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Four cases of hyperparathyroidism-jaw tumor syndrome in young patients with primary hyperparathyroidism in Russia

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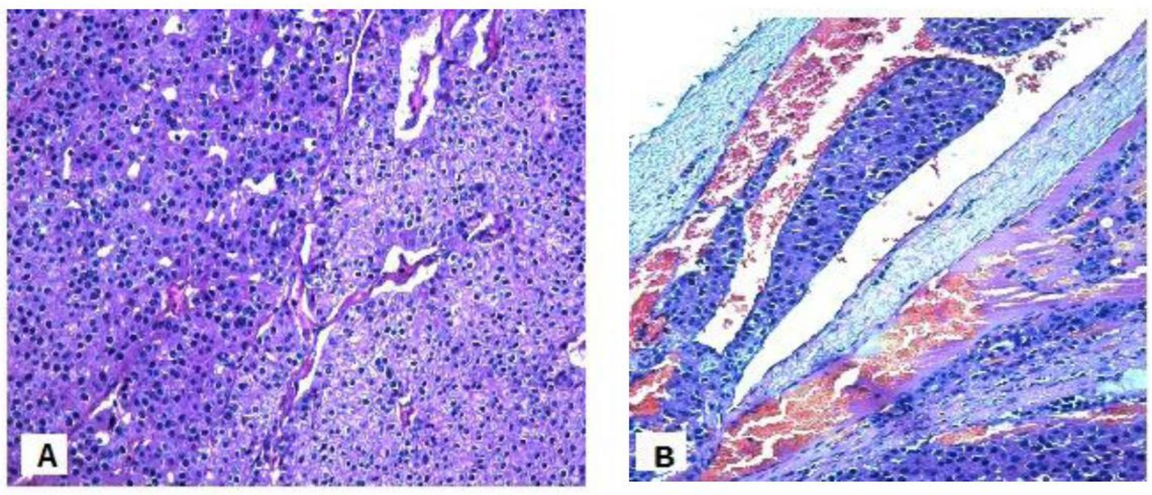
- **Introduction:** Hyperparathyroidism-jaw tumor (HPT-JT) syndrome is a rare autosomal-dominant disorder caused by mutations in *CDC73* tumor suppressor gene. To date about 80 mutations in *CDC73* have been described. Four patients among a cohort of young patients (<40 y.o.) with primary hyperparathyroidism (PHPT) underwent next-generation sequencing (NGS) (**Ion Torrent™ PGM™**, Thermo Fisher Scientific–Life Technologies, USA) using a custom-designed Ion AmpliSeq™ gene panel.

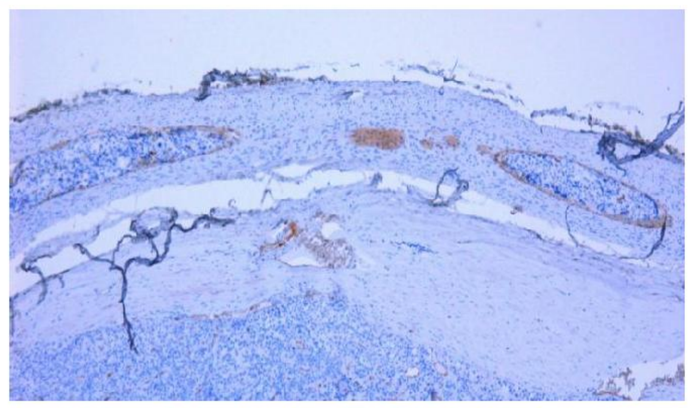
- **Case 1.** A female with PHPT manifestation at age 20, osteitis fibrosa cystica (OFC), kidney microlithiasis, serum Ca 4.09 mmol/l (2.15-2.55), parathyroid hormone (PTH) 2440 pg/ml (15-65) due to parathyroid carcinoma, and endometrial polyp at diagnosis. At age 26 her PHPT recurred as lung metastases of parathyroid carcinoma, requiring surgical intervention. NGS revealed a novel nonsense mutation in exon 3 p.R91X.

- **Case 2.** A female with PHPT manifestation at age 24, severe OFC, kidney microlithiasis, serum Ca 3.36 mmol/l, Ca^{2+} 1.56 mmol/l (1.03-1.29), PTH 558.8 pg/ml due to parathyroid carcinoma. A patient had positive family history, with polycystic kidney disease in her mother. NGS revealed a nonsense mutation in exon 6 p.Q166X.



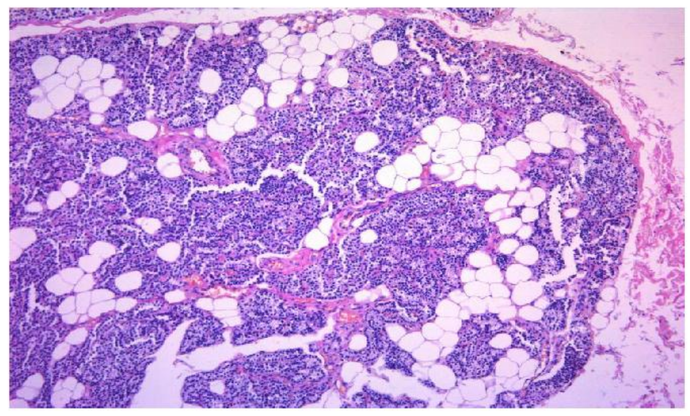
A – two types of chief cells, H&Ex200;
B – Vascular invasion, H&Ex400

- **Case 3.** A male with PHPT manifestation at age 22, severe OFC, serum Ca 3.9 mmol/l, Ca^{2+} 1.84 mmol/l, PTH 1441 pg/ml due to parathyroid carcinoma. NGS revealed a novel nonsense mutation in exon 7 p.R229X.



Vascular invasion, anti-CD31 antibodyx50

- **Case 4.** A female with mild PHPT manifestation at age 30, serum Ca 2.94 mmol/l, Ca^{2+} 1.24 mmol/l, PTH 125.1 pg/ml due to single parathyroid hyperplasia. NGS revealed a novel missense mutation in exon 8 p.R263C.



Parathyroid hyperplasia, H&Ex100

Conclusion: We describe four cases of HPT-JT syndrome in young patients with PHPT in Russia. 3 of 4 mutations are described for the first time. Occurrence of nonsense *CDC73* mutations in patients with parathyroid carcinoma and a missense mutation in a patient with parathyroid hyperplasia may reflect various degrees of parafibromin dysfunction.

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