Lindau's Disease—in the Hudson Valley*

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The group of manifestations of a peculiar developmental defect described by Lindau17,18 includes angiomatosis of the retina, hemangioblastoma of the cerebellum, medulla, and spinal cord, visceral cysts, hypernephroma, and cutaneous hemangiomas. The term “von Hippel’s disease” has been used by ophthalmologists to refer to angiomatosis of the retina alone, although 20 per cent of these cases will show manifestations of the disease in the central nervous system.17,18

The purpose of this paper is to present a family study in which 13 cases of Lindau’s disease and 8 cases of bilateral cataracts were found.

Review of Literature

The initial description of angiomatosis of the retina was made by Fuchs11 in 1882. Collins6 in 1894 reported the same condition in siblings, thus giving the first indication of the familial nature of the disease. Angiomatosis of the retina was established as a clinical entity in 1904 by von Hippel13 and has since been known by his name.

Jackson14 presented the initial description of hemangioblastoma of the cerebellum in 1872. Although Seidel36 had recognized a relationship between angiomatosis of the retina and hemangioblastoma, it remained for Lindau17,18 to correlate fully the involvement of multiple organs.10 Lindau’s report consisted of a detailed review of the literature, autopsy cases, and personal cases which clearly established this group of abnormalities as “Lindau’s disease.” He noted that while hemangioblastomas arise most commonly in the cerebellum, they may be found in the medulla and spinal cord,15 but never in the cerebrum, and that usually they were single lesions, but not uncommonly occurred as multiple cerebellar lesions or coexisted with lesions of the medulla or spinal cord.

The first pedigree to establish the transmission of the hereditary defect was that of Rochat.23 He described 6 affected members of a family in three successive generations. Möller,29 in his study of a large family, indicated that the inheritance was of a dominant autosomal type.

The inherited incidence has been reported by many observers,1–3,6,7,15,16,19–22,24,27,28,31 the most extensive pedigrees being those of Silver,27 Nicol,21 and Christoferson et al.4 Silver expressed the view that penetrance might be as high as 80–90 per cent were it not for deaths from other causes although his actual incidence was only 44 per cent. Christoferson et al. found only 12 per cent affected.

Lindau,17,18 and Cushing and Bailey8,9 emphasized the surgical treatment of cystic hemangioblastoma, recognizing that drainage of the cyst alone was not adequate and that the mural nodule must be excised for a cure. Stein et al.59 have shown that the prognosis following early and complete excision is very good and reported 1 case with a 23-year follow-up. Möller20 reported the first case in which the preoperative diagnosis of Lindau’s disease had been made and an operation deliberately carried out leading to a cure.

The treatment of the retinal lesions has not been entirely satisfactory.30 Among the treatments used have been fever therapy, roentgen ray, diathermy, vitamins, and enucleation. Recent work by Schepens38 on the surgery of retinal detachments associated

Received for publication May 14, 1963.
Revision received January 20, 1964.
Supported partially by funds from U.S.P.H.S. Grant No. 1GS-94, administered by the Research Grants Committee of the Albany Medical College.
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with angiomatosis of the retina has been very encouraging.

The general nature of the involvement of the central nervous system and retinal manifestations of the disease are basically the same, i.e., a benign primitive vascular tumor (hemangioblastoma) with an adjacent cyst, differing only in size in the anatomic sites of origin.

Materials and Methods

A pedigree of the involved family was constructed utilizing information from a number of sources including older family members, family Bibles, birth and death records, church and cemetery records, historical societies, and old newspaper clippings. Medical data were accumulated from family doctors, hospital records, pathological specimens, roentgenograms, and personal interviews and examinations. The data on the patients with cataracts were obtained from a local ophthalmologist who had operated on several members of the family, and from parents, children and siblings of the involved members.

Results

A family tree encompassing seven generations, 140 years, and 200 persons was established. Great difficulty was encountered in tracing the early members because there were no birth or death records kept in the up-state villages of New York State prior to 1885 and few good records prior to 1900. Factors that facilitated the study were the unusual family name and the fact that few of the family had migrated more than fifty miles from the village in the Hudson Valley where their ancestors had lived in the early 19th century.

Thirteen people in three generations had signs and/or symptoms of Lindau's disease. All living members of this group were located and examined, and the diagnosis was verified. The cause of death in the deceased was documented through hospital charts, and operative and autopsy reports. The hereditary pattern of the affected and the carriers of the trait are shown in Fig. 1.

In a parallel group stemming from the sister of the progenitor of the Lindau’s group, 8 people in three generations were found with bilateral cataracts of the usual senile type which were not associated with manifestations of involvement of viscera or central nervous system seen in the other group. The exact age of onset of symptoms from the lenticular opacities could not be determined, but was estimated in all cases to be within the fourth to sixth decades of life.

The pertinent clinical and pathological data are shown in Table 1.

Eight of 13 (62 per cent) patients with Lindau’s disease had angiomatosis of the retina (Table 2), three (23 per cent) with no other manifestations. Four of the 8 patients with angiomatosis of the retina (50 per cent) had retinal detachments from which 3 (38 per cent) had become blind in the affected eye. One patient was operated upon for a total retinal detachment and after 3 years had 20/30 vision in the affected eye. Of those with angiomatosis of the retina, the incidence of bilateral angiomatosis was 25 per cent, and of multiple unilateral and/or bilateral angioma, 50 per cent. Six of 10 (60 per cent) eyes with angioma had no alteration of function, 4 (40 per cent) had retinal detachments, and only 3 (30 per cent) were blind. Both the oldest patient (68 years) and the youngest patient (14 years) with angiomatosis of the retina had multiple lesions and were asymptomatic.

Five hemangioblastomas were present in the cerebellar hemispheres, 1 was in the vermis, and 1 was in the conus medullaris.