PAPILLOMA OF THE CHOROID PLEXUS IN CHILDHOOD

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Papilloma of the choroid plexus is an unusual but important intracranial tumor of early childhood. This tumor is interesting to the geneticist because of its occasional prenatal occurrence, to the physiologist because of its frequent association with communicating hydrocephalus and the possible role the tumor may play in overproduction or increased rate of circulation of cerebrospinal fluid, to the pediatrician because of the paucity of diagnostic symptoms and signs it produces in early childhood, to the radiologist because of the dramatic and diagnostic features of ventriculography, to the surgeon because of its common benign, noninvasive character and the frequent possibility of total excision with satisfactory end result, and to the pathologist because of its histological relation to normal ependyma and normal choroid plexus and also because of the relation of its occasionally more rapidly growing and invasive variants to other ependymal tumors.

Even when histologically benign, these tumors can prove fatal if not recognized early and subjected to definitive treatment before development of such complications as intraventricular hemorrhage and severe hydrocephalus. In general, the results of treatment of the patients reported previously have not been as good as the usual benign character of the lesion should warrant.

For these various reasons, it seemed worth while to review the literature briefly and to analyze the experience of the Children's Medical Center with 16 additional cases of papilloma of the choroid plexus seen during the period from 1941 to 1958. A few of these cases have been referred to elsewhere.29,30 There have been no other reports devoted specifically to this tumor in children since Friedman and Solomon20 collected 14 cases from the literature in 1936 and Rand and Reeves47 described 4 of their own cases in 1940.

INCIDENCE

In Cushing's31 series of 2,000 proven cases of intracranial tumor in all age groups the incidence of papilloma of the choroid plexus was 0.6 per cent. Norlén41 reported an incidence of 0.4 per cent in 3,664 cases of intracranial tumor. Zülch49 in 1956 also reported an incidence of 0.5–0.6 per cent. It is probable that papillomas of the choroid plexus are somewhat more common than these figures suggest since many cases in early childhood un-
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doubtedly have gone unrecognized and many more isolated tumors found post mortem have never been documented.

At the Children's Medical Center during the years 1941 to 1958 inclusive, there were 408 cases of intracranial tumor in children under 12 years of age, of which 16 were papillomas of the choroid plexus, an incidence in this age group of 3.9 per cent.

The possibility that this tumor is frequently of congenital origin is supported by the statistical data which indicate that it is seen most frequently in the first decade and particularly during the first 2 years of life, and gradually decreases in frequency with advancing age (Fig. 1).

![Figure 1](image_url)

**Fig. 1.** Age distribution of 88 children with papilloma of the choroid plexus collected from the literature and from the Children's Medical Center.

Posey in 1942 found that in 72 cases reported in the literature in which the age was stated, 27 cases, or 38 per cent, occurred before the age of 10 years. At the time of the present review, 48 per cent of all reported cases are in the first decade and 20 per cent are under the age of 1 year.

There is no doubt that papillomas of the choroid plexus can develop during prenatal life. Drucker reported a tumor in a newborn infant. Braunstein and Martin reported a 1-month-old infant with a history dating from birth. Matson has reported previously 1 of the present series (Case 9), an infant born prematurely with an enlarged head who had a papilloma of the choroid plexus removed before the normal expected date of birth. Another patient in this series (Case 14) had a huge tumor removed at 2 months of age.

In the present review of the literature, 67 children with well-documented papillary tumors of the choroid plexus have been identified. This includes reports from 53 different
authors, so it will be seen that for the most part these are individual case reports. The first was that of a 3-year-old child reported at autopsy by Guérard\textsuperscript{26} in 1833, and the most recent was that of van Hoytema\textsuperscript{28} in 1957. These children varied in age from birth to 14 years. The diagnoses in the early cases from the literature were all made post mortem. The first successful removal of a papilloma of the choroid plexus occurring in an adult was reported by Bielschowsky and Unger\textsuperscript{2} in 1906, but the patient did not survive. Perthes\textsuperscript{44} reported the first successful operation with survival in 1919, again in an adult. Dandy\textsuperscript{13} in 1927 successfully removed a tumor from the right lateral ventricle in a 14-year-old girl who survived. In 1929, Van Wagenen\textsuperscript{62} reported removal of a papilloma from the left lateral ventricle with survival in an infant 3 months of age.

Among these 67 children under the age of 15 years, operations were carried out on only 24, of whom 13 survived (Fig. 9). Of the survivors 2 died subsequently from recurrence of the tumor. One other had successful removal of a recurrent tumor but there was no further follow-up. Four were not followed postoperatively and the course of the remainder is reported for periods varying from 6 months to 8 years. Two of these patients died from other causes, but apparently were normal mentally and physically prior to their final illness. Of the 4 who survived on whom there are follow-up data, all showed normal physical growth and 3 had apparently normal mental development. One, the only 1 of the 4 who had a tumor in a lateral ventricle, showed mental retardation and petit mal attacks. An interesting 4-year-old patient was that of Obrador \textit{et al.}\textsuperscript{42} who, following removal of a tumor of the 4th ventricle, remained unconscious for 5 months and then made a complete recovery.

In the 67 cases collected from the literature, 11 of the tumors were considered to be malignant. Five of the patients died without operation, 1 died after operation, and 2 died from recurrence of the tumor, one showing metastases to lungs and pleura.\textsuperscript{64} One of these patients with so-called malignant tumor had removal of a recurrence but there is no further follow-up.\textsuperscript{13} One additional patient was not followed after operation\textsuperscript{41} and 1 was alive and well 4 years later.\textsuperscript{66} On the whole, therefore, the score in management of papillomas of the choroid plexus in children as reported in the literature has not been an encouraging one!

**MATERIAL**

It is our intention to make available the experience of treating 16 consecutive patients with papilloma of the choroid plexus seen at the Children's Medical Center between 1941 and 1958, 15 of whom were operated upon. There were 8 males and 8 females. The youngest patient was a 5-week premature baby admitted to this hospital at 3 weeks of age. The oldest was 8 years of age, and he was the only one over 3. The average age was 16 months.

In this series, the tumor was located in the left lateral ventricle in 8 cases,
the right lateral ventricle in 7, and the fourth ventricle in 1. A brief protocol of each case is found at the end of the paper.

CLINICAL EXAMINATION

The lack of diagnostic symptoms and signs is the most constant clinical feature of this condition. In most of the patients reported here, history relevant to the disorder was rather abrupt in onset and lasted only from 1 week to 2 months. In 2 patients, it was insidious in onset and of 12 and 20 months' duration, respectively. The commonest complaint was vomiting, which was noted in 10 patients (Fig. 2). Difficulty in walking was the main complaint in 2 patients while headache and convulsions lasting over a 5-month period were the chief complaints in 1 patient each. One patient had no complaints at all until a fall out of bed 3 days before admission led to sudden onset of persistent vomiting.

In 14 of our 16 patients there was enlargement of the head, and 1 older child had other evidence of increased intracranial pressure (Fig. 2). In the remaining patient, the head was slightly small and ventriculography showed no hydrocephalus. Seven patients had hyperactive deep tendon reflexes. Seven patients had ophthalmoscopic evidence of papilledema. Occasional findings were strabismus, ankle clonus, hypertonicity, and up-going toes in response to plantar stimulation. It is interesting that in 5 patients no abnormal physical findings at all were noted except for enlargement of the head and separation of the cranial sutures.

In 15 of the 16 patients, the cerebrospinal fluid pressure was measurably elevated at the time of lumbar or ventricular puncture or both (Fig. 3). In 7 of these patients a pressure of over 300 mm. of H₂O was recorded, and

![Fig. 2. Summary of the commonest presenting symptoms and signs at the time of hospitalization of 16 children with papilloma of choroid plexus.](image-url)
in it was as high as 600. The cerebrospinal fluid protein was elevated in 13 patients; in 10 of these it was more than 100 mg. per cent, and it was occasionally recorded as high as 500 mg. per cent. This was true whether the fluid was obtained from the lumbar space or directly from the ventricle. In 12 patients, the cerebrospinal fluid was xanthochromic. In all of the infants, subdural taps were performed and in each instance was found negative.

It is apparent that the "typical" young child with a papilloma of the choroid plexus might be expected to be hypertonic and irritable with an enlarged head or evidence of increased intracranial pressure and xanthochro-

mic spinal fluid under increased pressure with a total protein content well above normal. The absence of any part of this clinical picture, however, by no means rules out the diagnosis.

RADIOLOGICAL EXAMINATION

Plain roentgenograms of the skull in all patients but 1 of this series showed evidence of increased intracranial pressure consisting of separation of the cranial sutures and enlargement of the cranial vault in comparison to standard measurements and the size of the facial bones (Fig. 3). In no patient in this series was there calcification within the tumor, as has been noted in adults and in 2 children reported in the literature.50,62

Ventriculography proved to be informative in all cases and in most instances clearly defined the location and extent of the tumor (Fig. 4). A prominent feature in all but 1 patient was the marked degree of hydrocephalus. In 6 patients this apparently was caused by obstruction of the ventricular system by the tumor itself. In 9 other patients, however, hydrocephalus was of the communicating variety, that is, there was diffuse enlargement of the entire ventricular system as well as the surface subarachnoidal pathways,
with the lateral ventricle containing the tumor being perhaps slightly larger than that of the opposite hemisphere (Fig. 4). In 12 patients the tumor could be visualized lying freely within the ventricular lumen or completely filling a portion of it.

The combination of a large mass within one lateral ventricle associated with diffuse enlargement of the entire ventricular system and basilar cisternae (communicating hydrocephalus) occurred in 8 patients. This combination of findings is considered pathognomonic of papilloma of the choroid plexus. Only 3 of the 14 patients who showed hydrocephalus and a tumor within one lateral ventricle failed to show some shift of the ventricular system away from the side of the tumor. This indicated that the tumors were of large size even though the duration of symptoms was short. In the 1 patient in this series with a tumor in the fourth ventricle, although the tumor could not definitely be outlined in the ventriculogram, there was marked enlargement of the proximal fourth ventricle as compared to the rest of the ventricular system (Fig. 5). It is our feeling that when xanthochromic or high-protein ventricular fluid is found in hydrocephalus, or when there is any asymmetry of the lateral ventricles, ventriculography should be as complete as necessary to determine the presence or absence of an intraventricular tumor. A limited ventricular "bubble" study in this type of patient may miss tumor of the choroid plexus. Opportunity is taken here also to stress the danger of carrying out shunting procedures for hydrocephalus without doing ventriculography which rules out satisfactorily an intraventricular tumor.

Fig. 4. Case 7. Ventriculogram of 6-month-old infant which demonstrates a large tumor in the atrial portion of the lateral ventricle as well as communicating hydrocephalus. The study shows enlargement of the lateral ventricles, 3rd ventricle, aqueduct, 4th ventricle and cisterna magna.
Three patients in this series showed a porencephalic-like cyst in the cerebral hemisphere adjacent to the location of the intraventricular tumor; all of these 3 patients also demonstrated a shift of the lateral ventricles to the opposite side (Fig. 11). In 1 patient tumor was visible within the lateral ventricle at ventriculography. In the other 2 patients no tumor was seen and the preoperative roentgenographic diagnosis was porencephalic cyst. Only at operation was the tumor disclosed in these patients.

**Fig. 5. Case 6.** Anteroposterior and lateral ventriculograms of 14-month-old infant with papilloma of the choroid plexus in the caudal portion of the 4th ventricle. Here the hydrocephalus may be obstructive because of block of the outlets of the 4th ventricle as well as overactivity of the tumor itself.

**OPERATION**

Treatment of papilloma of the choroid plexus is total surgical excision with the least possible damage to normal brain tissue. Exposure of fourth ventricle tumors is by standard suboccipital craniectomy. Exposure of third ventricle tumors should probably be carried out by frontal transcortical approach across the dilated lateral ventricle of the nondominant hemisphere and through the corresponding dilated foramen of Monro. The majority of tumors in childhood, 14 out of our 16, have been located in the atrial region of the lateral ventricle (Fig. 4). Excision of these lesions is carried out through a posterior parietal cortical incision exposed by parietotemporal craniotomy. If the cerebral cortex has not been reduced in thickness appreciably by dilatation of the ventricles, it may be wisest to remove a cone of tissue 2–3 cm. in diameter down to the ventricle.

The tumor usually lies free within the lumen of the ventricle and is al-
ways attached of course to the choroid plexus, usually at the glomus (Fig. 4). It may be attached by light adhesions to the ependyma elsewhere. Occasionally the tumor protrudes subependymally into the substance of the parietal, temporal, or occipital lobe. This has been true particularly in those in which there has been associated formation of porencephalic cyst within the cerebral substance.

In removal of these tumors, an attempt is made to mobilize the mass and secure its blood supply from the choroid plexus promptly. As soon as this is accomplished, the tumor shrinks markedly in size and usually can be removed intact. It is important not to get into the tumor itself before dividing its pedicle, as bleeding will be difficult to manage. Intraventricular hemostasis should be perfect before the closure is carried out. The ventricular system is filled with physiological saline solution to support the brain before closure of the dura mater is performed. Patients should be protected during the operative and postoperative period with anticonvulsant therapy. Hypertermia may be a postoperative problem as with any intraventricular operation, particularly if hemostasis has not been accurate. There ordinarily is an immediate return to normal cerebrospinal fluid pressures if no postoperative complications occur.

**PATHOLOGY**

These tumors, when in the lateral ventricle, usually have grown to large size before diagnosis is made. In our series they have been roughly globular, 4–7 cm. in diameter, and conforming usually to some extent to the contours of the enlarged ventricle (Fig. 6). The surface is pinkish-purple or gray and roughly irregular, resembling a cauliflower. The tumor is soft, very vascular, and is contained within a thin transparent capsule. Although calcification has been reported in adults, it has not been seen in sections of the tumors in the present series except in the tumor removed from the 8-year-old child. The benign tumors do not invade neural tissue, but may displace it and come to lie partially within the confines of the cerebral hemisphere. One patient in this series exhibited seeding to distal ependymal surfaces.

Microscopically the cellular pattern is that of the normal choroid plexus itself (Fig. 7). There is a single layer of columnar or cuboidal epithelium supported by a vascular connective-tissue stroma. Russell pointed out that the epithelial cells of a papilloma are devoid of cilia and blepharoplasts and thus are distinguishable from those of a papillary ependymoma.

Malignant changes in these tumors, though rare, occur unmistakably (Fig. 8). These consist, first, in obvious invasion of the surrounding neural structures, at which points the characteristic pattern of papillary growth is lost and, secondly, in the appearance of malignant features within the epithelial cells themselves, namely, variation in size and shape of cells, and variation in the appearance of nuclei and frequent occurrence of mitotic activity.
In 5 tumors of this group there were malignant histological changes consisting of mitotic activity and evidence of invasion, and in 1 case there was seeding to other ventricular surfaces. There was no seeding found at autopsy in the patients with benign tumors who died, nor at operation in those who survived.

A few patients reported in the literature with malignant papillomas have survived for years after operation, and a few with apparently benign tumors who died following operation showed distant seeding. Both Herren and Norlén considered that the tumor seemed to be more malignant in its characteristics of local growth in children than in adults, even though benign histologically. In the literature, seeding was reported in 6 cases, 5 of them of benign papillomas and 1 of a tumor that had undergone malignant change.

RESULTS

Of the 15 patients who were operated upon, 3 died during the immediate postoperative period (Fig. 9). Two of them were moribund on admission and
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constituted extremely poor operative risks. One of these (Case 8) was a 20-month-old infant whose tumor was malignant histologically and invaded the surrounding brain in all directions; the patient died during a second attempt to remove the tumor. The second of these severely ill patients was a 4-month-old infant (Case 4) who also had an invasive malignant tumor with seeding to the meninges; this patient died 2 weeks following operation (Fig. 10). The third operative fatality was that of a 14-month-old infant (Case 6) whose tumor was removed totally from the fourth ventricle without untoward incident. However, the patient died 1 week postoperatively from massive hemorrhage from an acute duodenal ulcer. A fourth patient (Case 3), in whom two unsuccessful attempts were made to remove an invasive tumor of the choroid plexus, died 5 months later from extension of the lesion. One patient (Case 2), a 7-month-old infant, was critically ill at the time of hospital admission and although air studies revealed a tumor within the left lateral ventricle, death occurred rapidly before the patient’s condition could be improved sufficiently to warrant an attempt at excision.

The remaining 11 patients of this series survived operation and are still alive with the possible exception of 1 patient (Case 1) who was developing well 9 months after excision of a benign papilloma but has since been lost to all follow-up. Four patients (Cases 5, 9, 10 and 11), who have been followed from 2 to 7 years since operation, are alive and well but are mildly
Case 8. Malignant tumor of choroid plexus in 20-month-old infant. Above: Low-power photomicrograph shows invasion of tumor into surrounding cerebral tissue. Below: High-power photomicrograph shows (1) loss of normal choroid-plexus pattern, (2) mitotic activity, (3) variation in size of cells and nuclei, and (4) clumps of cells suggesting tumor emboli.
Summary of the results of surgical treatment of 24 children collected from the literature and 15 children from The Children's Medical Center.

to severely retarded mentally (Fig. 11). In all of these patients physical growth is apparently normal. Three additional patients (Cases 5, 12 and 13), who have been followed an average of 3 years since operation, appear normal in both mental and physical development (Fig. 12). Another patient (Case 14), who has been followed 2 years since operation, is developing normally mentally and physically but has petit mal seizures which are controlled satisfactorily with anticonvulsant medication. An additional patient (Case 15) has been followed a little more than a year with normal development.

Fig. 9. Summary of the results of surgical treatment of 24 children collected from the literature and 15 children from The Children's Medical Center.

Fig. 10. Case 4. Postmortem appearance of malignant tumor of choroid plexus in left lateral ventricle of 4-month-old infant who died 2 weeks after surgical exploration. The extreme degree of diffuse hydrocephalus as well as the normal-appearing choroid plexus in the opposite lateral ventricle are well shown.
in all respects. The last patient (Case 16) operated upon has been followed for 9 months; this patient has a mild spastic hemiparesis which is still improving and an homonymous hemianopia, but is otherwise asymptomatic and developing well.

In all but 1 of the living patients, it was felt at the time of operation that total excision of the tumor had been accomplished. There was no operative mortality in this series of patients in any of those having benign, non-invasive tumors except the infant (Case 6) with the tumor of the fourth ventricle who died of the bleeding Cushing-Rokitansky ulceration of the duodenum. A high proportion of the surviving patients have had one or more convulsive seizures, and it is recommended that all patients be protected during the immediate postoperative period with anticonvulsant medication.
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Fig. 12. Case 12. Upper left: Posteroanterior ventriculogram of 3½-month-old infant showing large intraventricular tumor, hydrocephalus, and separation of cranial sutures.
Lower left: Lateral roentgenogram at 3 years of age showing normal skull with no further evidence of increased intracranial pressure.
Right: Appearance of patient at 3½ years of age. Normal mental and physical development.

ROENTGEN-RAY THERAPY

In 3 patients of this series, deep roentgen-ray treatment was given in the amount of 3600 r to the area of the tumor and meninges. In 2 of the radiated patients, the tumor had proved widely invasive at operation and could not be removed totally. One of these died 5 months after operation (Case 3) and the other (Case 5) was alive and well 3 years after treatment, the only patient with malignant changes in the tumor to survive. The usefulness, if any, of roentgen-ray therapy in malignant papillomas of the choroid plexus is certainly not clear either from our experience or that reported in the literature. There would seem to be no indication for its use in cases of ordinary papilloma showing no malignant-cell changes microscopically. Total surgical removal here should be performed. In the in-
vasive tumors with histological evidence of rapid growth, or seeding from the parent lesion, roentgen-ray therapy is at least indicated theoretically.

Butterfield claimed that roentgen-ray treatment reduced the size and vascularity of a benign papilloma so that at a second operation he was able to remove the tumor intact. Vraa-Jensen employed roentgen-ray therapy following recurrence of a benign papilloma which became malignant. The tumor continued to grow and metastasized to lungs and pleura. In reviewing the literature, these appeared to be the only instances in which roentgen-ray therapy was used in children. Most authors expressed the opinion that radiation was of no value.

DIFFERENTIAL DIAGNOSIS

The variety of intraventricular tumors occurring in childhood is not great. There may be no way of differentiating a papilloma of the choroid plexus from other lesions occurring within the lateral ventricle until operation is performed. The most significant finding pointing toward a papilloma of the choroid plexus preoperatively is the combination of communicating hydrocephalus, xanthochromic ventricular fluid and a unilateral intraventricular mass.

Ependymoma constitutes a much more common intraventricular tumor in childhood than papilloma of the choroid plexus. Sometimes it can be differentiated only by microscopic study. An intraventricular ependymoma, however, usually causes an obstructive type of hydrocephalus involving only part of the ventricular system rather than the diffuse, communicating variety that occurs with papilloma. Calcification has occurred frequently in supratentorial ependymomas in children in our experience but never in papillomas.

Hemangiomas of the choroid plexus are said to be the only other intraventricular tumors capable of causing an increased production of cerebrospinal fluid and communicating hydrocephalus. There would seem to be no way to differentiate such a lesion from a papilloma except by pathological examination. Only a few cases have been reported in the literature.

Gangliogliomas occurring in the lateral ventricle have been seen at least 5 times in our experience in children. These usually have been associated with intracranial calcification and with an obstructive local hydrocephalus rather than the communicating variety. There usually have been other stigmata of tuberous sclerosis also in these patients.

Other rare tumors of the choroid plexus that have been reported include sarcomas, chondromas, myxomas and mixed tumors. These have seldom occurred in children.

Colloid cysts of the third ventricle occur chiefly in adults and have a characteristic clinical picture of intermittent increased intracranial pressure as well as a characteristic roentgen-ray picture on ventriculography. We have seen one colloid cyst of the third ventricle in a child of 11 years.

No report of metastatic carcinoma occurring in the choroid plexus of children could be found. van Hoytema and Wincke stated that the tumors
most likely to metastasize to the choroid plexus in children are Wilms's tumor, retinoblastoma and neuroblastoma.

Dyke\textsuperscript{17} reported 6 cases in adults of a mass in the area of the glomus of the choroid plexus within the lateral ventricle on ventriculography. These proved to be hematomas within the normal choroid plexus or local edema from the trauma of ventricular cannulation.

**DISCUSSION**

It is evident from our experience and review of the literature that in children papillomas of the choroid plexus occur mainly in the lateral ventricles, occasionally in the fourth ventricle and rarely in the third (Fig. 13).
times by roentgen-ray examination and sometimes by surgical or postmortem visualization. In a certain number of patients the hydrocephalus can be explained by the presence of the papilloma obstructing one foramen of Monro or the lumen of the third or fourth ventricle (Fig. 5). In a majority of instances of papilloma of the lateral ventricle, however, there is dilatation of all the ventricles and of the basilar cisternae without apparent obstruction to circulation or absorption of the cerebrospinal fluid (Fig. 4). Goodhart\textsuperscript{23} appears to be the first to have postulated that hydrocephalus was caused by increased production of fluid by the papilloma, and this view has been expressed by many subsequent authors. The demonstration by Ray and Peck\textsuperscript{18} of excessive formation of cerebrospinal fluid by this tumor in a patient who had a lumbar-ureteral shunt, and also the evidence cited by others\textsuperscript{20,29} of regression of hydrocephalus following operative removal of these tumors, provides excellent support, certainly, for this argument. Vigouroux\textsuperscript{63} reported an interesting patient who demonstrated a flow of 800 cc. of cerebrospinal fluid daily through a fistula from his ventricular system to his nasal cavity. Autopsy proved the presence of a papilloma of the choroid plexus. Laurence\textsuperscript{24} cited two informative experiences. The first concerned an 8-month-old child with severe hydrocephalus which had been rapidly progressive for 2 months. At autopsy there was diffuse hydrocephalus of all ventricles with dilatation also of the basilar cisternae and subarachnoidal pathways of the surface. Both choroid plexuses showed marked hypertrophy to 15 times that of normal weight. The second was a 15-month-old child with symmetrically dilated ventricles and basal cisternae by ventriculography; 300–400 cc. of cerebrospinal fluid were removed daily for 5 days until the child died. At necropsy a large papilloma of the choroid plexus was found in the right lateral ventricle. The subarachnoidal spaces of the surface were wider than normal and there was no obstruction.

Unfortunately, accurate clinical measurements under physiological conditions of the amount of cerebrospinal fluid formed daily in a patient with a papilloma of the choroid plexus in comparison with the amount in a normal patient are not available. Certainly a papilloma of the choroid plexus increases vastly the epithelized surface area in contact with the reservoirs of cerebrospinal fluid within the ventricular system.

Russell,\textsuperscript{51,52} on the other hand, suggested the necessity for considering alternative possibilities that must be excluded before attributing hydrocephalus to overactivity of the tumor. Because of the high incidence of xanthochromic cerebrospinal fluid, it seems probable that spontaneous hemorrhage must be a frequent complication of these tumors. Such bleeding, she pointed out, might be expected to initiate a low-grade basal leptomenigitis or ependymitis or both, which might be responsible for interruption of normal circulation or absorption of cerebrospinal fluid.

It is our feeling that the prompt and persistent relief of hydrocephalus following successful removal of a papilloma of the choroid plexus in 11 of
our 16 patients is rather overwhelming evidence against there being any obstruction of the surface subarachnoidal pathways of significance and in favor of the overproduction of fluid by the tumor as the sole cause of the communicating hydrocephalus.

Many patients have shown some edema of the brain adjacent to the tumor, and in 2 patients in this series the degree of edema was very marked. In 3 additional patients, as previously noted, there were large cysts in the cerebrum communicating with the lateral ventricle that contained the tumor. Davis and Cushing postulated that small cystic areas occurring in this tumor were caused by blocking of secretion of fluid from a local area of tumor that was being pressed against brain tissue by the increased pressure. No large cystic areas within brain substance have been reported previously in patients with papillomas of the choroid plexus. Their occurrence could be the result of blocking off of a portion of the lateral ventricle by the tumor, causing fluid to accumulate and force itself over a long period into an area of soft edematous brain. In retrospect, in the 2 patients in this series incorrectly diagnosed by ventriculography as having porencephalic cysts, the correct diagnosis should have been suggested by the combination of xanthochromic cerebrospinal fluid with a content of elevated total protein under increased pressure in patients with an enlarged head.

Gross and Ingraham and Matson have pointed out the difficulties in diagnosis of intracranial tumors during the first years of life. As a result of separation of the cranial sutures associated with increased intracranial pressure, symptoms are less severe than in adults and focal signs are often completely absent. In infants, any history at all is usually of short duration. The index of suspicion among young children with hydrocephalus must be high, and although papilloma of the choroid plexus is a rare cause of hydrocephalus in early life, it is one that must be thought of preoperatively and one in which only surgical removal of the tumor can provide a satisfactory outcome. Several writers have emphasized the need to carry out investigation of all infants with hydrocephalus to the extent of satisfactory ventriculography, and this is stressed here again. Certainly the earliest possible detection of this lesion before spontaneous hemorrhages have occurred, before hydrocephalus has become extreme and produced irreversible brain damage, and before the tumor itself has become excessively large, allows the best opportunity for a favorable result from surgical treatment.

SUMMARY

1. Sixty-seven cases of papilloma of the choroid plexus occurring in children under 15 years of age have been collected from the literature and reviewed briefly. Of these, 24 patients were operated upon with 13 survivals.

2. The cases of 16 additional children with papilloma of the choroid plexus treated at The Children's Medical Center between 1941 and 1958 are analyzed in some detail. The average age was 16 months. Of these patients,
15 were operated upon. One died without operation, and 4 died postoperatively. Of the 11 surviving patients, 4 are mentally retarded and 7 are developing satisfactorily.

3. In 4 of the 5 fatalities the tumors were malignant and invasive, and could not be excised totally at operation. Of the 11 surviving patients, 10 had a benign well-encapsulated papilloma, whose histological pattern reproduced that of normal choroid plexus.

4. The necessity for adequate ventriculography in all children with hydrocephalus to rule out the possibility of a tumor of the choroid plexus is emphasized.

5. The association of xanthochromic cerebrospinal fluid with a content of elevated total protein and the presence of hydrocephalus should suggest the diagnosis of papilloma of the choroid plexus.

6. Pneumographic demonstration of an intraventricular mass in the presence of communicating hydrocephalus is pathognomonic of this tumor. However, this combination of findings was present in only 50 per cent of patients. Large cysts were seen in the cerebrum adjacent to the lateral ventricle containing the papilloma in 3 of the 16 patients.

7. The treatment of this tumor is total surgical excision. Roentgen-ray therapy has been employed in malignant invasive lesions but its value is not clear.

8. The prompt and permanent relief of communicating hydrocephalus in all patients in whom a papilloma of the choroid plexus was removed successfully from a lateral ventricle would seem to be strong evidence that hydrocephalus was caused solely by overproduction of cerebrospinal fluid by the tumor and not by any associated obstruction of subarachnoidal pathways of the surface.

PROTOCOLS

Case 1. CMC #255853. R.S., an 8-month-old male, had convulsions gradually increasing in frequency for 5 months previous to admission. Prenatal and birth histories were normal.

Examination: He was a well-nourished happy baby with a head slightly smaller than normal, closed fontanelle, hyperactive reflexes and bilateral sustained ankle clonus. Lumbar puncture showed clear fluid under normal pressure, with a normal value of total protein. Ventriculogram showed a normal ventricular system without evidence of block and a mass in the right lateral ventricle. There was evidence of some cerebral atrophy.

At operation a papilloma of the right choroid plexus was removed.

Nine months later he was doing well, generally, and his petit mal attacks were well controlled by medication. He has been lost to further follow-up evaluation.

Case 2. CMC #271958. L.B., a 7-month-old female, had periodic vomiting for 1 month and increasing drowsiness and enlarging head for 2 weeks.

Examination: She was a very irritable well nourished, well developed infant with an enlarged head and bulging fontanelle. Craniotabes and beading of the ribs were present. The reflexes were increased and ankle clonus was present. There was in-
ternal strabismus. Ventricular tap yielded xanthochromic fluid under increased pressure with increased total protein of 530 mg. per cent. Pneumoencephalogram showed communicating hydrocephalus with a mass in the left lateral ventricle.

A diagnosis of possible tumor of the left choroid plexus was made; however, her condition had become rapidly worse and she died without operation being performed.

Autopsy showed a large papilloma of the choroid plexus of the left lateral ventricle.

Case 3. CMC #283392. D.D., a 2-year-old female, was noticed to have an unsteady gait 2 months prior to admission. Ataxia progressed until she was unable to walk. Vomiting occurred periodically. She had swelling of the right eye and arm for 1 week.

Examination: She was an irritable, restless child with an enlarged head and edema of the left optic disc. Reflexes were normal except for an up-going toe on the left. A small amount of bloody fluid was obtained on right ventricular puncture. Xanthochromic fluid under increased pressure of 200 mm. H₂O and with an elevated total protein of 162 mg. per cent was obtained from the left lateral ventricle. Ventriculogram showed dilatation of both lateral ventricles with shift to the left and a large mass filling the posterior part of the right lateral ventricle.

It was impossible to remove all of this highly malignant tumor of the choroid plexus on two attempts as it invaded the brain in all directions.

The patient died 5 months later because of widespread extension of the lesion.

Case 4. CMC #296810. N. L., a 4-month-old female, was admitted with the chief complaint of enlarging head of 5 weeks' duration. Occasional convulsions had occurred for 2 months.

Examination: She was a healthy looking baby with enlarged head, tense fontanelle and separated cranial sutures. Present were positive Babinski's signs and blurring of the left optic disc. Combined lumbar and ventricular taps showed a communicating hydrocephalus with a mass in the left lateral ventricle.

At operation it was impossible to remove the tumor which was found to invade the cerebrum in all directions.

The patient died 2 weeks following operation. Autopsy showed a malignant invasive tumor of the choroid plexus with seeding over the meninges of the brain (Fig. 10).

Case 5. CMC #307652. K. L., a 9-month-old male, had increasing lassitude, instability and periodic vomiting for 1 month. Two days before admission fever and convulsions developed.

Examination: He was a comatose baby with high fever, clonic convulsive movements of the arms and spastic extension of the legs. The head was large with a bulging fontanelle and separated cranial sutures. There was bilateral papilledema. Ventricular fluid was xanthochromic under increased pressure of 450 mm. H₂O and total protein level was 140 mg. per cent. Ventriculogram showed hydrocephalus. Patient was considered to have cerebellar tumor and suboccipital exploration was about to be carried out when a severe chill caused postponement of the operation. Ventriculograms were repeated subsequently and showed communicating hydrocephalus with a large mass in the left lateral ventricle.

At operation a malignant papillary tumor of the choroid plexus filled the left lateral ventricle. It was thought impossible to remove the tumor completely where it
seemed to invade surrounding brain tissue. In reviewing all the evidence now it seems probable that this tumor must have been removed completely.

Postoperatively the patient received roentgen-ray therapy (3600 r) to the brain and spinal cord. He made a good recovery with normal physical and mental development. He was reported to have some difficulties during his first year at school but was well 3 years later.

Case 6. CMC #335735. P. S., a 14-month-old boy, was admitted because of vomiting, listlessness and loss of weight of 2 months' duration.

Examination: He was a dehydrated, listless child with an enlarged head. No other abnormality was noted. The cerebrospinal fluid was xanthochromic with a total protein of 122 mg. per cent and a pressure of 300 mm. H2O. Ventriculogram showed dilatation of all ventricles, especially the fourth, with a block at that site (Fig. 5).

At operation a papilloma of the choroid plexus of the fourth ventricle was removed completely.

The patient died 1 week after operation from a bleeding duodenal ulcer. At autopsy there was no gross evidence of tumor in the fourth ventricle.

Case 7. CMC #369783. C. D., a 6-month-old girl, was admitted because of vomiting for 3 days following a fall. She was well previously.

Examination: She was a healthy baby with an enlarged head, bulging fontanelle, right internal strabismus and stiff neck. The cerebrospinal fluid pressure was increased to 400 mm. H2O and the fluid was xanthochromic with a total protein of 97 mg. per cent. Ventriculograms showed severe communicating hydrocephalus with a mass in the right lateral ventricle (Fig. 4).

A large papilloma of the choroid plexus was removed (Fig. 6).

A 2-year follow-up showed the child to be mentally retarded and in a state institution.

Case 8. CMC #376296. S. M., a 20-month-old female, had progressive weakness of the right leg and incoordination in the right arm of 3 weeks' duration. She was drowsy and lethargic. She had a squint of 1 week's duration.

Examination: She was a well developed, well nourished, irritable, acutely ill child with an enlarged head and bulging anterior fontanelle. The left pupil was slightly smaller than the right but both reacted sluggishly to light. There was marked bilateral papilledema. There was marked weakness of the right arm and leg with hyperactive reflexes on the right, ataxia of right arm and a positive Babinski's response on the right. Xanthochromic cerebrospinal fluid under increased pressure of 200 mm. H2O with a total protein of 80 mg. per cent was found on lumbar puncture. Ventriculogram showed moderate dilatation of the lateral ventricles and third ventricle with a shift to the right. There was a large mass filling the posterior part of the left lateral ventricle.

Two attempts were made to remove an extremely large malignant papillary tumor of the choroid plexus, which was invading the brain in all directions.

The patient died during the second operation. Autopsy showed residual tumor and dilatation of the third and fourth ventricles.

Case 9. CMC #378515. C. T., a 3-week-old male, who was delivered by caesarian section 5 weeks prematurely, had an enlarging head since birth.

Examination: He was a thin infant with an enlarged head, bulging fontanelles and separated sutures. Combined lumbar and ventricular taps showed a block of the
cerebrospinal fluid. The ventricular fluid was xanthochromic under increased pressure of 200 mm. H2O with an elevated total protein of 180 mg. per cent. Ventriculogram showed internal hydrocephalus, a large right porencephalic cyst and a shift of the ventricles from right to left. No tumor mass was seen.

At operation for the porencephalic cyst a reddish vascular tumor was seen in the floor of the cyst arising from the choroid plexus of the right lateral ventricle. The large tumor, a benign papilloma, was removed (Fig. 6).

A 7-year follow-up shows he is normal physically but is mentally retarded and attends a school for special students. His petit mal seizures are controlled partially by medication.

Case 10. CMC #408252. E. B., a 3-month-old female, was admitted because of an enlarging head. A bulging fontanelle had been noted for 2 months and the enlarged head for 3 weeks.

Examination: She had an enlarged head, bulging anterior fontanelle and separated cranial sutures. The remainder of the findings were normal. Combined lumbar and ventricular taps yielded xanthochromic cerebrospinal fluid under increased pressure and there was no block. Ventriculogram showed hydrocephalus and a large left porencephalic cyst. Left carotid arteriogram confirmed these findings.

At operation a large porencephalic cyst was entered that did not connect with the lateral ventricle. On entering the ventricle, a large tumor of the choroid plexus was found (Fig. 6). This was removed at a second operation. A communication was left between the cyst and the lateral ventricle.

The patient was readmitted 3 months later because the head was enlarging again. At operation the ventricles were normal but there was a very large subdural collection of fluid with an adherent inner membrane which was left intact. A left subdural-peritoneal shunt was performed.

Five-year follow-up has showed normal physical growth, moderate mental retardation and petit mal seizures which are fairly well controlled by medication (Fig. 11).

Case 11. CMC #411639. R. W., a 10-month-old male, had progressive enlargement of the head from birth. He did not sit up or grasp at things.

Examination: He was an apparently blind baby with an enlarged head, bulging fontanelle and bilateral internal strabismus. Lumbar and ventricular tap showed no block. The cerebrospinal fluid was xanthochromic under pressure of 120 mm. H2O and with total protein of 19 mg. per cent. Ventriculogram showed communicating hydrocephalus with a mass in the right lateral ventricle.

At operation the glomus of the choroid plexus was enlarged and contained a tumor nodule. This was removed.

Four-year follow-up shows no increase in his hydrocephalus but he is mentally retarded and partially blind. His petit mal seizures are fairly well controlled on medication.

Case 12. CMC #442878. T. M., a 3½-month-old male, was hospitalized because of vomiting for 8 days.

Examination: He was a very active, irritable infant with enlarged head and bulging fontanelles. Lumbar and ventricular combined tap showed no evidence of block. The cerebrospinal fluid was xanthochromic under increased pressure of 300 mm. H2O with an elevated total protein of 460 mg. per cent. Ventriculogram showed
communicating hydrocephalus with slight shift of the ventricles from left to right. A large mass was seen in the left lateral ventricle (Fig. 12).

At operation a well encapsulated benign papilloma of the left choroid plexus was removed (Fig. 6).

A 3-year follow-up shows normal physical and mental development; he has had one postoperative grand-mal convulsion at the time of an upper respiratory infection with fever (Fig. 12).

Case 13. CMC #446545. M. L., a 3-year-old male, was noticed to have an enlarged head 3 weeks prior to hospitalization. He was slow to sit up and did not walk until 18 months of age. He had been irritable for 1 year. He also had some vomiting and lethargy during the 3 weeks prior to admission.

Examination: He was a well developed, well nourished child with an enlarged head. Ventricular fluid was clear with a pressure of 130 mm. H₂O and with an increased total protein level of 188 mg. per cent. Ventriculogram showed communicating hydrocephalus with a mass in the atrium of the right lateral ventricle.

At operation a large benign papilloma of the choroid plexus was removed intact.

A 3-year follow-up has showed him to have normal physical and mental development.

Case 14. CMC #463417. A. Y., a 2-month-old female, had an enlarged head, increasing listlessness and vomiting of 1 week's duration.

Examination: She was a well developed, well nourished lethargic baby with an enlarged head and bulging fontanelles. The eyes deviated to the left and there was slight nystagmus. Reflexes were hyperactive bilaterally. Left ventricular tap was unsuccessful. On the right the fluid was under pressure of over 400 mm. H₂O with an increased total protein level of 189 mg. per cent. Ventriculogram showed air in a dilated right lateral ventricle which was shifted to the right, indicating an expanding lesion in the left cerebrum.

At operation a benign papilloma of the choroid plexus was removed intact from the left lateral ventricle. Marked edema of the surrounding cerebrum was found.

Two-year follow-up has shown normal mental and physical development. She has slight right-sided weakness and petit mal attacks which are well controlled on medication.

Case 15. CMC #469136. J. T., an 8-year-old male, had increasing headaches for 5 days. Two days prior to admission he became lethargic and vomited several times.

Examination: He had normal development and nutrition. He was drowsy and had slight ataxia on walking. He had bilateral papilledema with early acute hemorrhages. The ventricular fluid was xanthochromic, under increased pressure, with an elevated total protein value of 43 mg. per cent. Ventriculogram showed a single dilated lateral ventricle.

At operation no tumor was found in the left lateral ventricle. A window was cut through the septum pellucidum and a papilloma of the choroid plexus of the right lateral ventricle prolapsing into the foramen of Monro was removed intact.

One-year follow-up shows normal physical and mental development.

Case 16. CMC #479134. A. A., a 6-month-old female, was noticed to have an enlarged head 2 weeks prior to admission and increasing drowsiness for 4 days.

Examination: She was a well developed, well nourished infant who was irritable when aroused. She had an enlarged head, bulging anterior fontanelle, bilateral
papilledema and possible weakness of the left 6th cranial nerve. Ventricular fluid was clear under increased pressure of over 600 mm. H₂O, and raised total protein value of 69 mg. per cent. Ventriculogram showed communicating hydrocephalus with a mass in the posterior portion of the left lateral ventricle. A porencephalic-like cyst was also visible on the left, posteriorly.

At operation the cyst was found to be a very dilated occipital horn of the left lateral ventricle. A papilloma of the choroid plexus of the left lateral ventricle was removed intact.

Nine-month follow-up shows a right homonymous hemianopia and a slight right spastic hemiparesis. Mental and physical development appear to be normal.

REFERENCES

PAPILLOMA OF CHOROID PLEXUS IN CHILDHOOD


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