Non-functioning pituitary tumours

- mortality, morbidity and tumour progression

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Sahlgrenska Akademin vid Göteborgs Universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Academicum, Medicinaregatan 3, Göteborg, fredagen den 9 maj 2014, kl. 09.00

av:

Daniel S. Olsson

Fakultetsopponent: Professor Philippe Chanson
Assistance Publique-Hôpitaux de Paris
Hôpitaux Universitaires Paris-Sud &
Faculté de Médecine, Université Paris-Sud,
Le Kremlin-Bicêtre, France

This thesis is based on the following studies, referred to in the text by their Roman numerals.

Paper I. **Comparing progression of non-functioning pituitary adenomas in hypopituitarism patients with and without long-term GH replacement therapy.**
Olsson DS, Buchfelder M, Schlaffer S, Bengtsson B-Å, Jakobsson K-E, Johannsson G, Nilsson AG.
European Journal of Endocrinology, 2009 161 (5):663-669.

Paper II. **Tumour recurrence and enlargement in patients with craniopharyngioma with and without GH replacement therapy during more than 10 years of follow-up.**
Olsson DS, Buchfelder M, Wiendieck K, Kremenevskaja N, Bengtsson B-Å, Jakobsson K-E, Jarfelt M, Johannsson G, Nilsson AG.
European Journal of Endocrinology, 2012 166 (6):1061-1068.

Paper III. **Mortality in patients with non-functioning pituitary adenoma - a population-based study.**
Olsson DS, Johannsson G, Bryngelsson I-L, Trimpou P, Nilsson AG, Andersson E.
Manuscript.

Paper IV. **Mortality and morbidity in patients with craniopharyngioma - a population-based study.**
Olsson DS, Andersson E, Bryngelsson I-L, Nilsson AG, Johannsson G.
Manuscript.

UNIVERSITY OF GOTHENBURG

NON-FUNCTIONING PITUITARY TUMOURS
- MORTALITY, MORBIDITY AND TUMOUR PROGRESSION

Daniel S. Olsson

Department of Internal Medicine and Clinical Nutrition
Institute of Medicine at the Sahlgrenska Academy
University of Gothenburg, Sweden

ABSTRACT

Non-functioning pituitary tumours, i.e. non-functioning pituitary adenomas (NFPA) and craniopharyngiomas (CP), are histologically benign brain tumours. They are, however, associated with hypopituitarism, diabetes insipidus and other local symptoms caused by the tumour itself or its treatment. Previous studies have shown an excess mortality in patient populations with hypopituitarism, caused by various aetiologies. The mortality rates and factors predicting the mortality in NFPA and CP patients are largely unknown. Modern replacement therapy for patients with hypopituitarism includes treatment with growth hormone (GH) replacement therapy (GHRT). GH has known mitogenic effects, and is considered to possibly increase the risk of tumour progression in patients with a history of pituitary tumours.

This thesis is based on four studies aimed to investigate whether GHRT influences the risk of tumour progression and to study mortality and morbidity in patients with NFPA or CP.

In two case-control studies the frequency of tumour progression was investigated in patients with NFPA or CP treated with and without GHRT. The 10-year tumour progression free survival rate in NFPA patients with and without GHRT was 74% and 70%, respectively. The corresponding figures for CP patients were 88% and 57%. In a population-based registry-study of 2795 NFPA patients an excess mortality was demonstrated in women and in patients diagnosed at or before 40 years of age. In another population-based registry-study of 307 CP patients, mortality and morbidity were highly increased, especially in patients with a childhood-onset of the disease. The incidences of type 2 diabetes mellitus, cerebral infarction and severe infection were 5-fold elevated compared to the general population.

In conclusion, GHRT does not affect the frequency of tumour progression in patients with NFPA or CP. Furthermore, there is an increased mortality in women and young patients with NFPA and an excess mortality in CP patients, especially in patients with childhood-onset of CP.

Key words: Non-functioning pituitary adenoma, Craniopharyngioma, Mortality, Morbidity, Growth hormone replacement therapy, Residual tumour, Radiation therapy, Tumour progression

ISBN: 978-91-628-8957-9 (Printed edition)
ISBN: 978-91-628-8960-9 (Electronic edition)
E-publication: http://hdl.handle.net/2077/35193