

## **A Cocktail of Disorders**

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Disorders of the parathyroid glands, calcium metabolism and bone

A 23 year old Asian lady was first seen in endocrine clinic in February 2006, referred to from her son's genetic clinic where she was noted to have short 4<sup>th</sup> and 5<sup>th</sup> metacarpals in both hands. She was obese, short and seemed to have mild learning difficulties. Past medical history included treated left sided cervical lymph node TB in 2001. Hand and feet X rays confirmed short right 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> metacarpals and short left 4<sup>th</sup> and 5<sup>th</sup> metacarpals as well as short 4<sup>th</sup> left metatarsal. She had a calcium of 2.62 mMol/L and raised PTH of 262 pg/ml (Normal 9-72). Thyroid function, phosphate, magnesium and alkaline phosphatase were all normal.

She had clinical features of pseudo- or pseudopseudo- hypoparathyroidism. However, the markedly raised PTH level with marginally raised calcium instead suggested co-existing vitamin D deficiency with autonomous hyperparathyroidism. Also, GNAS 1 gene mutation was not detected on genetic testing, and FISH analysis for 2q37 deletion was normal. Vitamin D levels confirmed severe Vitamin D deficiency at 2.1 mg/ml (moderate deficiency <20mg/ml; severe deficiency <10mg/ml). Incidentally her son was also diagnosed to have Vitamin D deficiency.

She was treated with a course of intramuscular ergocalciferol. A parathyroid MIBI scan at this time on subtraction imaging suggested a large right parathyroid adenoma originating from the right inferior parathyroid. However, on detailed review of scans this appeared to be due to a large cold nodule of the thyroid in the right lower pole of the thyroid raising the possibility of a false positive parathyroid scan.

On examination, she was indeed noted to have a hard and discrete thyroid nodule and ultrasound scan of the thyroid confirmed a large inhomogeneous mass in the right lobe of the thyroid 3X2.2 cm. Fine needle aspiration did not reveal any definite diagnosis so a neck exploration is planned with a suspicion of thyroid cancer and possible parathyroid adenoma.

Most recent biochemistry on two tablet of Adcal D3 twice a day showed adjusted calcium at 2.87 mMol/L, with PTH at 100 pg/ml and Vitamin D level at 28.1 mg/ml. The dose has been reduced to one tablet of Adcal D3 twice a day.

In summary, this 23 year old Asian lady has a number of coexisting endocrine pathologies, not previously described in any syndrome: severe Vitamin D deficiency, somatic features of pseudo/ pseudohypoparathyroidism not confirmed by gene testing, cold thyroid nodule possibly malignant, and also autonomous hyperparathyroidism which may be tertiary due to longstanding Vitamin D deficiency or parathyroid adenoma (to be ascertained on neck dissection). Her history of treated cervical tuberculosis in neck glands may complicate neck dissection.

This case raises a few interesting learning points.

1. Not all patients have a single unifying diagnosis. Some patients have more than one problem.
2. Vitamin D deficiency is a common and often under-diagnosed problem, especially in the South Asian population. This may co-exist with autonomous hyperparathyroidism.
3. 99m Tc-MIBI scan is highly sensitive in detecting parathyroid adenomas but with the possibility of false positives in the presence of thyroid adenomas and carcinomas, an examination of the thyroid is important before requesting the scan, and results should be interpreted with caution.

4. The absence of a gene mutation associated with a disorder does not necessarily exclude a genetic disorder.