THE OCCURRENCE OF HEMANGIOBLASTOMAS (TWO CEREBELLAR AND ONE SPINAL) IN THREE MEMBERS OF A FAMILY

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The familial character of hemangiomatous cysts and tumors of the central nervous system has been stressed by numerous writers, this characteristic perhaps being true particularly of patients having associated angiomatosis of the retina as well as cysts of other organs such as the kidney, pancreas, liver, and so forth, the so-called Lindau-von Hippel disease. Lindau himself believed that about 20 per cent of all cases showed a family incidence.

Although hemangiomatous cysts in the cerebellum with or without similar associated lesions elsewhere are by far the most frequent form of this tumor situated in the central nervous system, nevertheless the spinal cord occasionally has been found to be the seat of hemangiomatous or angiomatous growths. Cushing and Bailey felt that spinal lesions of this nature were extremely rare. However, Sargent stated that he had operated upon 6 patients with spinal cord angiomas, and Wagener, Kernohan and one of us (W.McK.C.) reported several cases of typical hemangioblastoma of the spinal cord in which no other lesion was clinically demonstrable. One of these patients had histologically verified cerebellar and spinal cord hemangiomas, and from his history it is evident that his disease was familial, although it was not possible to verify the lesions in other members of his family except for an angioma of the retina in 1 sister. In 1938 Dorothy Russell reported a case of capillary hemangioma of the spinal cord associated with syringomyelia, noting the great rarity of the condition.

The 8 patients to be reported here present several interesting features. In the first place, the hemangiomatous cysts of the cerebellum in the mother (Case 1) and 1 daughter (Case 2) have been verified histologically. The mother likewise had a probable angioma of the retina (and kidney?) and was reported previously by one of us. One daughter (Case 2) had two separate verified hemangiomas, one in each cerebellar hemisphere. The other daughter (Case 3) has angiomatous or hemangiomatous tumors, identified by inspection, involving both the cervical and lumbar portions of her spinal cord.

Case 1. Slowly developing cerebellar symptomatology with retinal hemangioma difficult to recognize. Ventriculography with removal of hemangioma in the left cerebellar hemisphere. J.F., aged 42, was referred to the Mayo Clinic in September 1937 for examination. She had had some loss of vision in the right eye for 11 years which had
been diagnosed as chorioretinitis with scotoma. Recently intermittent headaches and vomiting had developed.

**Family history** was negative except for questionable migraine headaches in the mother.

**Present Illness.** The patient noticed difficulty in vision of the right eye which had been present for 11 years with no other symptoms and was considered to be chorioretinitis of tuberculous origin. Because of the headaches, an encephalogram was done, which was negative. She returned in June 1938, with a history that following encephalography there had been some relief of the headaches and very few neurologic symptoms. Four months before re-examination headaches, projectile vomiting, and some unsteadiness of gait had developed.

**Examination.** The patient was ambulatory, cooperative and fully oriented. There was marked incoordination of the left arm and leg with slight ataxia. Examination of the eyes revealed nystagmus on looking to the right, and papilledema of 4 D. on the right and 5 D. on the left. The left visual field was normal; the right showed a loss of the temporal field and the nasal upper quadrant, with diminution of vision which could have been explained by the retinal lesion. The retina had the appearance of proliferating retinitis with detachments of the lower portion of the retina in the right eye. In view of the development of cerebellar signs, the retinal lesion was reconsidered and the consensus was that it might be an angiomatous lesion of Lindau-von Hippel's disease.

**Operation (W.McK.C.).** On June 24, 1938, ventriculography was performed with removal of several ounces of fluid. Subsequent roentgenograms revealed dilation of the lateral and 3rd ventricles with some elevation of the posterior horn of the left lateral ventricle.

A suboccipital craniotomy was done in the upright position under intratracheal anesthesia. When the dura was opened, the inferior tonsil of the left cerebellar lobe was found to be herniated below the level of the 1st cervical vertebra. The convolutions of the left cerebellar lobe were broadened and flattened and the entire lobe was covered with large, engorged, tortuous vessels (Fig. 1, a). A needle was inserted and 0.5 cm. below the surface a cyst was encountered from which 5 cc. of fluid were removed. The fluid was yellow and coagulated on standing. The vessels on the surface of the cerebellum were ligated and coagulated. An incision was made into the cyst and a nodule was found lying on the lateral wall (Fig. 1, b). The cyst wall, including the mural nodule, was removed completely. Convalescence was satisfactory.

**Subsequent Course.** An examination in March 1945, 7 years after operation, revealed no papilledema and no neurological disturbances. Vision was normal except for the defect due to the retinal lesion of the right eye which had not increased in size.

**Pathologic Report.** The tumor, which weighed 5 gm. and measured 3×2×2.5 cm., was a hemangio-endothelioma. On microscopic examination it was found to contain more large thin-walled blood spaces than are usually seen in hemangio-blastomas. There were regions in which numerous small blood spaces were lined by endothelial cells, some of which were swollen and contained vacuoles that gave the cells a typical foamy appearance. There were, however, more foam cells between the blood spaces than actually lining the spaces. Staining showed the vacuoles of the foam cells to contain fat. The relationship of the xanthic cells to the walls of the blood spaces was best demonstrated with a combination of Perdrau’s silver impregnation method for connective tissue and scarlet red staining for fat.
Comment. Like many patients with hemangiomatous cysts of the cerebellum this patient presented a difficult diagnostic problem since only minimal evidences of loss of cerebellar function were present. Even the early encephalographic studies were inconclusive and this has been true of other patients suffering from the same type of tumor. However, there eventually developed intracranial hypertension and cerebellar signs.

Case 2. Meager cerebellar symptomatology. Dilated ventricular system by ventriculography. Disclosure and complete removal of hemangiomas in both cerebellar hemispheres. E.F., aged 18, was referred to the Lahey Clinic and admitted to the New England Deaconess Hospital on Aug. 16, 1942. She is a daughter of Mrs. F. (Case 1),
and had been complaining of headaches, nausea and vomiting for 2 or 3 months.

**Family History.** Her mother, as noted, had been operated on by one of us (W.McK.C.) at the Mayo Clinic 4 years previously and an hemangiomatous cyst of the cerebellum removed. Her past history was negative for serious illness or head trauma.

**Present Illness.** The patient had been well until 2 to 3 months before admission when she began to have headaches which were frontal and occipital in situation. These were dull and of short duration at first, but became severe and almost constant. She had also suffered from occasional morning nausea and vomiting, had become slightly unsteady, and had noticed some numbness of her extremities.

![Fig. 2. Case 2. Dilated lateral and 3rd ventricles together with dilatation of upper portion of aqueduct of Sylvius.](image)

**Examination.** The patient was conscious, cooperative and fully oriented. Her pupils were equal and reacted normally. There was a persistent nystagmus vertically and on looking to either right or left; otherwise the ocular movements were normal. Examination of the fundi showed slight blurring of the nasal margins of the disks with filling in of the optic cups. Visual acuity and fields were normal. No other neurological abnormalities were found other than absent abdominal reflexes. Roentgenograms of the skull were negative.

Lumbar puncture revealed an initial pressure of 400 mm. of water with the patient well relaxed. There were no cells; total protein was 43 mg./100 cc.

In view of the high CSF pressure, ventriculography was carried out on Aug. 19, 1943; 90 cc. of fluid were obtained, and replaced by a similar amount of air. The subsequent x-ray films showed a greatly dilated ventricular system with the upper portion of the aqueduct also visualized and dilated (Fig. 2). Immediately following ventriculography, a suboccipital craniotomy was performed.
Operation (G.H.). The suboccipital region was exposed by the usual curved incision and a wide bony opening secured over both sides.

When the dura had been opened an obvious small tumor was at once apparent on the lower lateral surface of the right cerebellar hemisphere. It consisted of a bright red central portion, some 3 to 4 mm. in two diameters, and surrounding this there was a greyish-yellow area about 1 cm. in size. This whole area was quickly and easily excised completely, using the electrosurgical apparatus, and was preserved intact for pathologic study (Fig. 3).

It was noted that the cerebellar tonsils were herniated far through the foramen magnum and it was thus obvious that the small tumor that had just been removed could not be responsible for this. Upon inspecting the cerebellar hemispheres, the left showed widened convolutions, and toward its lateral portion the convolutions were likewise discolored. A needle introduced into this area secured a few cc. of yellow cystic fluid. The cerebellum was incised down to the cyst and thus exposed a large, solid, red-colored tumor extending from the lateral wall of the cyst outward and upward to the tentorium (Fig. 4). This solid tumor was roughly the size of a hen's egg, and was finally removed completely after an extremely difficult session occasioned by severe hemorrhage.

Fig. 3. Case 2. Photograph of small tumor in right cerebellar hemisphere (see Fig. 4). (Natural size)

Fig. 4. Case 2. Elaboration of operative sketch of the two cerebellar tumors: small superficial tumor in right hemisphere; large, partly cystic but largely solid tumor of left hemisphere.
The patient made an excellent but somewhat prolonged convalescence and was discharged on Sept. 30, 1942.

Subsequent Course. On Aug. 6, 1947, 5 years postoperatively, the patient was seen for a follow-up examination. She was in perfectly normal health; had been married 1 year after operation and has had 1 child. She had no cerebellar or pressure symptoms of any kind.

Pathologic Report. Microscopic sections from the large tumor presented quite a variable picture. For the most part it was composed of two elements, endothelial lined spaces filled with blood, and clusters of mesenchymal cells. The vascular channels exhibited a wide range in size, several being almost a low power field in diameter while the majority were much smaller, of approximately the diameter of liver sinusoids. The larger vessels had a definite fibrous or fibromuscular wall. The smaller vessels were delineated by a single thick membrane against which one or two endothelial cells might be found in each space. In some channels the endothelial cells and membrane appeared to be one unit; elsewhere they appeared to separate (Fig. 5).

The cellular component consisted of small clusters, 2 to 5 usually, of varying-sized clear cells lying between the vascular channels described above. These clusters were surrounded by a thick membrane which, with the small vessel walls, formed a reticulated pattern. The cells themselves had a clear white cytoplasm with hematoxylin and eosin stain or a cytoplasm that was composed of homogeneous tiny
vacuoles. Their nuclei were generally oval or wrinkled, and ranged from approximately 10 to 25μ in greatest dimension and had a sparse amount of chromatin. Mitoses were not seen (Fig. 6).

The histologic picture was that of an hemangioma.

Microscopic sections from the small tumor in the right hemisphere were similar.

Comment. The 2 patients whose records have just been cited, although having almost identical lesions in the left cerebellar hemisphere, nevertheless presented contrasting clinical features. Although the mother (Case 1) had had symptoms 1 year previous to her first neurological survey, an air study failed to show any changes in the ventricular system. On the other hand, her daughter (Case 2) showed great ventricular dilatation after only 2 or 3 months of headaches, and in the absence of cerebellar signs other than nystagmus. The paucity of clinical localizing criteria has been a feature in other patients with similar lesions and emphasizes again the great value of ventriculography as well as its occasional misleading evidence.

The extreme operative difficulties due to hemorrhage from enormous, friable blood vessels, especially in the presence of a large solid portion of an hemangioblastoma, was a common feature of both mother and daughter.

Case 3. Progressive symptoms of spinal cord pressure for 3 years. Disclosure by operations of angiomatous or hemangiomatous lesions at cervical and lumbar enlargements. V.C.F., younger daughter of Case 1 and sister of Case 2, was first admitted to the New England Deaconess Hospital on May 24, 1944, complaining of pain in the back and progressive weakness of the legs for 3 years.

Family History. As noted, her mother and sister had been operated upon previously for hemangiomatous cysts of the cerebellum.

Present Illness. The patient had been well until 3 years previous to admission when she first noted pain in the middle and low back region. This pain gradually increased in severity and radiated around both sides of the trunk at the level of the lower ribs. It had been sufficient to awaken her in the morning. During the past 6 to 8 months she had had pain likewise in the left axillary region running down the left arm, and this pain was increased by coughing.

About 1 year before admission she had first noted some weakness of the legs, particularly awkwardness in running. This weakness progressed so that she had become unsteady and her right leg sometimes collapsed under her. Both legs had felt numb as if she were “walking on cushions.”

Neurological Examination. The fundi and other cranial nerves were negative except for complete nerve deafness on the right side which had been present for 4 or 5 years. Motor System. There was general weakness of both legs in all muscle groups, but no atrophies. She could stand and walk by herself, but unsteadily and on a wide base. There was slight relative weakness of the left hand as compared with the right and slight atrophy of the intrinsic muscles of the left hand on its dorsal aspect. Sensory System (Fig. 7). There was fairly complete loss of pain sensation over the thoracic dermatomes from the 1st to the 8th or 9th level on the left side, and both thighs were analgesic up to the level of the 12th thoracic or 1st lumbar dermatome. Some disturbance of sensation was present over the lower legs and feet, but this was less marked than over the thighs. There was some slight diminution to pin pricks over the whole abdomen above the 12th dermatome. In addition, position
and muscle sense were lost in both feet, and both feet were cold. There was marked ataxia in the heel-to-shin test with both legs and a positive Romberg's sign. Deep reflexes were active and equal throughout in both arms and both legs. Plantar responses were normal and there was no ankle clonus.

Roentgenograms of the skull and the entire spine showed no abnormalities.

Lumbar puncture was attempted on May 25, 1944. No fluid could be obtained throughout the lumbar area and at the 12th thoracic interspace.

Preoperative diagnosis: Spinal cord tumor (single or multiple). It was felt that the growth might be an intramedullary hemangioma in view of the family history.

Operation I (G.H.). On May 26, 1944 laminectomy was carried out from the 3rd cervical to the 1st thoracic vertebra. The bone was over-vascular, especially on the left side where the bone was softer than on the right. There was no pulsation of the dura. When the latter was opened throughout the exposed area there was immediate bulging of the cord through the dural incision. The cord seemed to fill out the arachnoid completely so that it gave the appearance of being expanded by a tumor within its substance. The surface of the cord had the appearance of a diffuse angioma or hemangioma, being covered with large, tortuous blood vessels throughout the extent of the area exposed. No attempt was made to deal with these vessels, but the dura was left widely open for decompressive purposes.

The patient made a rather prolonged convalescence and was given a course of 18 roentgen treatments directed to the entire cord.

Nov. 14, 1944—5½ months after operation. The patient came for a check-up examination. She had improved gradually and walked by herself with only slight unsteadiness.
Jan. 7, 1945. She was readmitted to the hospital because of progressive ataxia and loss of position sense in her legs.

Motor Examination. The patient had regained the full strength and use of her hands and arms, was able to sew, knit and carry out all normal movements with her hands. Her legs were weaker and much more ataxic. The heel-to-shin test was done extremely poorly with both legs and there was complete loss of postural sense in both legs. Sensory Examination. This showed hypesthesia to all modalities over both lower extremities, but sparing the sacral segments. The area of hypesthesia extended upward over the abdomen to the level of the 12th thoracic segment on the right, and on the left there was lowered sensation up to the 5th cervical segment.

![Fig. 8. Case 3. Chart of sensory loss on 2nd admission, Jan. 7, 1945.](image)

Deep Reflexes. The triceps reflexes were either absent or equivocal on either side, but all other deep reflexes were active and equal. Plantar responses were inactive on both sides.

Lumbar puncture and oxygen myelography were carried out on Jan. 13, 1945. A needle introduced between the 2nd and 3rd lumbar vertebrae encountered slightly xanthochromic fluid. There was a complete subarachnoid block by jugular compression. Subsequent roentgenograms showed that the upper level of the oxygen was at the 1st lumbar level, no gas being present above this. The total protein content of the fluid was 2,515 mg./100 cc.

Operation II (G.H.). On Jan. 16, 1945 a laminectomy from the 9th thoracic to the 1st lumbar vertebra inclusive was performed. The dura when exposed was of a bluish-red color and there was a distinct bulge in the dura at the level of the 10th and 11th thoracic areas. The dura felt firm to palpation. The following is a quotation...
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from the operative note: "The dura was opened over the area exposed and an extraordinary picture presented itself. Toward the upper end of the dural opening there was a lesion which was bright pink in color and smooth in contour. This pink area covered the cord like a saddle with sharply demarcated upper and lower margins and extended around on either side of the cord as far as one could see. Above and below this area of presumed hemangioma there was a tangle of large and small interlacing blood vessels, and from the lower side one particularly large vessel in the

form of a corkscrew seemed to come up and enter the under surface of the pink saddle area between the latter and the cord (Fig. 9). By retracting the blood vessel mesh below the pink area one could see what may have been a further extension of tumor anterior to the mesh of vessels, this extension being yellowish-grey in color. A similar appearing area could be seen by retracting the vessels above the pink saddle area. The dura was left open for decompressive purposes."

The patient was discharged on Mar. 12, 1945. She was able to get about in a walking frame. Her legs were very weak and numb and she had marked ataxia.

Check-up Examinations. Aug. 7, 1946—1 year and 8 months following 2nd opera-
tion. In the interim the patient had been given 3 courses of x-ray treatment covering her entire spinal canal by Dr. Lawrence Reynolds of Detroit.

She was now able to walk fairly well, usually with a single cane, but could walk without any support. Her legs had become considerably stronger than they were when she left the hospital, but they felt numb and she had difficulty in knowing where her feet were placed. She had no pain.

Examination showed that her arms and hands were normal in strength and in all movements. Her legs showed fairly good strength and there were no atrophies. Sensation. There was a band of hypesthesia to all modalities from the 8th cervical to the 3rd thoracic dermatome inclusive on the left side, and likewise hypesthesia over both legs and both sides of the trunk up to the level of the 6th thoracic on the right and the 8th thoracic on the left. Deep reflexes were normal at both elbows, but somewhat overactive at both knees and both ankles. There was normal plantar flexion on both sides.

Aug. 5, 1947—2½ years after 2nd operation. The patient had lost some ground so far as her legs were concerned. A year previously she had reached the highest point in her recovery and had been able to play a few holes of golf.

Examination showed that both hands and both arms were of normal strength without atrophy. The right leg was extremely weak in all muscle groups, while the left leg still retained fair strength throughout. Sensation was about as charted in Fig. 8, except that there was now some slightly lessened sensation over the right side of the upper abdomen and chest up to the level of the 4th thoracic segment. The deep reflexes were present and equal at both biceps, but rather underactive. The knee jerks were likewise present and equal, but less active than normal. The Achilles reflexes were active on both sides, but greater on the left. There was no response to plantar stimulation on either side.

Nov. 15, 1948. The patient was last seen on this date, having been readmitted to the hospital for observation and any possible treatment several weeks previously. At this time it was evident that the weakness of her legs, particularly the right, had become more marked so that she was unable to stand or walk. Her arms and hands showed excellent strength and no sensory loss. The sensory changes over her trunk and legs were about the same, except that the loss now was bilateral up to the 4th thoracic dermatome.

SUMMARY

The 3 patients whose histories have been detailed are reported largely to put on record another instance of the familial incidence of hemangioblastomas of the central nervous system. Certain unusual features were at hand, namely, the presence of tumors in both cerebellar hemispheres in Case 2, and either two separate tumors involving different regions of the spinal cord in Case 3 or else the possibility that the angioma or hemangioma may run throughout the entire length of the cord.

Certain marked differences in the symptomatology and clinical findings in the 2 patients with cerebellar tumors have been mentioned. In one, normal ventricles were disclosed after intracranial pressure symptoms had been present for a year, while in the other there was great ventricular dilatation only 2 to 3 months after such symptoms had appeared.

So far as treatment is concerned, both patients with cerebellar tumors
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have apparently been cured by the complete removal of their growths which in both instances, however, was accomplished only after extreme operative difficulties. Operative removal of the spinal lesion or lesions in Case 3 was obviously impossible, but an arrest of the condition by deep roentgen therapy sometimes may be hoped for. In a similar lesion of less wide extent so treated we have seen a return to perfectly normal cord function which is still present 10 years following laminectomy and x-ray therapy.

We are greatly indebted to Dr. James B. Ayer of Boston for his valuable consultations in connection with Case 3.

REFERENCES