A rare case of SDHB mutation in a male individual with pituitary adenoma, and paraganglioma/phaeochromocytoma syndrome.

Valentinos Kounnis, Saeed ElMuhtadi, Aparna Pal, Mike Tadman, Bahram Jafar-Mohammadi

The Oxford Center for Diabetes, Endocrinology and Metabolism, University of Oxford, UK

Introduction

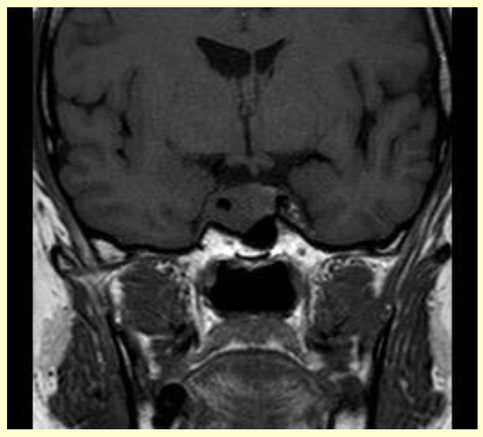
Herein we provide clinical, biochemical, histological and radiological evidence of a rare case of a male patient who was diagnosed with pituitary macroadenoma (prolactinoma), phaeochromocytoma and a lung typical-carcinoid tumour on a background of SDH gene mutation encoding the succinate dehydrogenase enzyme.

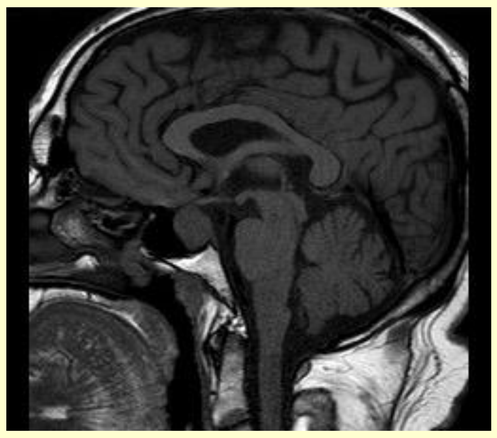
Test	Result	Reference Range
Prolactin	**9723**	**45-375 mU/L**
Testosterone	**7.5**	**8.4-28.7 nmol/L**
LH	**0.5**	**1.5-9.3 IU/L**
FSH	2.0	2.0-20 IU/L
FT4	1.99	0.35-5.5 mU/L
IGF1	14.4	10.5-20 pmol/L
SST	535 -> 766	

Initial Biochemistry

Test	Result	Reference Range
Normetadrenaline	**3.88**	**0 – 3.45 µmol/24h**
Metadrenaline	1.12	**0 – 1.4 µmol/24h**
3-Methoxytyramine	**4.01**	**0 – 2.55 µmol/24h**

Urinary Metanephrines





Initial Imaging

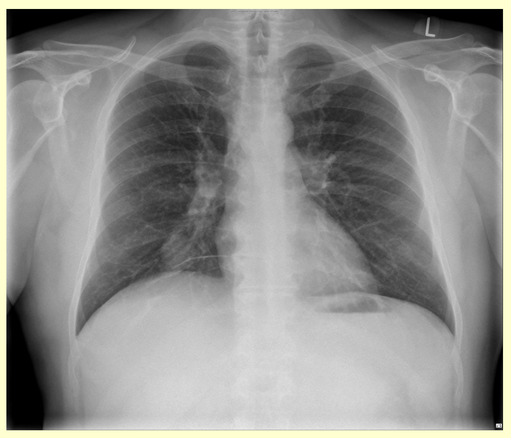
Presentation of Case

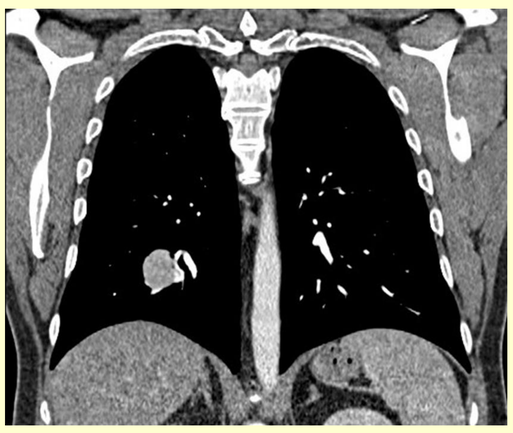
A 42 year old male individual, was initially diagnosed with a pituitary macroadenoma (prolactinoma) after complaining of persisting severe headaches, for which cabergoline treatment had been initiated.

His positive paternal history of phaeochromocytoma, led to further genetic screening which revealed a c.600>A, p.(Trp200*) mutation in the SDHB gene and further biochemical and imaging studies confirmed the presence of a phaeochromocytoma, which was surgically excised.

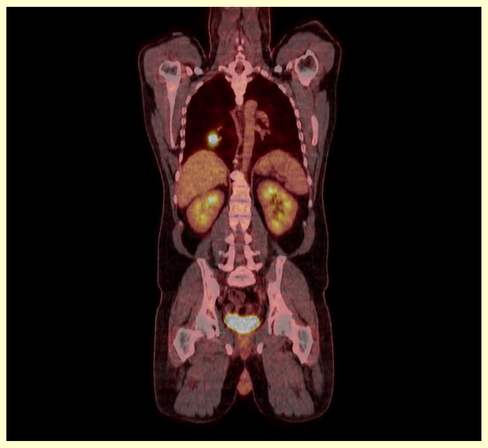
Following a random hospital visit, a plain chest radiograph raised concerns over a right lower lobe mass which ultimately led to advanced imaging studies with CT and PET, confirming the presence of a neoplastic lesion with no evidence of lymphadenopathy of other evidence of metastatic disease.

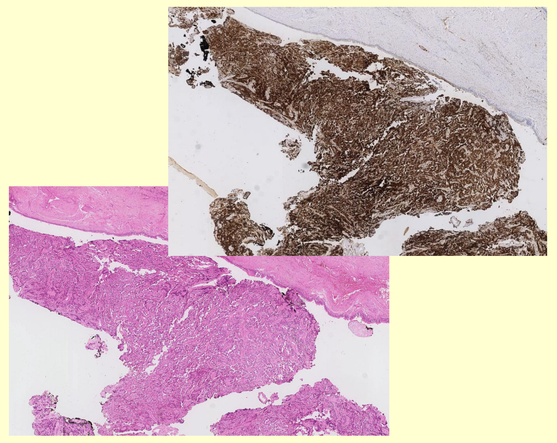
A subsequent lobectomy and Histopathological analysis (positive for chromogranin and synaptophysin) confirmed the diagnosis of a typical carcinoid tumour (stage pT1b N0 Mx).





Two months post initial presentation





PET scan and Histology sample/ +ve for Chromogranin

Discussion

The role of mutations in the genes encoding the succinate dehydrogenase (SDH) subunits, in tumorigenesis has been described previously and especially the predisposition to the development of the hereditary paraganglioma/phaeochromocytoma syndrome (HPGL/PCC).

To our knowledge this may be the first reported case of a lung neuroendocrine tumour, phaeochromocytoma and pituitary macroadenoma on the background of a mutation in the SDHB gene.

References

1. Bardella, C., P.J. Pollard, and I. Tomlinson, SDH mutations in cancer. Biochim Biophys Acta, 2011. 1807(11): p.1432-43.
2. Couldwell, W.T. and L. Cannon-Albright, A heritable predisposition to pituitary tumors. Pituitary, 2010. 13(2): p. 130-7.
3. Efstathiadou, Z.A., et al., Unusual case of Cowden-like syndrome, neck paraganglioma, and pituitary adenoma. Head Neck, 2014. 36(1): p.E12-6.
4. Lefebvre, M. and W.D. Foulkes, Pheochromocytoma and paraganglioma syndromes: genetics and management update. Curr Oncol, 2014. 21(1): p.e8-e17.
5. Zhan, X., X. Wang, and T. Cheng, Human Pituitary Adenoma Proteomics: New Progresses and Perspectives. Front Endocrinol (Lausanne), 2016. 7: p.54.