Reviewer's report

Title: Three cases with unusual presentation of primary hyperparathyroidism and review of the literature

Version: 3
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Reviewer: Søren Daugaard

Reviewer's report:

Major compulsory revisions
None

Minor compulsory revisions
Title: “… and a review of the literature” should be left out. This is not a systematic review of all previously published cases, as one would normally assume when that designation is used.

Abstract: line 23: “…for difficulties in diagnosis” is ungrammatical and can be left out.

Key words: replace “giant cells tumour” with “giant cell lesion”.

Background: The authors should explain the three stages of HPT: increased osteoclastic activity with fibrosis, osteitis fibrosa, and osteitis fibrosa cystic with brown tumors as the final stage. The giant cells are osteclasts, and they have a tendency to cluster in areas of hemorrhage. The clinical and radiological differential diagnoses are different from the histopathological ones, and different in the peripheral skeleton vs. the facial bones – I think that is what the authors wish to say, but the last sentence in the first paragraph is not comprehensible.

Case 1: “Superficial-erosion” and “polynesic” – what does this mean?

Case 3: The incidental finding of a papillary thyroid carcinoma is not a rare event. But the size of the tumour should be stated, together with the presence or absence of any metastases.

Discussion:

1. The incidence of HPT is difficult to establish – it seems to be increasing, but that may be due to more testing due to growing awareness of the disease. There may regional or racial differences, too – the authors should take a look at Yeh MW et al., Incidence and prevalence of primary hyperparathyroidism in a racially mixed population, J Clin Endocrinol Metab 2013; 98(3): 1122-9.

2. The histopathological differential diagnoses are mainly as stated, but there are subtle differences between the entities. GCT usually exhibits larger osteoclasts than the others, and should not (or at least only with great caution) be diagnosed when the lesion is located outside the epiphysis of long bones, if multifocal (as illustrated in case 3), or if found in the facial bones. Giant cell (“reparative”) granuloma is histologically indistinguishable from brown tumour, and this
diagnosis should always accompanied by a reminder to check for HPT. These considerations should be added.

Discretionary revisions


Case 1: The pathological diagnosis was a giant cell lesion – unspecified? Or do the authors mean a giant cell granuloma? (Not all of the laboratory findings appear to be relevant, perhaps they could be left out and the important ones put in table 1).

Case 2: Line 114: “..in other positions” – what does this mean?

Discussion: Line 153: “phenotype” -> syndrome, or variant; it is generally called ‘normocalcemic HPT’. Line 155-160: This is a repetition and can be left out. There are also some repetitions in the next paragraph. Line 169: “head bones” -> facial skeleton. Line 172: don’t the other cases illustrate this, too? Line 175: “tumor” -> neoplasia. Line 176: “neoplasm -> malignancy. Line 185: “challenging” -> variable, “mimics” -> can mimic. Line 193: “uncommon” -> extremely rare.

Conclusion: Line 222: “GCT” -> other tumors, tumor-like lesions and…

Figure legends: Fig. 1: “superficial-erosion” - ? Consider adding a microphoto of one of the lesions.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests: No competing interests.