Baishideng Publishing Group

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Reviewer#1

Specific comments to authors

The reported case is rare, but interesting. My main concern is about the patient's follow up: we know that at one month her calcium remained normal, however, how frequently she needed (or is expected to need) zoledronic acid? Was the tumor treated?

Reply: Yes. She is planned for carboplatin, paclitaxel, pembrolizumab regimen.

how was it response to therapy?

Reply: We don't know the response to treatment at this point.

Moreover: I couldn't find an evaluation of the calcium excretion (24h urine calcium, urine Ca/Cr ratio, etc): is there any?

Reply: 24 hr urine ca was not done. Ca/ cr ratio- was not performed.

Are there the values for the serum/plasma ionized calcium?

Reply: Ionized calcium- 7.5 mg/dL (4.5- 5.6)

Do you have any magnesium measurement? or phosphate?

Reply: Mg – 1.9 mg/dL (1.8- 2.4). Phos- 2.4 mg/dL (2.5 – 4.9)

Any of these could have "suggested" the diagnosis, given the suppressed PTH?

Reply: With calcitriol elevation- PTH, PTHrP, 25 hydroxy vitD, phosphorus level are expected to be suppressed which is consistent with the findings in our case.

Is there any analytical problem (ie circadian rythm, preanalitic bias, etc) the reader should know about calcitriol measurement?

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Reply: No there was no analytical problem associated with our case.

Why did you choose to treat the patient even if the severe hypercalcemia was asymptomatic (or paucisyntomatic)?

Reply: Paucisymptomatic and rapidly rising calcium level.

1 week prior to presentation corrected calcium level was noted to be 13.3 mg/dL. Decision was made to monitor and repeat labs. 1 week later, corrected calcium was 14.3 mg/dL so was sent to ER for further evaluation. She presented to ER 12 hours later and repeat value showed further worsening to corrected Ca 15 mg/dL.

Totally agree that biphophonates should be a first line therapy of hypercalcemia. I think most authors/readers could agree on this point (ie: Treatment of Hypercalcemia of Malignancy in Adults: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2023;108(3):507) The case by Shah et al (https://doi.org/10.1530/EDM-22-0371) could be included in the introduction. I was wondering if a reduced/altered liver metabolism of calcitriol ore 24,25-vitD could partially explain the degree of hypercalcemia

Reply: Yes that's the possibility but our discussion highlights the mechanism behind hypercalcemia.

Keywords are missing: please add them Units are not SI units, but they are clear enough and should not be changed.

Reply: Keywords have been added.

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Reviewer#2

Specific comments to authors

Why you dont use immunohistochemistry in the study of the liver core biopsy?

Reply: Markers for lungs primary squamous cell ca – p63 +, cytokeratin 5/6 – heterogeneous +,

Thyroid transcription factor -1 negative, CK 7 negative, CDX2 negative, GATA3 negative (typical IH for lung adenocarcinoma)

PDL-1 high expression

In figure we notice in the upper pole of the spleen a well limited lesion with a low density.

Reply: Radiology read: normal spleen parenchyma

Is it related to a metastatc spr Spread? Please detail clearly what you mean by "granulomatous disease"?

Reply: Granulomatous diseases such as sarcoidosis, tuberculosis, fungal granuloma etc.

The title of the 13th bibliography reference must be writed in minuscule letters.

Reply: Edited to match format