



OP-3-4

GENETIC CHARACTERIZATION OF A FAMILIAL PATHOGENIC VARIANT OF MAX GENE ASSOCIATED WITH PHEOCHROMOCYTOMA, PARAGANGLIOMA AND DUODENAL/PANCREATIC NEUROENDOCRINE TUMOURS

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Stefanie Parisien-La Salle,¹ Frédéric Mercier,² Gilles Corbeil,¹ Nadine Dumas,³ Franck Vandenbroucke-Menu,⁴ Hugues Widmer,⁵ Bich Ngoc Nguyen,⁶ Mathieu Latour,⁶ Isabelle Bourdeau^{1,3}

¹Division of Endocrinology, Department of Medicine, Research Center, Centre Hospitalier de l'Université de Montréal (CRCHUM), Montreal, Canada

²Division of Surgical Oncology, Department of Surgery, Centre Hospitalier de l'Université de Montréal (CHUM), Montreal, Canada

³Division of Genetics, Department of Medicine, Research Center, Centre Hospitalier de l'Université de Montréal (CRCHUM), Montreal, Canada

⁴Division of Hepatopancreatobiliary and Liver Transplantation, Department of Surgery, Centre Hospitalier de l'Université de Montréal (CHUM), Montreal, Canada

⁵Division of Urology, Department of Surgery, Centre Hospitalier de l'Université de Montréal (CHUM), Montreal, Canada

⁶Department of Pathology and Cellular Biology, Centre Hospitalier de l'Université de Montréal (CHUM), Montreal, Canada

OBJECTIVES

A 30-year-old male was diagnosed with pheochromocytoma based on hypertension, imaging and biochemistry. He underwent a 14-susceptibility gene panel for PPGLs (Invitae, USA) that revealed a germline pathogenic nonsense heterozygous MYC-associated factor X (MAX) variant (c.223c>t p.arg75*). The patient's father (61 years old) was found to carry the same germline mutation which led to the diagnosis of a functional abdominal paraganglioma and two neuroendocrine tumors (NETs) in his pancreas and his duodenum that were operated on.

Our objective was to determine the causal role of the familial germline MAX pathogenic variant in the development of PPGLs and NETs.

METHODOLOGY

Leucocyte DNA was extracted from blood cells and tumoral DNA was extracted from FFPE tissues. All 5 exons of the MAX gene (nm_002382.4) were studied by Sanger sequencing. The amplicons were directly sequenced using the applied biosystems 3730xl DNA analyzer (McGill University, Genome Quebec, Qc, Canada).

RESULTS

The germline MAX mutation (c.223c>t p.arg75*) was confirmed in both leucocyte DNA and all tumoral DNA (son: PHEO, father: PGL and NETs). The wild-type max allele was lost in the tumoral DNA of the father's PGL. A second somatic pathogenic variant of MAX c.263t>c (p.leu88pro) was identified in the duodenal NET and was predicted to be likely deleterious (CADD score 31).

CONCLUSION

We report the rare association of a familial germline MAX mutation presenting with PPGLs and NETs. A second hit in the MAX gene in the duodenal NET supports the hypothesis that MAX mutations might be associated with multiple endocrine tumors.