Multiple endocrine neoplasia type 1 (MEN1) is an autosomal dominant condition characterized by varying combinations of endocrine tumors and commonly accompanying hyperplasia within the parathyroid gland, anterior pituitary and gastrointestinal tract (1-4). Heterozygous occurring cases (7). Until now over 1000 germline mutations and 200 somatic, have been identified in patients with MEN1 (7). Here we describe novel pathogenic mutations p.V220E and split-site c.30G>T in two separate families presenting MEN1 manifestation.

**RESULTS**

**Family 1**
A 45 - year - old male patient suffered from pancreatic neuroendocrine tumor, parathyroid adenoma, diabetes mellitus type 2, hypertension, anemia, chronic kidney disease, hepatic hemangioma, hysterectomy and oophorectomy. Genetic testing of the patient, revealed heterozygous substitution c.30G>T (p.Leu=), which may predispose to MEN1. Her 48 - year old daughter also suffered of PHPT. Parathyroidectomy had been performed in 2009. During hospitalization 9 mm tumor of the segmental bronchus was detected at computed tomography. According to clinical findings, the diagnosis of MEN1 was highly suspected. Genetic testing of the patient revealed a missense mutation p.V220E (c.659T>A, g.3394T>A) in exon 3 of MEN1 gene.

**Family 2**
A 68-year old woman had been diagnosed with primary hyperparathyroidism in 2011. The proband had also history of depression, anxiety disorders, anal fissure, cortical and subcortical atrophy, right breast tumor (2001), Hashimoto’s thyroiditis, nodular goiter, diabetes mellitus type 2, hypertension, anemia, chronic kidney disease, hepatic hemangioma.

In both families, novel pathogenic mutations were identified. Mutations and locations were searched in the literature and genomic databases but so far no such abnormalities were reported. Missense mutations represent 20% of MEN1 changes while splice site mutations accounts only for 9%. Others, such as frameshift deletions, insertions and nonsense mutations are more common (7). Studies have shown that in patients with MEN1, nonsense mutations are more common (7). Studies have shown that this gene has been established (9). Patients presenting solid components of MEN1 syndrome should be routinely screened for mutations in a coding sequence of menin gene. There is limited understanding of tumor biology, behavior, and heterogeneous clinical presentation in MEN1. Abundance of genetic alterations in menin as well as lack of mutational hot spots, prompt the usage of wider genetic analysis including MEN1 interacting genes. This work also indicate the necessity of thorough analysis of synonymous alterations as potentially pathogenic splice site mutations that are commonly overlooked.

**CONCLUSIONS**

In both families, novel pathogenic mutations were identified. Mutations and locations were searched in the literature and genomic databases but so far no such abnormalities were reported. Missense mutations represent 20% of MEN1 changes while splice site mutations accounts only for 9%. Others, such as frameshift deletions, insertions and nonsense mutations are more common (7). Studies have shown that this gene has been established (9). Patients presenting solid components of MEN1 syndrome should be routinely screened for mutations in a coding sequence of menin gene. There is limited understanding of tumor biology, behavior, and heterogeneous clinical presentation in MEN1. Abundance of genetic alterations in menin as well as lack of mutational hot spots, prompt the usage of wider genetic analysis including MEN1 interacting genes. This work also indicate the necessity of thorough analysis of synonymous alterations as potentially pathogenic splice site mutations that are commonly overlooked.

**Bibliography:**