Hyperparathyroidism-Jaw Tumor Syndrome (HPT-JT) is a rare autosomal dominant disorder characterized by primary hyperparathyroidism (PHPT), ossifying fibromas of the mandible or maxilla, kidney lesions and uterine tumors. This is caused by a heterozygous germline pathogenic mutation in CDC73. To our knowledge, this is the first reported case of an ovarian granulosa cell tumor (GCT) associated with HPT-JT.

A 31 year old woman with persistent abdominal pain was found to have a heterogenous 3cm right (R) ovarian cyst on pelvic ultrasound and MRI. A laparoscopic R ovarian cystectomy was performed which revealed an adult GCT. She was referred to gynecology oncology. Surgical staging with possible bilateral salpingo-oophorectomy was planned. She was also referred to endocrinology for low bone density although values were within the expected range for age.

Her history was significant for PHPT at age 23 with calcium (Ca) 10.8 mg/dL (8.6-10.2 mg/dL), ionized Ca 1.48 mmol/L (1.18-1.33 mmol/L), PTH 107 pg/mL (15-72 pg/mL), and 24 hour (24h) urinary Ca 275 mg (100-321 mg/24h). She underwent 1-gland parathyroidectomy. Of note, her mother also had PHPT with 1-gland removal as well as history of renal cysts. Her brother and 2 maternal aunts have reportedly normal Ca levels.

There was no history of fractures. Her examination was normal. Ca, creatinine, phosphorus, PTH, 25-OH vitamin D, and 24h urinary Ca were also normal. Due to personal and familial history of PHPT, she underwent germline gene sequencing and deletion/duplication analysis of genes associated with PHPT including CASR, CDC73, CDKN1B, MEN1 and RET. Result showed a CDC73 gene pathogenic mutation (c.687_688dupAG) which creates a premature translational stop signal causing loss-of-function. Due to the history of GCT, 52 other tumor predisposition genes, including STK11, were analyzed which did not show pathogenic mutations.

She underwent a R salpingo-oophorectomy with fertility sparing staging surgery. No residual disease was noted on final pathology (Stage IC). The uterus and left ovary were preserved.

CDC73 is a tumor suppressor gene that encodes the protein parafibromin. HPT-JT is a CDC73-related disorder associated with PHPT (~15% malignant), benign fibro-osseous jaw tumors, benign or malignant renal tumors and cysts, and benign or malignant uterine tumors. We found no reports of ovarian tumors with HPT-JT. However, there is a report of bilateral ovarian GCT in a patient with MEN-1.

GCTs are rare, accounting for less than 5% of all ovarian tumors. They usually occur in a younger age group who present with nonspecific symptoms such as abdominal pain or distention. Genetic syndromes associated with GCT include Peutz Jeghers (STK11) and Ollier Disease/Maffucci syndrome (IDH1 or IDH2).

In summary, we reported a patient with CDC73 mutation causing PHPT who also has a rare adult GCT. We believe that ovarian GCT may be another tumor associated with HPT-JT.