.

3. Does the Introduction explain the relevance of the case to the medical literature?

Yes. Consider elaborating on the diagnosis, prognosis, and treatment of osteosarcoma in the background section. Also it is helpful to quantify incidence and prevalence of osteosarcoma, metachronous osteosarcoma, and extraskeletal sarcoma.
Response:

Incidence of metachronous osteosarcoma is reported as 1-10% of all cases of osteosarcoma. Extraskeletal osteosarcoma accounts for approximately 1% of soft tissue sarcomas and 4% of osteogenic sarcomas. Contrary to conventional osteosarcoma, its extraskeletal counterpart more commonly affects adults (>40 years), with the lower extremity being the most common location. It usually demonstrates a central pattern of ossification which shows contrast enhancement on magnetic resonance imaging and positron emission tomography (PET) avidity. On histology this variant mimics its conventional subtype. Treatment modalities include primary surgery, multi-agent chemotherapy (both neoadjuvant as well as adjuvant), and radiotherapy (palliative as well as adjuvant). Chemotherapy protocols include high-dose methotrexate (HD-MTX), doxorubicin, cisplatin, and ifosfamide. Karyotyping to reveal a possible clonal relationship between these tumors may help in estimating prognosis and guiding therapy intensiveness.

4. Does the article report the following information? Where information is missing, please specify.
   
a. The relevant patient information, including:
      
      - De-identified demographic information (age, gender, ethnicity)
      - Main symptoms of the patient
      - Medical, family and psychosocial history
      - Relevant past interventions and their outcomes

b. The relevant physical examination findings

c. Important dates and times in this case (if appropriate, organized as a timeline via a figure or table); if specific dates could lead to patient identification, consider including time relevant to initial presentation, i.e. initial presentation at T = 0, follow up at T = 1 month.

d. Diagnostic assessments, including:
- Diagnostic methods
- Challenges (e.g., financial, language/cultural)
- Reasoning and prognostic characteristics (e.g., staging), where applicable

e. Types and mechanism of intervention

f. A summary of the clinical course of all follow-up visits

Comments:
a) Include patient demographics, past medical history.
b,c,d,e,f are well covered.
Response: Patient demographics and past medical history have been included.

5. Is the interpretation (discussion and conclusion) well balanced and supported by the case presented?
Comments:
Yes

6. Is the anonymity of the patient protected? Please consider any identifying information in images such as facial features or nametags, whether the patient is named etc. If not, please detail below.
Yes
7. Is the Abstract representative of the case presented?

Comments:

Yes

8. Does the case represent a useful contribution to the medical literature?

Comments:

Metachronous and extraskeletal osteosarcoma are both rare entities, it is interesting to see them both present simultaneously.

9. Additional comments for the author(s)?

- Listing of Amstutz classification of osteogenic sarcoma within the manuscript is unnecessary, unless it has been contributed to or modified by the authors.

Response:

Listing of Amstutz classification has been removed.

- What was the histology of the original osteosarcoma and how does it compare to the recent lesion?

Response:

The histology of the original osteosarcoma was similar to that of the present lesion.

- Further elaborate on the treatment used in the original lesion, if available. Was there a possibility of treatment failure despite negative PET scan?

Response:

For the original lesion, wide local excision was performed followed by chemotherapy (methotrexate, doxorubicin). Despite advanced imaging studies, not all micrometastatic disease foci are able to get detected. (Kayton ML, Huvos AG, Casher J, Abramson SJ, Rosen NS,

Reviewer #2: This manuscript clearly shows a case about metachronous extraskeletal epithelioid osteogenic sarcoma. However, it is best to add what medications the patient is taking for chemotherapy.

Response:

The patient has undergone wide local excision followed by chemotherapy (methotrexate, doxorubicin, cisplatin)

Also, the authors should not use acronyms that where shown at the first time in the text. (PET, CECT, AP, H&E, IHC, CK, EMA, SMA, LCA, CD)

Response:

Full forms have been used at first time use in text.

There are two misspelled words in this manuscript. (i.e. immunohistochemistry, haemorrhage)

Response:

The spellings have been corrected.