



VON HIPPEL-LINDAU DISEASE - REPORT OF TWO CASES-

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INTRODUCTION: Von Hippel-Lindau (VHL) disease is a rare **autosomal dominant syndrome** (1/36,000 live births) with highly penetrance that predisposes to the development of **benign and malignant, highly vascularized tumours** in many organs. VHL results from a mutation in the **tumor suppressor VHL gene** on **chromosome 3p25.3**. Mutations in this gene prevent production of the VHL protein or lead to the production of an abnormal version of pVHL which results in the promotion of angiogenesis and uncontrolled cell proliferation (a lack of blocking hypoxia-inducible transcription factor- HIF).

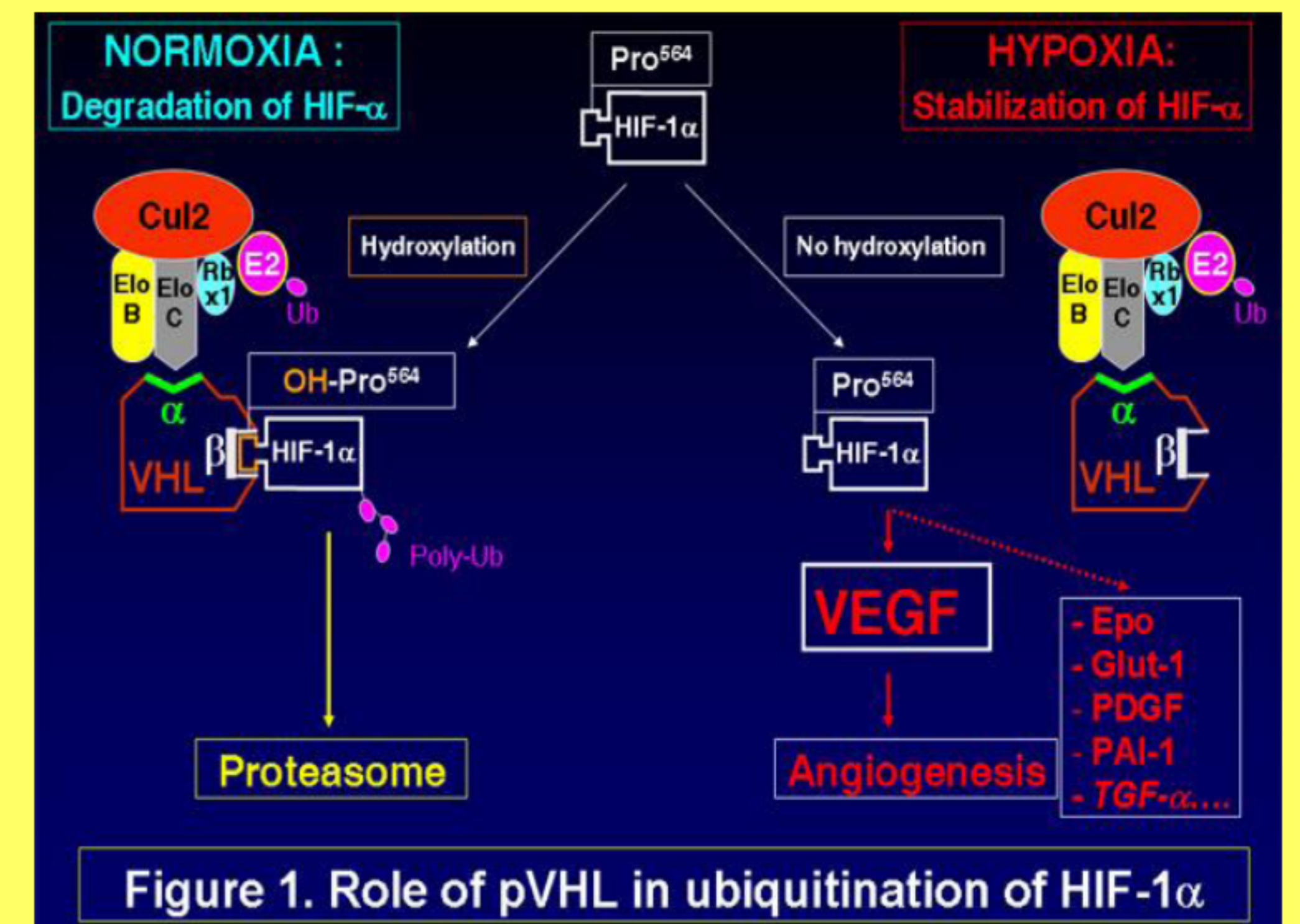


Figure 1. Role of pVHL in ubiquitination of HIF-1α
Ref. Atlas of Genetics and Cytogenetics in Oncology and Haematology 2002; 6(2):106-110.

CASE REPORTS: Two women with VHL, without family history of VHL, were admitted to Department of Endocrinology for checkups. The diagnosis was made based on genetic tests.

Patient A: a 53-year-old woman with **VHL type 2C**, after partial right adrenalectomy in 1976 and total left adrenalectomy in 1979 due to **bilateral pheochromocytoma**. At present, she has no hypertension and typical symptoms of adrenal insufficiency. Hormonal tests revealed normal concentrations of serum cortisol and 24-h urinary cortisol in the presence of elevated serum ACTH that may indicate low adrenal reserve. The administration of hydrocortisone (10-20mg/day) was recommended, in case of stress. The levels of serum chromogranin-A, dopamine and noradrenaline as well as 24-h urinary methoxycatecholamines were in normal range. All body scintigraphy and abdomen CT scan did not show pheochromocytoma recurrence.

Fig 1. Patient A- abdominal CT scan

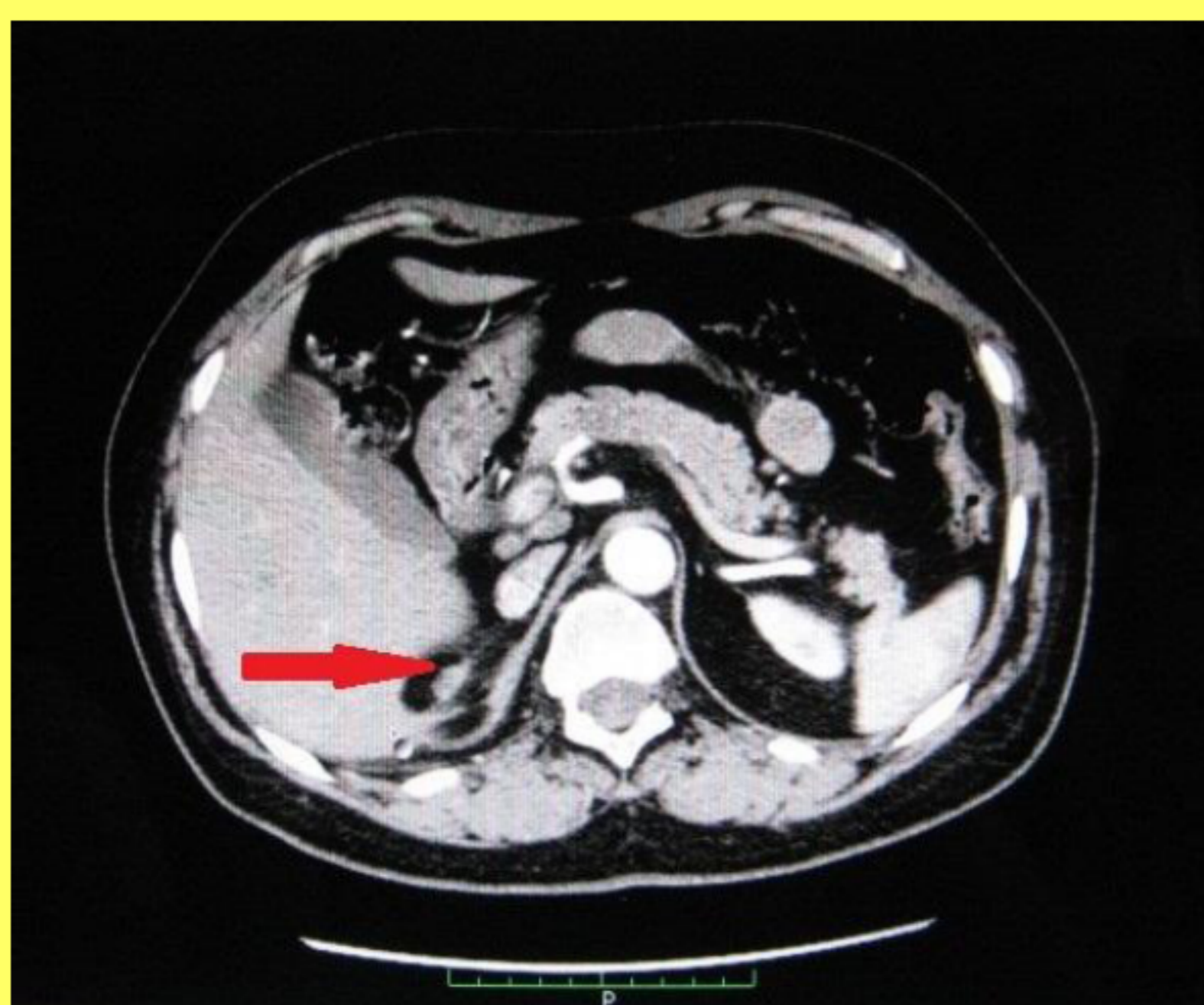


Fig. 2. Patient B- somatostatin-receptor scintigraphy

Patient B: a 44-year-old woman, with **right retina haemangioblastoma** leading to blindness, after resection of **cerebellum haemangioblastoma** (with right hemiparesis and) and **clear-cell carcinoma of the left kidney**, with renal cysts. At present, she has no hypertension. Hormonal tests revealed normal concentrations of serum ACTH and cortisol and 24-h urinary cortisol as well as serum chromogranin-A, dopamine, noradrenaline, urinary 5-HIAA. Abdomen CT scan showed **hepatic vascular malformations** and **2 pancreatic tumours**. In head MRI scan, the lesions: in right frontal lobe and in right eyeball were found. Somatostatin receptor scintigraphy confirmed increased radioisotope accumulation in pancreas and in right orbit. We excluded pheochromocytoma. The diagnosis of pancreatic NETs, without hormonal activity, was made and the surgery is considered. Moreover, stereotactic radiotherapy for brain lesion was recommended.

CONCLUSIONS: Some manifestations of VHL cause that endocrine care is needed to optimize patients' treatment.