**ABSTRACT**

Von Hippel Lindau syndrome is a rare familial syndrome involving multisystem of the body characterized by abnormal growth of blood vessels. The lesions that includes retina, cerebellum, spinal cord haemangiomas, renal cell carcinoma, adrenal pheochromocytoma, angiomatic cystic lesions of the kidneys, pancreas and epididymis.

We are reporting a case of unilateral lesion due to exudative retinal detachment as initial manifestation of Von Hippel Lindau disease associated with renal cell carcinoma and bilateral renal cyst (Fig. 1) and multiple pancreatic cysts, secondaries in both lungs in a male aged 57 years for 10 days. He was thoroughly investigated, diagnosed as Von Hippel Lindau syndrome which is a very rare hereditary disease that runs in the family. Hence studied and reported.

**KEYWORDS:** Retinal haemangioma, exudative retinal detachment, pancreatic cyst, renal cyst, renal cell carcinoma

**INTRODUCTION**

Von Hippel Lindau syndrome is a multisystem familial cancer syndrome of autosomal dominant inheritance caused by mutation in short arm of chromosome 3p 25-26 characterized...
by abnormal growth of blood vessels. It predisposes to various benign and malignant tumours of central nervous system, retina, kidneys, pancreas, adrenal gland, epididymis.\textsuperscript{[1 and 2]} In VHL disease, retinal hemangioblastomas occurs in 43\% to 67\% patients.\textsuperscript{[3 and 4]} Retinal hemangiomas although benign tumours, they can be asymptomatic for years, but usually grow and cause visual impairment due to exudative retinal detachment, optic atrophy, cataract, glaucoma.\textsuperscript{[5]}

**Case Report**

A 57 year male patient admitted in urology ward for complaints of pain in right loin for past 1 month. He was referred to ophthalmology outpatient department for complaints of painless defective vision right eye for the past 10 days.

**Family history**

Out of his 7 children, 2 of them were affected. Affected son had central nervous system tumor and died at the age of 33 yrs. Affected girl 27yr old has pancreatic cyst and retinal angioma of the right eye.

**Past History**

He is a known case of hypertension for the past ten years and he is on treatment.

On clinical examination

**General Examination**

1. Fair, afebrile, no cyanosis, no clubbing, no lymphadenopathy, no pallor.
2. Cardiovascular system and Respiratory System - Normal.
3. Abdomen soft, right loin tenderness present, bimanually palpable and ballotable mass present in right loin which is typical of renal mass.

**Ocular examination**

Vision Right eye - Perception of light - present, Projection of rays defective superiorly.

Left eye - 6/6. Anterior segments of both eyes were normal.

Dilated fundus of the right eye with +90D lens showed retinal angioma with inferior exudative retinal detachment. Left eye was normal.
Fundus photography

Laboratory investigations

<table>
<thead>
<tr>
<th>Test</th>
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<tr>
<td>Hemoglobin</td>
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<tr>
<td>ESR</td>
<td>10 mm/hr</td>
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<tr>
<td>BT</td>
<td>2 min</td>
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<td>Urea</td>
<td>26 mg%</td>
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<tr>
<td>Creatinine</td>
<td>1.2 mg%</td>
</tr>
</tbody>
</table>

Imaging studies

1) **CT abdomen** shows bilateral renal cell carcinoma and bilateral renal cyst and multiple pancreatic cysts
2) **CT thorax** shows bilateral lung secondaries

![CT thorax image]

3) **MRI brain** - right eye exudative retinal detachment

![MRI brain image]
DISCUSSION

VHL disease is a hereditary cancer syndrome caused by germline mutations of VHL tumour suppressor gene located in short arm of chromosome 3.\textsuperscript{[6]} Prevalence is 1 in 50000. No sex predilection.\textsuperscript{[7]} In 1904, Dr. Eugen Von Hippel a German ophthalmologist published a clinical description of a vascular tumour of retina but in 1926 Dr. Arvid Lindau, a Swedish pathologist linked CNS angiomatosis to retinal angiomatosis.\textsuperscript{[8]} Diagnosis of VHL disease based on family history and clinical presentation of hemangioma, renal cell carcinoma, pheochromocytoma, pancreatic cysts and visceral cysts.\textsuperscript{[9]} There are 3 types of VHL disease - Type 1 (without pheochromocytoma), Type 3 (with high risk of pheochromocytoma) and Type 2, which has 3 subtypes. Type 2a (low risk of pancreatic tumours and renal cell
carcinoma), Type 2b (full multitissue subtype) and Type 2c (pheochromocytomas only). VHL Syndrome was named in 1969 and VHL gene was mapped in 1993.\[10\]

Retinal hemangioblastoma is the presenting sign in 50% of VHL patients and is bilateral and multifocal. Seen in 60% of patients with VHL disease. On fundus examination, lesions have an easily recognizable globular reddish appearance with a dilated feeding artery and a tortuous draining vein. Although it is a benign tumor and has a slow growing course, it can cause vision threatening complications like macular edema, exudative retinal detachment, neovascular glaucoma, vitreous hemorrhage, phthisis bulbi.\[1 and 11\] It can be diagnosed by fundus fluorescein angiography. Usually VHL patients with retinal angiomas have very poor visual prognosis, however early detection and treatment results in good prognosis.

Treatment is based on the size and location of retinal hemangioma. Careful observation for juxtapapillary and peripheral retinal angiomas, less than 500 micrometer diameter angiomas that are not with exudation or subretinal fluid and are not visually threatening. For retinal angiomas less than 4.5mm diameter Argon LASER treatment advised. Lesions more than 4mm diameter cryotherapy advised. Other treatment modalities are plaque radiotherapy, antiangiogenic drugs, photodynamic therapy, transpupillary thermotherapy, parsplana vitrectomy.\[12\]

Renal manifestations include renal cysts, renal cell carcinoma, hemangiomas and benign adenomas. Renal cysts are bilateral, multifocal and high chances for malignant transformation. Clear cell type of renal cell carcinoma is associated with VHL. It is the primary cause of morbidity and mortality in VHL patients. Diagnosed by ultrasonogram, CT, MRI. Treatment depends upon the size and stage of the tumor. Treatment options are tumor excision and partial nephrectomy, nephron sparing surgery. Antiangiogenic drugs therapy is done for advanced metastasis. For recurrent cases, bilateral nephrectomy with life long dialysis or renal transplant are the options.\[13\]

CNS hemangioblastomas are the second most common cause of morbidity and mortality in VHL patients. 80% of CNS hemangioblastomas originate from cerebellum and 20% from spine. Surgical resection is indicated in patients with neurological deficits. Other clinical manifestations of VHL disease are pancreatic cyst, pheochromocytoma, endolymphatic sac tumors of inner ear, bilateral epididymal papillary cyst in males and papillary cystadenoma of broad ligament in females.\[14\] Mortality in VHL patients is mainly due to metastatic renal cell
carcinoma and complications of cerebellar hemangiomas.\textsuperscript{[15]} Clinical management of VHL disease is challenging and requires a co-ordinated multidisciplinary approach. However early detection of VHL tumors by annual surveillance has improved the prognosis VHL gene carriers.

**Present Study**

This case of Von Hippel Lindau syndrome is seen in male patient aged 57 years who came with gradual diminution of vision right eye and pain in the right loin from past one month. On examination of the right eye there was retinal angioma with inferior exudative retinal detachment. Left eye was normal. Systemic examination revealed a palpable mass in the right loin. CT abdomen showed bilateral renal cysts with renal cell carcinoma associated with multiple pancreatic cyst. C-T thorax showed bilateral lung secondaries. MRI brain was normal except for the right eye exudative retinal detachment. MRI brain with contrast was normal.

**CONCLUSION**

In summary, Von Hippel Lindau syndrome is a disease which is inherited and lifelong with severe morbidity due to involvement of more than one systems. Since it is familial, all the members should undergo thorough clinical examination with relevant investigation along with molecular genetic screening, while patient should undergo annual clinical screening to know about progress of this syndrome as early diagnosis and treatment could save the life of the patient.

**REFERENCES**


