SCREENING FOR A 10-GENE PANEL IN A GROUP OF 90 PHAEOCHROMOCYTOMAS

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Background

Several new gene mutations have been reported in recent years to be associated with a risk of familial phaeochromocytomas. However, it remains unclear as to whether there is a genotype-phenotype correlation that could be used in clinical decisions in a similar fashion as is currently done for RET and VHL mutations

Methods

Clinical data of consecutive unselected as operated for phaeochromocytomas (PHAEOs) over a decade in a tertiary referral centre were reviewed. Genetic screening was performed using a 10-gene panel comprising RET, VHL, SDHB, SDHD, SDHA, SDHC, SDHAF2, MAX, TMEM127 (TMEM127 and SDHB if >45 years, NF1 when indicated)

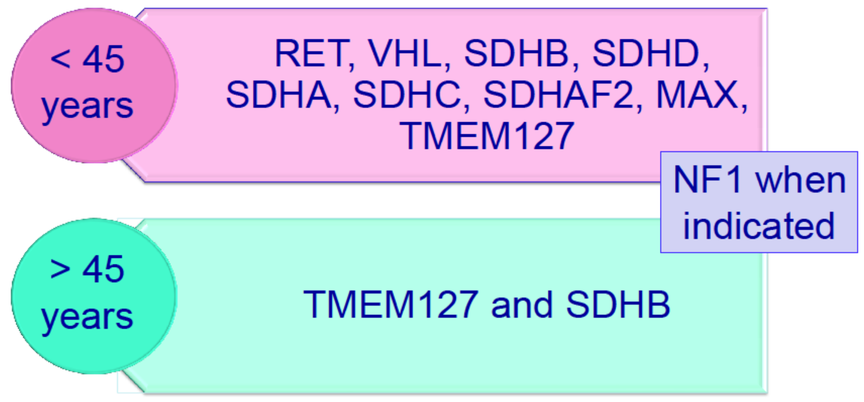

Fig. 1: Genetic screening according to age at presentation

Results

A total of 157 patients (68 males: 43%, 89 females: 57% 6-86 years, median 50.3±17.4 years) underwent laparoscopic (85%), open (10.5%), or laparoscopic converted to open (4.5%) adrenalectomy for unilateral (92%) or bilateral (8%) adrenal phaeochromocytomas: 90 patients underwent genetic screening, in particular 60/90 (67%) patients presented with apparently sporadic tumours and 30/90 (33%) patients had genetic mutations. These were more frequently bilateral (p=0.02). In particular, mutations were seen in 11/90 patients for VHL (12%), 9/90 NF1 (10%), 6/90 RET (7%), 2/90 patients SDHD (2%) and 2 patients MAX (2%). During a median follow-up of 50.4 months (1-240 months), 12 patients (8%) presented with recurrence in the controlateral adrenal (n=8: 5%) or with metastatic disease from malignant phaeochromocytomas (n=11: 7%). Younger patients showed a significant higher percentage of mutations compared to older patients (24/54: 44% vs 6/36: 17%); 20/74 (27%) mutations were identified in patients who presented with unilateral phaeochromocytoma and showed no disease recurrence within 5 years vs 10/16 (62%) in the recurrent-bilateral-metastatic group. 6/7 (86%) patients with bilateral disease had germline mutations (2 VHL, 2 RET, 1 NF1, 1 MAX)

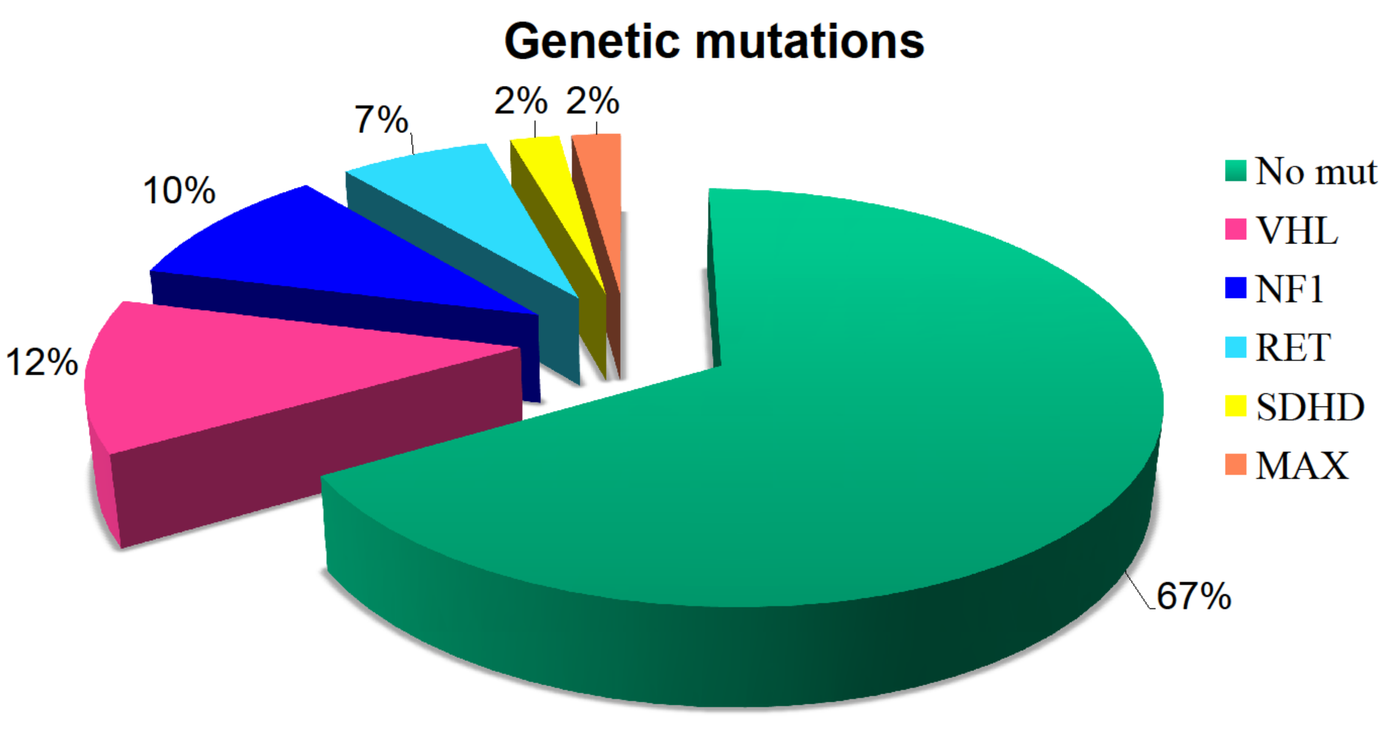

Fig. 2: Distribution of genetic mutations in our population

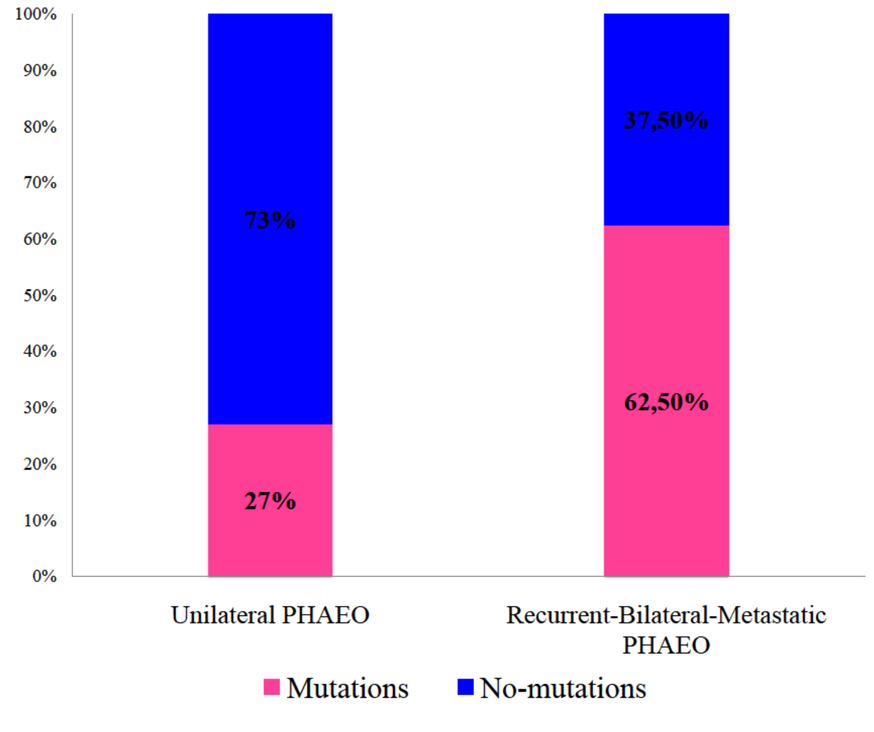

Fig. 3: Distribution of genetic mutations in unilateral vs recurrent-bilateral-metastatic PHAEO

Conclusions

The advent of rapid genetic screening for 10-gene panel makes it feasible to screen large cohorts of patients, and allows for the prediction of bilateral and malignant disease and screening of family members.

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