Author’s response to reviews

Title: A patient with extensive cerebral calcification due to Pseudohypoparathyroidism: a case report

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Author’s response to reviews:

Dr. Ciaran Martin Fitzpatrick,
Editor,
BMC Endocrine Disorders

Dear Dr Fitzpatrick,

A patient with extensive cerebral calcification due to Pseudohypoparathyroidism: a case report

We have made the changes requested by the reviewers. Our responses to the points raised by the reviewers are below. Please consider publication of this revised version in your journal.

Best wishes,

Suren William De Silva, MBBS; Sawanawadu Dilantha Neomal De Silva, MBBS; Chintaka Eshan De Silva, MBBS, MD, MRCP, FCCP

Editor Comments:

-reformatting of Abstract section - Done
- remove figure in the main ms - Done
- move figure legend after References section - Done
- reformatting of Declarations section - Done
- headings
  - fix number superscripts on title page - Done
- put examination section into a title – We have limited headings to abstract, background, case summary, discussion and conclusion as suggested by reviewer
- legend and refine timeline figure - Done

Reviewer reports:

Bashir Ahmad Laway, D.M. (Reviewer 1): Review of case report

Comments:

1. Limit the headings to abstract, background or introduction, case summary, discussion and conclusion - Done

2. Need not write biochemical values and reference ranges in abstract part and case summary – we have included some reference ranges as requested by reviewer 2.

Kindly tabulate the investigations – done

Mention about assays used for measurement of 25(OH)D and PTH.

3. Arrange keywords alphabetically - done

4. Background: correct grammatical errors in 2nd paragraph - done

5. Case presentation

  • Better to write in a paragraph rather than under headings of history, examination, diagnostic assessment, therapeutic intervention and outcome - done

  • Mention only positive findings on examination - done

  • Flowchart is not informative; just a repetition of case summary – Timeline has been modified
• Needs only brief note about treatment and follow up; no need for detailed description – We have given details requested by reviewer 2.

• Write only relevant investigations - done

• Tabulate the investigations as much as possible along with change in biochemical investigations with treatment - done

• Avoid discussing differential diagnosis in case presentation part – differential diagnosis moved to discussion.

6. Discussion:

• Discuss differential diagnosis here - done

• 2nd paragraph adds little to discussion - removed

• Do not repeat treatment and follow up in discussion part - removed

• PPHP presenting so late (59 years) in life for the first time – needs reference and description in discussion part – reference given in 1st paragraph of discussion

• Why the patient presented with acute symptoms?? What’s the triggering factor?? – We couldn’t find a triggering factor for hypercalcaemia. However there are case reports of PHP presenting in late adult life which we have mentioned in paragraph 1 of discussion.

• Hypomagnesemia induced PTH resistance is a definite possibility in this case. How was it ruled out?? If this possibility cannot be excluded, then patient needs genetic analysis for making the diagnosis of PHP – this has been explained in discussion 1st paragraph

• What about other hormonal axes that functions through GSα receptors like thyroid hormones. Were those axes checked?? – Yes. TSH was normal which is compatible with a diagnosis of PHP Ib. this is mentioned in last paragraph of discussion.

7. Conclusion:

• Kindly discuss regarding why this case is reportable. What’s unique in this case?? – Conclusion has been modified.

8. References are too old. Kindly quote recent references as much as possible – references have been edited.

Gemma Marcucci (Reviewer 2): PHP is a rare disease, and it is important to describe as many clinical cases as possible. The clinical case described here is interesting, but some aspects need to be improved.
Revisions

- I suggest that a native english speaker reviews carefully the text.

Abstract:

- "His muscle power was grade four in all limbs": Which scale do you refer to? – MRC grades
- "elevated phosphate level of 9.5 mg/dl": to add normal range - done
- "His 25 hydroxyvitamin D levels were only marginally low at 22.1 μg": is the unit of measurement correct? - corrected

- The conclusions of the abstract are generic and not very original – conclusions modified

Background and differential diagnosis:


- Examination: "Muscle tone was slightly high in all the limbs.": did you use a specific scale of assessment? – no specific scale was used for muscle tone

Diagnostic assessment:

"an elevated phosphate level of 9.5 mg/dl(Normal 2.7-4.5 mg/dl) were noted": to add "serum phosphate level". - done

- "hypomagnesaemia": was urinary 24h excretion rates of magnesium evaluated? - No

- I think that biochemical exams should be inserted in a table, and in the text there should be the description. - Done

- was MOC DEXA performed? - No

- an evaluation by a neurologist specialist was made? – Yes. This has been mentioned in paragraph on management

Figure 1 and 2: to insert "arrows" – Timeline has been edited
Therapeutic interventions:
- Doses and duration of calcium and magnesium supplementation should be added - done
- "Serum ionized calcium levels gradually improved from 0.5 to 0.93 mmol/l. Inorganic phosphate levels reduced from 9.5 mg/dl to 5.3 mg/dl, intact PTH reduced from 76.3 pg/ml to 67.7 pg/ml. Serum magnesium levels improved from 1.4 mg/dl to 1.9 mg/dl. With the resolution of tetany CPK levels reduced from 1294 U/L to 574 U/L.": when did these changes occur? during the follow up, how often were the biochemical examinations monitored? a graphic figure could be done – in one week. We have added it to the text
- "Upon both clinical and biochemical response patient was discharged with calcium, magnesium and 1αcholecalceferol replacements.", which doses? – This has been added

Discussion:
- "Seizures are thought to occur due to hypocalcemia and intracranial calcification that occurs in vascular and perivascular locations5. PTH exerts its action through the PTH2 receptor in the brain and an endogenous brain specific hypothalamic neuropeptide has been identified as its natural ligand. Diminished activation of PTH2 receptor due resistance as seen in PHP is also presumed to result in neuro-psychological abnormalities as manifested as altered behavior in this patient.": It lacks references and a specific recent bibliographic research – this part was omitted as suggested by reviewer 1.
- was there a fragility fractures history? - no
- "Perera et al described……": I suggest to add also a table with the all other cases described in literature.
- "Conclusion" is too synthetic – conclusions have been modified

References:
- they should be expanded. – references have been modified