Can Parathyroid carcinoma or Functional Parathyroid cyst be predicted preoperatively

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Introduction:
Parathyroid carcinoma (PTHCa) is a rare malignant tumour with less than 700 cases reported since 1904. Although it is associated with higher calcium and parathyroid hormone (PTH) levels at presentation and younger age group, it can only be diagnosed on histological basis. Recent studies have shown a logarithmic formula (using Calcium, PTH and age) can predict PTHCa, with a sensitivity and specificity of 100% and 30% respectively. Functional parathyroid cyst (FPC) although biochemical and clinically quite similar to PTHCa, is however even rarer with less than 30 cases described in literature. The authors here present a rare case of FPC where application of similar formula may have helped in identifying PTHCa but was unable to differentiate between FPC and PTHCa.

Case History:
A 43 years old man presented with new onset worsening lethargy, thirst and constipation over last 2 weeks. History was not suggestive of any previous medical problems or exogenous supplements. On examination, a soft mass was palpable in the left anterior triangle of the neck with no other pertinent findings.

Past Medical History:
He had no previous known medical problems but he admitted to having polyuria and polydipsia over the last few months to years but he did not seek any medical advice or investigations for this.

Investigations on Admission:
His initial investigations showed corrected calcium level 4.74mmol/L, PTH 35.2pmol/L, Urea 9.5 mmol/L and Creatinine 206 umol/L. All other investigations were unremarkable.

Treatment:
He was treated with aggressive intravenous hydration and zolendronate which improved his calcium levels to 2.79 mmol/L with normalization of renal function. His neck ultrasound showed 4.2 x 6.7cm cystic parathyroid mass. His probability for PTHCa as calculated via non-invasive formula by Karakas et al (figure 1) was more than 90%. The patient was referred for surgical removal on an urgent basis.

Surgery however confirmed large parathyroid cyst with a translucent collapsed thin-walled cyst 58 x 55 x 5mm with a small amount of firm tissue at one end measuring 30mm in maximum extent. Histology confirmed right parathyroid cyst showing hypercellular parathyroid gland with cystic change, consistent with parathyroid adenoma or hyperplasia on microscopy.

The patient’s calcium normalized after surgery and was reassured of the benign yet rare diagnosis. FPC, which are 10% of all parathyroid cysts, may behave biochemically much like PTHCa and the radiological confirmation of cyst may be the only differentiating feature.

Figure 1: Formula for calculating risk of Parathyroid carcinoma

\[ \ln \left( \frac{1}{1-p} \right) = 2.13 \times \ln \text{PTH} + 10.97 \times \ln \text{Ca} - 0.0511 \times \text{age} - 27.46 \]

Conclusion:
The parathyroid cysts are derived either from embryological remnants of the third or fourth branchial clefts, coalescence of pre-existing microcysts, simple retention of parathyroid secretions, or cystic degeneration in pre-existing adenomas. Haemorrhage in a parathyroid cyst/adenoma has been associated with hypercalcaemic crisis in previous reports and it may have been the likely the cause here as well.

Points for discussion:
The case highlights the importance of identifying PTHCa and FPC as strong clinical similarities exist between parathyroid cyst and parathyroid carcinoma which increase the risk of misdiagnosis. Early detection of PTHCa and differentiating it from FPC and parathyroid adenoma affects the surgical technique, waiting time as well as long-term patient outcome.