The Turkish Journal of Pediatrics 29:243 - 248, 1987

VON HIPPEL-LINDAU DISEASE: REPORT OF AN ADOLESCENT CASE EMPHASIZING THE DIAGNOSTIC ASPECTS*

*Keriman Tınaztepe MD***, Sevgül Bilgiç MD***, Behsan Önol MD****
*Aykut Erbengi MD*****, Aydın Yuluğ MD******

Key words: Von Hippel-Lindau disease, retinal angioma, cerebellar hemangioblastoma.

Von Hippel-Lindau disease is an autosomal dominant disorder characterized by hemangioblastomas of the central nervous system and retina, and other cystic and neoplastic lesions in various organs[1-3]. Since the disease generally does not present with symptoms prior to the age of twenty, it is rarely seen by pediatricians. In atypical cases, if the syndrome is not suspected, the diagnosis of multiple system involvement may be delayed. We would therefore like to report an adolescent case with an intracranial mass in order to emphasize the following points:

i) The disease is occasionally seen in adolescents.

ii) When an angiomatous tumor of the posterior fossa is found, this syndrome should be considered and other possible components of the disease should be searched for.

iii) A detailed family history is very important in evaluating all cases.

Case Report

A 13-year-old girl was admitted to our hospital in December 1979 with complaints of severe headaches of six months duration which did not respond to analgesics. She had been vomiting for five days. A complete physical examination on admission revealed the following pathologic findings: the head was tilted to the right, the uvula was also deviated to the right and there was bilateral severe papilledema. With the tentative diagnosis of an intracranial mass, a brachial arteriography, contrast ventriculography and brain scintigraphy were performed

* From the Departments of Pediatrics, Ophthalmology, Pathology, and Neurosurgery, Hacettepe University Faculty of Medicine, Ankara.

** Professor of Pediatrics, Pediatric Pathologist, Hacettepe University Faculty of Medicine.

*** Associate Professor of Opthalmology, Hacettepe University Faculty of Medicine.

**** Professor of Pathology, Hacettepe University Faculty of Medicine.

***** Professor of Neurosurgery, Hacettepe University Faculty of Medicine.

****** Research Assistant in Ophthalmology, Hacettepe University Faculty of Medicine.

and found to be within normal limits. Due to the persistence of the complaints, a computed tomography scan was performed which revealed a mass in the posterior fossa. Following a posterior fossa exploration, a 6×5 cm encapsulated cystic mass was found in the left cerebellar lobe and was totally removed. Microscopically, the tumoral mass was diagnosed as a hemangioblastoma as seen in Figs. 1 and 2.

The presence of a cerebellar hemangioblastoma suggested the possibility of von Hippel-Lindau disease. The fundi were reevaluated by indirect ophthalmoscopy and with a three-mirror contact lens examination which showed that two of the temporal retinal vessels were dilated in the right fundus which led to a protuberant reddish mass of anastomosing vessels three disc-diameters in size and about ten disc-diameters from the papilla in the temporal quadrant (Fig. 3). The tumor was then better demonstrated with the aid of fundus fluorescein angiography. For treatment, the periphery of the tumor was photocoagulated in a double-row manner.

The patient was seen again two years later with no complaints. The only pathologic physical findings were that the papillae were slightly atrophic and the laser spots could be observed in the right fundus due to the treatment applied.

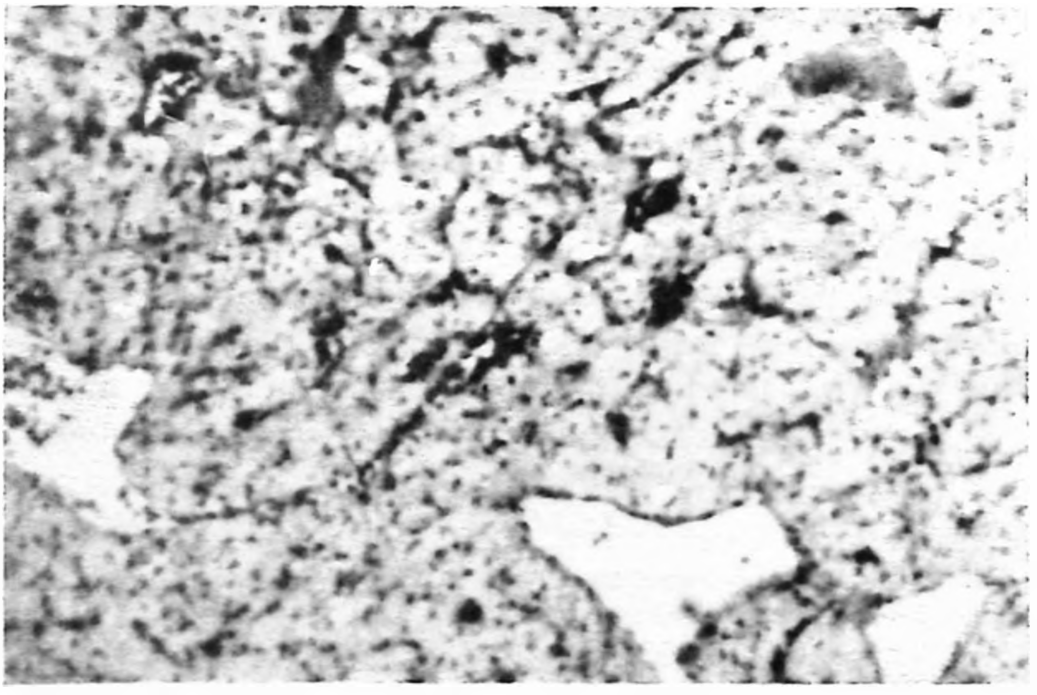

Fig. 1: A section showing vascular channels varying in size; In between there are large polygonal cells with pale cytoplasm containing small, red, round, dark-staining nuclei (HE X 250).

Fig. 2: A section showing a vascular tumor rich in reticulin fibers (silver impregnation technique X 250).

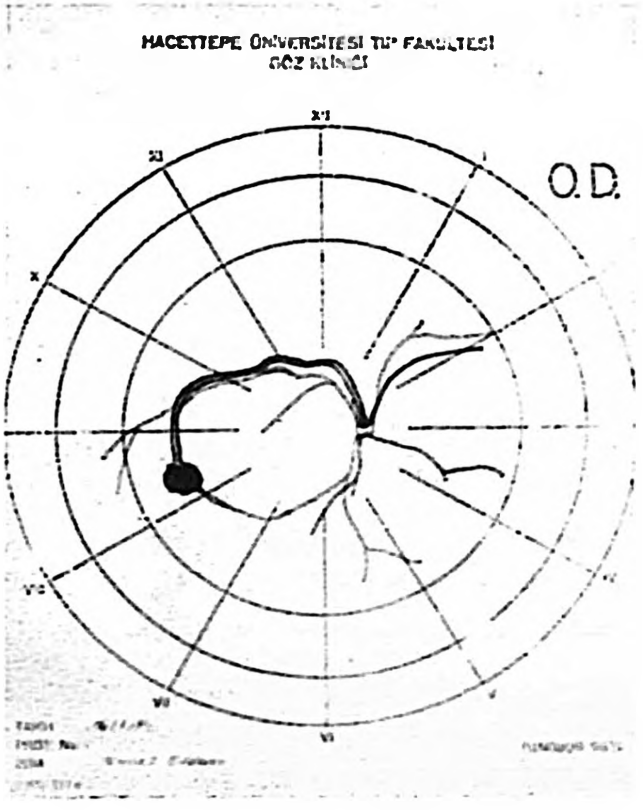

Fig. 3: Fundus chart of right eye showing retinal angioma and its vessels.

Discussion

After von Hippel described patients with retinal angioblastomas in 1904, Lindau demonstrated the occurrence of cerebellar hemangioblastomas in these patients and the eponym "Von Hippel-Lindau disease" was established. The cardinal features of this disease are angiomas of the retina and hemangioblastomas of the cerebellum[3]. The disease generally manifests itself in early adulthood but, like our patient, may occasionally present itself in adolescence[4].

Cerebellar hemangioblastomas which are the most significant lesions of the disease are the most frequent cause of initial symptoms and death. They are usually cystic and are found in more than one-third of the patients[5]. Symptoms generally occur in early adulthood. All symptomatic posterior fossa hemangioblastomas should be excised surgically[6]. Our patient also had a cystic hemangioblastoma of the cerebellum but presented with symptoms earlier than usual.

Retinal angiomatosis is present in over half of those affected[5]. The angiomas may be multiple in the same or both eyes[7]. They typically appear as a greatly dilated artery/vein pair which lead to a peripheral reddish nodule. Fundus fluorescein angiography may reveal the lesion before the onset of the ophthalmoscopically visible alterations[8]. Retinal angiomas have a tendency to progress[9]. When left untreated, they frequently lead to exudation, retinal detachment, glaucoma and blindness. The treatment of retinal lesions is by photocoagulation, and occasionally by cryosurgery or diathermy[6,10]. In our case, the retinal angioma was detected before the onset of complications, but only after a cerebellar hemangioblastoma was established which led to a detailed fundus examination and fluorescein angiography.

Other less frequent manifestations of the disease are hemangioblastomas of the cerebrum, medulla and spinal cord; cysts of the pancreas, kidney and epididymis; pheochromocytoma, and hypernephroma[3].

A detailed family history is very important as an autosomal dominant mode of inheritance has been reported regarding this disease[5,9]. A family history is especially important in diagnosing cases without extensive involvement. It was not possible to obtain a detailed family history from our patient since she was an adopted child.

A case has recently been reported where the ANA titer was high, thus simulating connective tissue disease[4]. When the hemangioblastoma was removed, the titer returned to normal. Therefore, it is suggested that the ANA titer may be useful as a tumor marker. It is also emphasized that the mistaken diagnoses that were arrived at could have been avoided by a detailed family history.

In conclusion, we would like to emphazise that when a benign hemangioblastoma of the cerebellum is found, the ocular fundi must be thoroughly evaluated by indirect ophthalmoscopy, three-mirror contact lens examination and fundus fluorescein angiography with the aim of finding a retinal angioma. It is also suggested that when a retinal angioma is diagnosed, the patient should be screened for a cerebellar lesion[3]. An abdominal ultrasound is necessary in order to detect other organ involvement.

Since pediatricians now also have adolescent patients, they must be aware of the various components of this disorder for detection of the syndrome. By doing so, they will be able to provide appropriate medical evaluation and genetic counseling, thus avoiding many of the disease's complications.

Summary

An adolescent case of von Hippel-Lindau disease is reported. The patient presented with symptoms of an intracranial mass and a cerebellar hemangioblastoma was excised. With the tentative diagnosis of von Hippel-Lindau disease, a more detailed fundus examination including fluorescein angiography was carried out and asymptomatic retinal angioma was detected. The angioma was then treated by photocoagulation.

Even though the disease usually manifests itself in early adulthood, it may occasionally be seen in adolescence. Therefore, pediatricians should recognize the various manifestations of the disease and search for the other possible components when one of them is detected.

REFERENCES

1. McKusick VA. *Mendelian Inheritance in Man* (7th ed). Baltimore: Johns Hopkins Univ. Press, 1986, pp 758-759.
2. Warkany J. *Congenital Malformations.* Chicago: Year Book Medical Pubs, Inc, 1971, pp 1266-1267.
3. Melmon KL, Rosen SW. Lindau's disease: review of the literature and study of a large kindred. *Am J Med* 36:595, 1964.
4. Seitz ML, Shenker IR, Leonidas JC, et al. Von Hippel-Lindau disease in an adolescent. *Pediatrics* 79:632, 1987.
5. Horton WA, Wong V, Eldridge R. Von Hippel-Lindau disease: clinical and pathological manifestations in nine families with 50 affected members. *Arch Intern Med* 136:769, 1976.
6. Kuppersmith MJ. Angiomatosis retinae. In Fraunfelder FT, Roy FH (eds). *Current Ocular Therapy* 2. Philadelphia: WB Saunders Co, 1985, pp 162-163.
7. Delaney WV Jr. *Physicians' Guide to Oculosystemic Diseases.* New Jersey: Medical Economics Books, 1982, pp 152-155.

8. Blodi FC. Vascular anomalies of the fundus. In Duane TD, Jaeger JA (eds). *Clinical Ophthalmology*, Vol 3. Philadelphia: Harper & Row, 1985, Chapter 22.
9. Salazar FG, Lamiell JM. Early identification of retinal angiomas in a large kindred with von Hippel-Lindau disease. *Am J Ophthalmol* 89:540, 1980.
10. Fison L. The treatment of vascular retinal lesions. *Trans Am Acad Ophthalmol Otolaryngol* 77:25, 1973.