Oncogenetic testing for persons with paraganglioma and phaeochromocytoma

Phaeochromocytomas are tumours arising from adrenomedullary chromaffin cells that commonly produce catecholamines.

Paragangliomas are tumours derived from extra-adrenal chromaffin cells of the sympathetic paravertebral ganglia of thorax, abdomen, and pelvis, or from parasympathetic ganglia located along the glossopharyngeal and vagal nerves in the neck and at the base of the skull.

Phaeochromocytomas and paragangliomas can be components of endocrine tumour syndromes (e.g. MEN2, von Hippel-Lindau disease), but they can also occur sporadically, i.e. without syndromic features. Several susceptibility genes have been described, with SDH mutations occurring most frequently.

In 2011, 16 phaeochromocytomas and 9 paragangliomas were registered at the Belgian Cancer Registry (personal communication), with a European Standardized Rate of 0.14 and 0.06 per 100 000 person years, respectively. However, these incidences are probably underestimated because of underregistration.

Clinical Recommendations

- Pre- and post-test genetic counselling should be offered to all patients with phaeochromocytoma / paraganglioma (Strong recommendation)
- In patients with phaeochromocytoma / paraganglioma and syndromic features, targeted genetic testing (e.g. for MEN2 and VHL) should be offered (Strong recommendation)
- All patients with phaeochromocytoma / paraganglioma that lack syndromic features should be offered genetic testing for SDHx genes (SDHD + SDHB + SDHC subtypes), VHL and RET (in this order) (Strong recommendation)
- If tumour tissue is available, SDHB immunohistochemistry testing could be considered as a triage test before proceeding with genetic testing for SDHx genes (Weak recommendation)
- In patients with phaeochromocytoma / paraganglioma and clinical features suggestive of a mutation (i.e. age < 35 years, metastatic disease, recurrent disease, bilateral tumours and/or familial disease), who test negative for SDHx, VHL and RET, further genetic testing may be considered (Weak recommendation)
- Once a germline mutation has been identified in a proband, mutation analysis should be offered to all first-degree relatives irrespective of age (Strong recommendation)

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