SATURDAY, OCTOBER 13 **8:00 AM - 9:00 AM**
Vancouver Convention Centre – West Building
Meeting Room: 301-305

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PLENARY LECTURE

Familial Isolated Pituitary Adenomas

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LEARNING OBJECTIVES

At the end of this session, participants should be able to:

- Recognize this new hereditary disease and make better diagnosis.
- Use appropriate genetic testing in patients with pituitary adenomas

Pituitary adenomas represent about 15% of primary intracranial neoplasms and have a prevalence of 1/1000 inhabitants in cross-sectional case-finding studies in developed countries such as Belgium and the United Kingdom (1,2). Most arise in a sporadic setting with >5% developing as a part of familial syndromes, predominantly MEN1 and as part of familial isolated pituitary adenomas (FIPA), while they also occur in other rarer hereditary conditions like Carney complex and MEN4 (3,4,5). Mutations in MEN1 and PRKAR1A genes are found in the majority of MEN1 and CNC patients respectively (5). About 15-20% of FIPA kindreds have mutations in the AIP gene (6,7). Mutations in the CDKN1B gene, encoding p27Kip1 were identified in MEN4 cases (8).

Familial pituitary tumors may have specific clinical characteristics. In MEN1 and FIPA they are more aggressive and affect patients at younger age, therefore justifying the importance of early recognition. AIP mutation-related pituitary adenomas have a particularly early onset (50% in children/adolescents) and there is a large predominance of somatotropinomas (80%; gigantism is frequent), followed by mixed GH/PRL tumors, prolactinomas and non-secreting tumors. These tumors are usually very large at diagnosis and appear to be more frequently resistant to pharmacological treatment (9).

Based on the now-established clinical characteristics of AIP mutation related pituitary adenoma patients, it is reasonable to assess affected members of FIPA kindreds for AIP mutations. Patients with apparently sporadic aggressive adenomas, diagnosed at age <30 years, is a clinically delimited population that is enriched for AIP mutation positive cases, and in whom unrecognized familial mutation carriers are often noted. However, there is a need for a pragmatic clinical approach to this developing area of research. Such an approach would seek to avoid widespread genetic testing in unselected sporadic pituitary adenoma populations, as the likelihood of identifying AIP mutations is low. The risk of subsequent pituitary tumor development in unaffected AIP mutation carriers remains unclear, so unnecessarily invasive follow-up in the absence of good clinical evidence should be avoided. Regular clinical review and the opportunity for hormonal assessments should be considered and an initial MRI may be discussed with the patient. The optimal interval for follow up hormonal surveillance remains to be determined in longitudinal studies.