

Incidentally discovered adrenal tumours, adrenal metastases, and pheochromocytomas

Clinical and epidemiological aspects

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien vid Göteborgs Universitet kommer att offentligens försvaras i hörsal Ivan Ivarsson, Medicinaregatan 3, Göteborg, fredagen den 6 maj 2011, kl. 9:00

av

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Leg läkare

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Avhandlingen baseras på följande delarbeten:

- I. Lilian Hammarstedt, Andreas Muth, Bo Wängberg, Lena Björnelid, Helga A. Sigurjónsdóttir, Galina Götherström, Erik Almqvist, Håkan Widell, Sture Carlsson, Stefan Ander & Mikael Hellström: Adrenal lesion frequency: A prospective, cross-sectional CT study in a defined region, including systematic re-evaluation. *Acta Radiologica*, 2010 Dec; 51(10): 1149-56.
- II. Andreas Muth, Lilian Hammarstedt, Mikael Hellström, Helga A. Sigurjónsdóttir, Erik Almqvist & Bo Wängberg: Cohort study with two-year follow-up of incidentally discovered adrenal lesions in an unselected population undergoing radiological examinations. *British Journal of Surgery*, in press.
- III. Andreas Muth, Charles Taft, Lilian Hammarstedt, Lena Björnelid, Mikael Hellström & Bo Wängberg: Patient reported impacts of a conservative management programme for the clinically inapparent adrenal mass. Submitted.
- IV. Andreas Muth, Fredrik Persson, Svante Jansson, Viktor Johanson, Håkan Ahlman & Bo Wängberg: Prognostic factors for survival after surgery for adrenal metastasis. *Eur J Surg Oncol*, 2010 Jul; 36(7): 699-704.
- V. Andreas Muth, Frida Abel, Svante Jansson, Ola Nilsson, Håkan Ahlman & Bo Wängberg: Prevalence of germ-line mutations in patients with pheochromocytoma or abdominal paraganglioma and sporadic presentation: a population-based study in western Sweden. Manuscript.



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Abstract

Incidentally discovered adrenal tumours, adrenal metastases, and pheochromocytomas – Clinical and epidemiological aspects

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With increasing use of high resolution radiological imaging incidentally discovered adrenal tumours (adrenal incidentalomas, AI) have become a common clinical problem. The aim of work-up and follow-up of patients with AI is to detect malignant (primary or metastatic) and/or hormone-producing tumours. The frequency of AI, and the clinical and patient reported outcomes of a two-year follow-up programme for AI was investigated in an unselected population undergoing radiology at all departments of radiology in Western Sweden during 18 months. The results of surgery for adrenal metastasis, and the impact of background variables on survival was analysed in a consecutive series of patients treated at the Sahlgrenska University Hospital (1996-2007). Pheochromocytomas (Pheo) and paragangliomas (PGL) are rare catecholamine-producing tumours originating from the adrenal medulla and sympathetic and parasympathetic ganglia that may be detected as AI. The frequency of germ-line mutations (in the *RET*-, *SDHB*-, *SDHC*-, *SDHD*- and *VHL*-genes) was studied in all living patients with Pheo and abdominal PGL with apparently sporadic presentation registered in the National Cancer Register for Western Sweden 1958-2009.

At focused evaluation of abdominal computed tomography the frequency of AI was 4.5 %. In patients with AI (without extra-adrenal malignancy) 6.6 % were operated on suspicion of malignant or hormone-producing tumours; hormone-producing tumours were verified in 3.1 %. No primary adrenal malignancy was found. All patients with hormone-producing or malignant tumours were identified at first evaluation. Further follow-up had low impact on Health-Related Quality of Life, but did not confer any benefit. Surgery for adrenal metastasis was associated with low perioperative morbidity and mortality. Factors associated with prolonged survival were potentially curative surgery, tumour type, no previous surgery for metastases, and long disease-free interval. It should be considered for all patients with isolated adrenal metastasis, and may be part of the multi-modal treatment in disseminated disease. Germ-line mutations were found in 5.6 % of patients with apparently sporadic Pheo/abdominal PGL, which was fewer than in other published series. All mutations were seen in *SDHB* and *RET*. Notably, no patient with *SDHB*-mutation has evidence of malignant disease after 16-28 years follow-up, even though this genotype has been associated with a high rate of malignancy.

Keywords: Incidental Findings; Adrenal incidentaloma; Adrenal Gland Neoplasms; Adrenalectomy; Follow-Up Studies; Quality of Life; Pheochromocytoma/epidemiology; Pheochromocytoma/genetics; Paraganglioma/epidemiology; Paraganglioma/genetics

