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An unusual ocular presentation of a case of von Hippel- Lindau disease

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Abstract
We report a case of 40- year- old male, presented with complaints of pain abdomen associated with blurring of vision in right eye. Ocular examination showed features of juxta papillary retinal capillary haemangioma in right eye. Comprehensive systemic work up in conjunction with magnetic resonance imaging of abdomen illustrated well encapsulated lesion in supra renal, superior mesenteric and left paraaortic region. Further imaging by I-131 MIBG whole body scan revealed bilateral pheochromocytoma. Here is a report of a rare case of Von Hippel-Lindau disease having juxtapapillary haemangioblastoma in association with pheochromocytoma.

Keywords: Von Hippel-Lindau disease**,** retinal capillary hemangioma, laser photocoagulation

Introduction
Von Hippel-Lindau (VHL) disease is a type of phakomatosis characterized by hamartomas (abnormal proliferations of tissue normally found in the involved organs) involving multiple organs with a predilection for the central nervous system (CNS) and retina [1]. Principal lesions are retinal and CNS hemangioblastomas.
VHL disease is a rare genetic disorder with incidence of approximately 1 in 40,000 live births [2]. It has autosomal dominant inheritance with variable penetrance with gene locus mapped to chromosome 3p [6]. VHL disease is of particular relevance to the ophthalmologist because retinal capillary hemangioma is the most frequent and often the earliest manifestation [3]. Other lesions associated with VHL disease are central nervous system hemangioma, renal cyst, renal carcinoma, pancreatic cysts and adenoma, pancreatic islet cell tumors, pheochromocytoma, endolymphatic sac tumor of the inner ear and epididymal cystadenoma [1, 2]. It is a potentially lethal disease, with renal cell carcinoma the most common cause of death [1]. This case highlights the importance of heightened awareness for the thorough systemic workup and imaging in patients with retinal vascular lesions.

Case report
A 40 year old serving soldier reported to a tertiary care hospital with complaints of pain in right side of abdomen for 2 months associated with blurring of vision in right eye. Abdominal pain was dull aching, non-radiating and not associated with vomiting, fever or jaundice. During evaluation, he was found to have an increased blood pressure. Ultrasonography (USG) examination of abdomen revealed mild cortical scarring of inferior pole of right kidney. Magnetic resonance imaging (MRI) abdomen revealed well encapsulated lesion in supra renal (4.5x2.8x3.9cm), superior mesenteric (2.0x17.8x15cm) and left paraaortic (5x3.6x4.7cm) region. (Fig 1) Patients 24 hour urinary catecholamine excretion showed elevated metanephrine (78.21µg/ g of creatinine) and normetanephrine (1977.37µg/ g of creatinine). I-131 MIBG whole body scan was done in the patient and images were acquired at 24, 48 and 78 hours. An abnormal focus of tracer concentration was seen in right subhepatic region and left paravertebral region in 24 hr image which persisted and more intense at 48 and 78 hours. Based on findings diagnosis of bilateral pheochromocytoma made. On ophthalmic evaluation, visual acuity in right eye was 6/9, not improving further and 6/6 in left eye. Anterior segment examination was essentially normal. Pupillary examination revealed no afferent papillary defect. Dilated fundus examination showed a polypoidal orange-red colored exophytic mass of 3 disc diameter size in juxtapapillary region temporal to the disc with dilated and tortuous feeding vessels-suggestive of juxtapapillary retinal capillary haemangioma. Retinal folds were seen over macula (Fig.2). The left eye fundus was normal. Intraocular pressure by applanation tonometry was 14 and 16mm Hg in right and left eye respectively. USG B-scan right eye showed a well demarcated globular mass lesion extending into vitreous with high internal reflectivity. Fundus fluorescein angiography confirmed a highly vascular lesion with feeder vessels with no leakage of dye (Fig.3). Patient underwent complete neuroimaging to look for associated lesions. However, MRI of brain and spinal cord revealed no hemangiomas.
In view of retinal haemangioma along with a visceral lesion in form of pheochromocytoma, diagnosis of VHL disease was made [2, 3, 4]. The patient underwent exploratory thoracolaprotomy with excision of right adrenal pheochromocytoma and interaorta caval paraganglioma. Histopathological report confirmed the same (Fig. 4).
Considering near normal visual acuity and juxtapapillary location of the lesion, patient has been placed under observation with three monthly follow up visits.

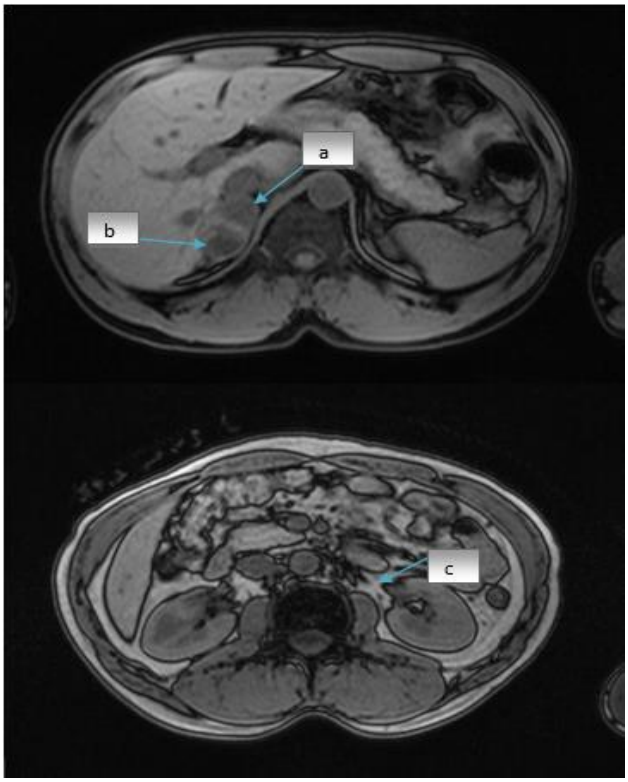

Fig 1.a: Magnetic resonance imaging (MRI) abdomen showing well encapsulated lesion 4.5x2.8x3.9cm in right supra renal location.
b: Another lesion of similar intensity of size 5x3.6x4.7cm noted at aorta caval region
c: Lesion 2.0x17.8x15cm is noted in the left paraaortic region, inferior to left adrenal gland

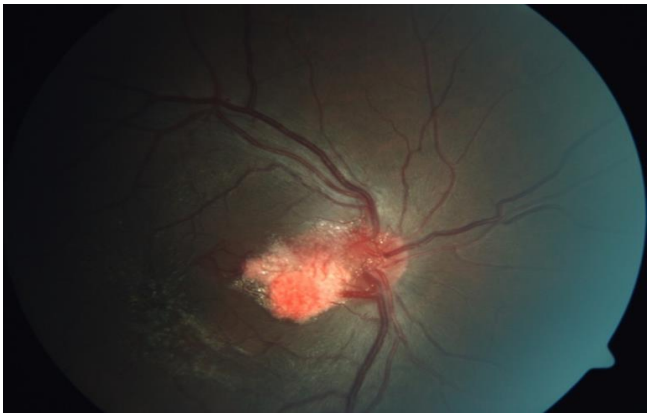

Fig 2: Fundus photograph showing retinal capillary haemangioma

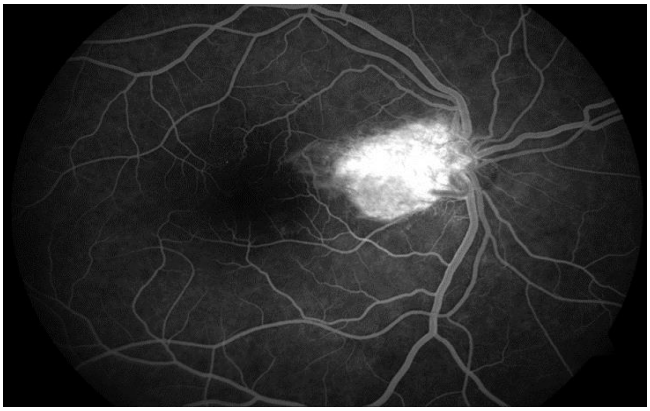

Fig 3: Fundus fluorescein angiography (FFA) show a highly vascular lesion with feeder vessels with no leakage of dye.

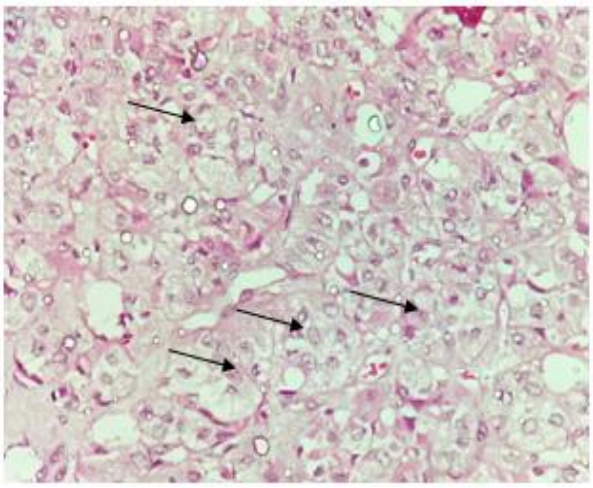

Fig 4a: Histopathological section of excised tumor showing characteristic zellballen arrangement of tumour cells in nests (H and E, 400x)

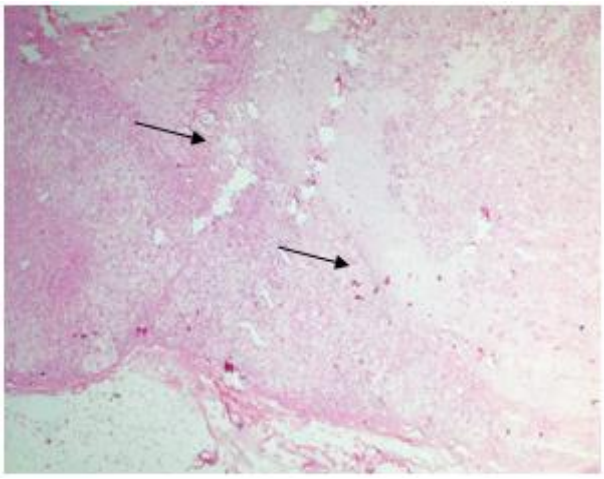

Fig 4.b: Histopathologicl section of excised tumour showing adrenal capsule and surrounding peri-adrenal fat tissue along with nested arrangement of tomour cells (H and E,40x)

Discussion

The salient features of this case were absent family history, non exudative, exophytic juxtapapillary retinal capillary hemangioma in one eye with bilateral pheochromocytoma. This fulfills the criteria of VHL disease [2, 3, 4, 5]. The diagnostic criteria for VHL disease are based on the observations of Melmon and Rosen [2]. With a negative family history, presence of two or more hemangiomas or one hemangioma (retinal or central nervous system) and a visceral lesion is required to establish the diagnosis of VHL disease [2, 5, 10]. Visceral lesions include renal cysts, renal carcinoma, pheochromocytoma, pancreatic cysts, islet cell tumors, Epididymal cyst adenoma or endolymphatic sac tumor.

Retinal capillary hemangiomas are most frequent manifestation of VHL disease seen in about 50% of patients. [7] Retinal angiomas generally develop in the third decade but maybe present from birth [7]. Of those patients with retinal hemangioblastomas, 25% to 80% will have VHL disease [1, 7]. The tumors are often multiple and bilateral in more than 50% of the cases. Most angiomas are present in the temporal periphery but may present anywhere in the retina [2, 7]. The juxtapapillary retinal capillary hemangioma which is present in this case occurs in 11–15% of cases of

VHL disease and it can be the sole retinal manifestation of VHL disease in one or both eyes in only to 6% of cases [8]. This underlies the rarity of presentation in this case.

Overall, less than 20% of all patients with VHL disease have pheochromocytoma which is often multiple and bilateral [2, 9]. Up to 19% of patients presenting with apparent sporadic pheochromocytoma may have underlying VHL disease [9]. This shows the need to actively look for associated lesion in such cases. The detection retinal haemangioblastoma clinched the diagnosis of VHL disease in present case.

Central nervous system (CNS) hemangioblastomas are the second most common cause of morbidity and mortality in patients with VHL disease [2]. Among patients with retinal angiomas, 25% have associated cerebellar hemangioblastomas. CNS hemangioblastomas were absent in this case.

Depending on the clinical circumstances, retinal capillary hemangioma may be managed by observation, laser photocoagulation, Cryotherapy or plaque radiotherapy [2]. Observation as an initial management of juxtapapillary retinal capillary hemangioma should be considered, because some of them have been observed to be stable for many years [8]. However, they can be progressive, particularly in young patients with VHL disease. The treatment of juxtapapillary retinal capillary hemangioma should be undertaken only if the vision is reduced or if there is progression of the lesion, as treatment usually leads to significant reduction of visual acuity due to adverse effects on the optic nerve and major retinal vessels [8].

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