Hereditary Pheochromocytoma

Bertil Hamberger
Professor of Surgery
Karolinska Institutet,
Stockholm, Sweden
Familial paraganglioma-pheochromocytoma

- Multiple endocrine neoplasia type 2 (MEN2, 10q)
- Von Hippel Lindau (3p)
- Neurofibromatosis type 1 (von Recklinghausens disease, 17q)
- Succinate dehydrogenase subunit B and D (SDHB 1p, SDHD 11q)
- Uncommon like Familial pheochromocytoma with unknown genetics, Tuberous sclerosis
Paraganglioma-pheochromocytoma

Always consider the possibility of familial disease. In “sporadic” cases it may be close to 25%.
Multiple Endocrine Neoplasia type 2 (MEN 2)

- Medullary thyroid carcinoma
- Pheochromocytoma, 10-50%
- Hyperparathyroidism (2A) or marfanoid habitus and mucosal neurinoma (2B)
- Mutations in the RET gene on chromosome 10
- Genetic testing mandatory
- Prophylactic thyroidectomy early in childhood
Von Hippel Lindau (VHL)

- Retinal hemangiomatosis
- Cerebellar hemangioblastoma
- Renal cysts or carcinoma
- Pancreatic cysts and tumors
- Pheochromocytoma, 10-20%
- Mutations in tumor suppressor gene on 3p
Neurofibromatosis type 1 (von Recklinghausens disease, NF1)

- Café au lait spots,
- Neurofibromas
- Optic glioma
- Pheochromocytoma, 1%?
- Mutations on tumor suppressor on 17q
Succinate dehydrogenase subunit B and D (SDHB 1p, SDHD 11q)

- Nuclear genes encoding mitochondrial proteins
- Frequently found in familial paraganglioma
- Screening in healthy first degree relatives detect new paraganglioma
Succinate dehydrogenase subunit B and D (SDHB 1p, SDHD 11q)

**SDHB**
- Higher risk for extraadrenal disease
- Higher risk for malignant disease
- Median age for penetrance 47 years

**SDHD**
- More often multiple tumors
- Head and neck paraganglioma
- Median age for penetrance 31 years

European-American Paraganglioma Study group JAMA 292 943-951 2004

International SDH consortium, Benn et al JCEM 91 827-836, 2006
Suggested genetic testing in paraganglioma/pheochromocytoma

- Positive family history or below 30
- Extraadrenal and/or malignant
- Bilateral
- VHL
- RET
- SDHB
- SDHD

Suggested by a workshop at the First International Symposium on Pheochromocytoma NIH October 2005
Surgical options for adrenal disease in hereditary cases

- Usually bilateral adrenal medullary hyperplasia with development of tumors slowly and not symmetrically
- If unilateral tumor only remove one side and continue following patient
- In patients with malignancy or high risk for malignant pheochromocytoma adrenalectomy
- If not consider conservative cortex-sparing operation
Surgical options for adrenal disease in hereditary cases

- If bilateral and low risk for malignancy, conservative treatment with partial resection can be recommended
- This can be done with knife or stapler, open or laparoscopically
- The tumor can recur and may need reoperation

Life long steroid supplementation after total adrenalectomy has a considerable morbidity and some mortality
Conclusions

• A potentially lethal, curable and usually benign adrenal tumor

• More often hereditary than previously thought

• Program for genetic testing advisable

• Preservation of cortical tissue valuable in bilateral disease