THE RADIOLOGICAL APPEARANCES OF AGENESIS OF THE CORPUS CALLOSUM

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The first case of agenesis of the corpus callosum was reported by Reil in 1812. Eighty-two cases, in which the condition was encountered incidentally at necropsy, were collected from the literature up to 1933 by Baker and Graves.

Despite the introduction of pneumo-encephalography by Dandy in 1918 it was not until 1934 that Davidoff and Dyke established its value in the diagnosis of agenesis of the corpus callosum. In the first of three cases described by these authors the pneumo-encephalogram was interpreted as showing a cyst of the septum pellucidum. However, at necropsy, following a craniotomy, complete agenesis of the corpus callosum was found. The diagnosis is now usually made on the encephalographic findings, and Davidoff and Dyke (1934) enumerate the following diagnostic points: (1) marked separation of the lateral ventricles; (2) angular dorsal margins of the lateral ventricles ("bicornuate" appearance of Hyndman and Penfield, 1937); (3) concave medial borders of the lateral ventricles; (4) dilatation of the posterior horns of the lateral ventricles; (5) enlargement of the interventricular foramina; (6) dorsal extension and dilatation of the third ventricle; (7) a radial arrangement of the medial cerebral sulci around the roof of the third ventricle and extension of these sulci through the zones normally occupied by the corpus callosum.

In 1937 Hyndman and Penfield reported a series of five cases in which pneumo-encephalograms had been performed, and confirmed the importance of the above criteria. They consider that the bicornuate appearance of the lateral ventricles, together with the raised roof of the third ventricle, are diagnostic, but Bunts and Chaffee (1944) in a review of the encephalographic appearances of all published cases, find that while the third ventricle is always raised, the bicornuate shape is not constant.

Hyndman and Penfield also describe the appearances which they consider to be due to partial

agenesis and which they call "fish-tailing" of the posterior part of the third ventricle. It may be doubted, however, whether this is anything more than enlargement of the suprapineal recess of the third ventricle (Robertson, 1946) and is thus quite independent of the condition of the corpus callosum itself (Fig. 1). If, however, it is indicative of partial agenesis this condition must be much more common than is suspected, since the appearance is found fairly frequently by chance in otherwise normal ventriculograms and encephalograms.

Since then over 20 cases have been reported in

FIG. 1.—Erect lateral film of an encephalogram on a patient with a temporal lobe abscess.

A chance finding was the very large suprapineal recess which reaches up between the lateral ventricles. (Part of the third ventricle is covered by a burr-hole and the abscess cavity contains thorotrast.)

which the diagnosis has been based on pneumo-encephalographic criteria.

The appearances seen in carotid angiograms in this condition have not previously been reported. In the two cases presented the angiograms showed signs which are probably diagnostic. The position and course of the anterior cerebral artery were unusual and reflected the absence of the corpus callosum. The ascending part of the anterior cerebral artery ran almost directly upwards (Fig. 2a) and then the artery bent sharply backwards. This occurred at a much lower level than in a normal case, and the curve as the artery turned round the genu was absent. The remainder of the course of the pericallosal artery lay immediately above the roof of the third ventricle (Fig. 4). This was in contrast to the normal condition in which the pericallosal artery lies above the corpus callosum and is about 2 cm. superior to the roof of the third ventricle.

The internal cerebral vein lay higher than usual and was also above the roof of the third ventricle. The normal curve of the great cerebral vein was greatly diminished and was situated above and in front of its usual position (Fig. 2c).

In one case the anterior cerebral artery followed a very irregular, wavy course in the antero-posterior views, possibly due to absence of "splinting" by the corpus callosum, but it did not cross the midline (Fig. 2b). In the second case the artery ran a much straighter course in the antero-posterior view

Case Histories

Case 1 (R.I.85311).—This patient, a man aged 28, was admitted to the Radcliffe Infirmary in August, 1950, with a history of fits since the age of 10. They were preceded by an unpleasant sinking feeling in the epigastrium. This was followed by a twitching in the left arm and left leg for about one minute. In the past he had had occasional attacks involving the right side of the body. No loss of consciousness occurred and he understood what people were saying during an attack, though he was unable to speak until it had ended. He had been given anticonvulsant drugs since a few months after the onset of the first fit.

There was nothing relevant in the past personal or family history.

Clinical examination revealed a fit looking, well grown, selfconscious young man. He appeared mentally normal at interview, and psychometric tests revealed no definite impairment, though he seemed to lack any real ambitions and interest in life, and appeared to be very dependent on his parents. The central nervous system was normal, apart from some astereognosis of the left hand. No other clinical abnormality was present.

Straight radiographs of the skull were normal. Examination of the cerebrospinal fluid showed it to be under normal pressure, with a protein content of 150 mg./100

ml. and a Lange curve of 1122111100. The serum and cerebrospinal fluid Wassermann and Kahn reactions were negative. The electro-encephalogram showed a precisely localized spike focus in the right precentral region, with an anterior bilateral dysrhythmia.

A lumbar air encephalogram (Figs. 3a and b) showed the points described by Davidoff and Dyke (1934) apart from the radiate arrangement of the medial sulci, which were not examined. The inner borders and the bodies of the lateral ventricles were concave and greatly separated, and the superolateral angles were pointed. There was marked enlargement of the posterior portion of the bodies and posterior horns.

The third ventricle was dilated and its roof was raised to a level only 1 cm. below that of the superolateral margins of the lateral ventricles. The floor, antero-inferior recesses, and anterior wall looked normal (Figs. 3a and b). The region of the pineal body was not well shown, and thus the relationship of the suprapineal recess to the great cerebral vein could not be demonstrated. The foramina of Monro were very large.

In view of the high cerebrospinal fluid protein, the possibility of a neoplasm, for example, lipoma or meningioma, associated with an agenesis was considered, and ventriculograms were therefore also done. However they showed no evidence of a space-occupying lesion.

A right percutaneous common carotid angiogram performed by Dr. Ingmar Wickbom showed that the anterior cerebral and pericallosal arteries ran a very irregular and wavy course. The normally well marked curve of the pericallosal artery passing round the genu of the corpus callosum was absent and was replaced by a sharp kink as the artery turned posteriorly (Fig. 2a). The horizontal portion was low, and was shown to lie immediately above the roof of the third ventricle (Fig. 4). In the antero-posterior arteriogram the anterior cerebral and pericallosal arteries ran a very irregular, loose course always in or just to the right of the midline (Fig. 2b).

The internal and great cerebral veins were shown well in the first and second phlebograms (taken four and eight seconds after the beginning of the injection of 10 ml. of 35% solution of diodone). These were very high in position. The curve of the great cerebral vein, usually caused by passing round the splenium of the corpus callosum, was greatly diminished so that the vein was shortened in the infero-posterior direction. The origin of the straight sinus was not accurately visualized (Fig. 2c).

Other vessels appeared normal in all phases.

Case 2.—This patient, E. B., a man aged 24, was first seen in December, 1950. He gave a five-month history of repeated focal motor cerebral seizures involving the left side of the body. The attacks were always followed by a very transient weakness and numbness involving the left side of the body. He was otherwise symptom-free apart from occasional headaches.

There was nothing relevant in the past personal or family history.

FIG. 2a.—Case 1 : lateral arteriogram. The anterior cerebral artery runs straight up and then turns sharply posteriorly instead of curving smoothly round the genu of the corpus callosum.

FIG. 2b.—Case 1 : A. P. arteriogram showing the wavy, "wandering" course of the anterior cerebral and pericallosal arteries.

FIG. 2c.—Case 1 : lateral phlebogram showing lack of curvature and high position of the internal and great cerebral veins.

FIGS. 3a and b.—Case 1 : A. P. and lateral views of encephalogram. The roof of the third ventricle is considerably raised and lies between the bodies of the lateral ventricles, which are widely separated. The outer angles of lateral ventricles are angulated.

FIG. 4.—Case 1 : a composite drawing showing the relationship of the anterior cerebral and pericallosal arteries to the roof of the third ventricle.

Examination of the central nervous system revealed no abnormality apart from minimal pyramidal signs in the left upper and lower limbs in the form of increased tendon reflexes. There was no evidence of any mental impairment. No other clinical abnormality was detected.

Straight radiographs of the skull were normal. The serum and cerebrospinal fluid Wassermann reactions were negative. The cerebrospinal fluid was under normal pressure with a normal protein content.

An electro-encephalographic tracing showed a good deal of generalized theta activity which was most persistent in the right temporal region and was increased by hyperventilation.

A right internal carotid angiogram showed appearances mainly similar to those reported in the previous case. There was, however, one difference, in that the anterior cerebral and pericallosal arteries ran a much straighter course in the antero-posterior arteriograms. (The lateral films have been lost and cannot be reproduced.)

An air encephalogram subsequently carried out showed marked dilatation and upward extension of the third ventricle, which looked normal in its lower part (Figs. 5a and b). The lateral ventricles were thrust

apart from above, the medial surfaces were concave, the superomedial angles pointed, more so on the left side (Fig. 5a), and the bodies were dilated posteriorly.

In view of the shape of the lateral ventricles and the high position of the roof of the third ventricle, it was considered that this could only be a case of agenesis of the corpus callosum.

Discussion

Symptomatology.—It is difficult to assess the symptoms of agenesis of the corpus callosum *per se* because the condition is usually associated with other developmental defects of the brain.

From a review of the literature it seems that the most frequent symptoms are epilepsy and a varying degree of mental impairment. The former symptom was present in both the cases reported in this paper, and both showed slight lateralizing signs but no evidence of mental impairment in either case. However, Cameron and Nicholls (1921) and others consider that even total agenesis is possible without any pathognomonic alteration in physical or mental capacity. Bruce (1889), quoting from his own cases and those of others, stated that when the brain is otherwise well developed there may be "no disturbance of mobility, co-ordination, general or specific sensibility, reflexes, speech, or intelligence". Moreover, Dandy (1931) and others have divided the whole of the corpus callosum in the sagittal plain at operation, and have noted no untoward sequelae.

In the rare cases where the agenesis is accompanied by a tumour of the corpus callosum symptoms are usually present, but these depend on the size and position of the tumour and are not referable to the defect.

Agenesis of the corpus callosum may be associated with extracranial anomalies, such as cleft palate, hare lip, thoracic stomach, and cryptorchidism, but no such abnormalities were found in the cases reported.

Embryology.—The embryology of the corpus callosum and associated structures is of importance in explaining the radiological appearances of agenesis. For this reason it is described at length.

The corpus callosum first appears in the third month of intra-uterine life as a thickening of the lamina terminalis, lying on the dorsal aspect of the hippocampal commissure. The anterior part develops first, and while the initial fibres lie within the limits of the lamina terminalis the corpus callosum gradually increases in size by extending in a cephalic, dorsal, and then caudal direction beyond these limits to form the rostrum and genu. While this is occurring part of the nearby cortex on the medial

FIGS. 5a and b.—Case 2: A. P. and lateral films of encephalogram. The angulation of the superolateral margins of the bodies of the lateral ventricles are well marked.

surface of both cerebral vesicles is cut off by the developing corpus callosum to form the two leaves of the septum pellucidum.

The body of the corpus callosum continues to grow caudally, carrying with it on its under surface the septum pellucidum and the hippocampal commissure. The commissures come to lie in the midline between the two parts of the body of the fornix. The latter is really a paired structure and the position of the hippocampal commissure assists in its fusion. Thus a single midline structure is formed which acts as an additional roof to the third ventricle, the true roof of which is the original epithelial covering of the neural tube. At the same time the corpus callosum invades the upper part of the hippocampal formation, which becomes thinned out on its surface to form the induseum griseum.

Development is not complete until the fifth month. Agenesis may be complete or partial. Partial agenesis, depending on the state at which arrest takes place (Bruce, 1889) varies all the way from the development of only a rudimentary bundle of fibres to a structure which is almost complete, except for a defect in the splenium (Hyndman and Penfield, 1937).

As the corpus callosum extends backwards, the arrangement of the sulci on the medial surface of the cerebral hemisphere changes from the foetal radiate pattern to the normal adult one. In cases of agenesis the radiate pattern persists.

Abnormalities which are found with agenesis of the corpus callosum may be divided into two groups :—

(1) *Directly Consequent upon Under-development of the Corpus Callosum.*—Under-development of the hippocampal commissures and lack of fusion of the crura of the fornix to form the body of the fornix, with consequent elevation of the third ventricle ; dilatation of the posterior part of the bodies and of the posterior horns of the lateral ventricles ; radiate arrangements of the medial sulci ; absence of the septum pellucidum in cases of complete agenesis.

(2) *Due to Under-development of the Brain in General.*—Polygyria, agyria, microgyria, and pachygyria ; absence of the olfactory nerves ; incomplete separation of the frontal lobes ; microcephaly ; porencephaly.

Occasionally agenesis may be accompanied by a lipoma of the corpus callosum or a meningioma. Such new growths filling the defect or replacing part of the corpus callosum are likely to arise from developmental disturbances in the meninges. Thus occasionally even a typical meningioma may arise

at the place of defect. The aetiology of this condition is unknown as is that of many other congenital anomalies.

Differential Diagnosis.—If the radiological appearances of agenesis of the corpus callosum are kept in mind it is unlikely that the abnormality will be missed.

In both the cases reported in the present paper all the criteria of Davidoff and Dyke (1934) were found, with the exception of the radiate pattern of the medial cerebral sulci. Other conditions which may cause confusion are symmetrical tumours of the corpus callosum, notably lipomata, and secondly, cysts and symmetrical tumours of the septum pellucidum.

The most important evidence of a lipoma of the corpus callosum is an area of translucency surrounded by a zone of calcification, situated in the region of the genu, which may be seen on preliminary radiographs of the skull (Sosman, 1946 ; Sutton, 1949). A lipoma is very frequently accompanied by agenesis. Under such circumstances there will be the usual encephalographic signs of agenesis, but the roof of the third ventricle will not be raised as much as usual and will be flattened. The radiological appearances of a lipoma of the corpus callosum without agenesis were described by Mullen and Hannan (1950). The encephalogram showed that the lateral ventricles were dilated, the anterior horns separated by a midline tumour, and the medial borders were concave. The third ventricle was enlarged but the roof was not raised.

Other symmetrical tumours of the corpus callosum are rare. They may cause some concavity of the superior and medial surfaces of the bodies of the lateral ventricles, and possibly angulation of the supero-lateral margins, but the third ventricle will not be raised in position.

Cysts of the septum pellucidum may or may not communicate with the lateral ventricles. A communicating cyst may superficially resemble agenesis of the corpus callosum if the third ventricle is confused with the air-filled cavum septi pellucidi, but in such a case there will be no suggestion of a bicornuate appearance of the lateral ventricles.

Non-communicating cysts cause widening of the septum pellucidum, 3 mm. probably being the upper limit of normal width (Echternacht and Campbell, 1946). The third ventricle is not raised in position, and hydrocephalus may be caused by pressure on the foramina of Monro. While this condition may be confused with a tumour of the corpus callosum or septum pellucidum, it does not resemble agenesis of the corpus callosum.

Agenesis of the corpus callosum should be easily differentiated from above mentioned conditions, provided the position of the third ventricle is well shown.

Symmetrical tumours of the septum pellucidum are also rare. Figs. 6a and b show the appearances of the ventricles found with a longstanding calcified tumour of the septum pellucidum. The nature of this tumour was unverified but was believed to be an oligodendroglioma. In this case the bodies of the lateral ventricles were separated by a midline tumour, which caused a concave filling defect of the medial borders. The superior borders, however, were distended from within, and the supero-lateral margins were rounded in contrast to the angulated appearance found with agenesis of the corpus callosum. Most important was the lack of filling

FIGS. 6a and b.—A. P. and lateral films of ventriculogram of a case of oligodendroglioma of the septum pellucidum showing widening of the septum pellucidum.

The bodies of the lateral ventricles are separated by a midline space-occupying lesion.

The outer angles of lateral ventricles are not angulated as in agenesis of the corpus callosum. The upper part of the third ventricle is considerably depressed.

FIG. 6c.—Tracing of a lateral arteriogram showing how the anterior cerebral artery and pericallosal arteries run a rounded, stretched course in the midline.

of the upper part of the third ventricle due to pressure on the roof by downward extension of the tumour. Percutaneous carotid angiography (Fig. 6c) showed the pericallosal artery to be raised and stretched and the anterior part to be rounded, in contra-distinction to the appearances seen with agenesis of the corpus callosum. This was partly due to a slight degree of hydrocephalus and possibly partly to extension of the tumour into the corpus callosum. There was no lateral displacement. In addition a pathological circulation could be seen on the phlebograms.

Use of Angiography in Differential Diagnosis.

The study of these two cases indicates that angiography should be of help in doubtful cases. Apart from the changed position and direction of the midline arteries, one of the most notable findings in these cases of agenesis of the corpus callosum has been the "wandering," irregular character of the courses of these vessels contrasting with the tight stretching and deviation found in cases in which arteries lie close to tumours (Wickbom, 1948). The pericallosal artery runs a normal course in the case of a cyst of the septum pellucidum, but where there is an infiltrating tumour of the corpus callosum the artery is usually displaced and stretched upward and laterally.

No report of the angiographic findings in a case with a lipoma has so far been published. It may be doubted whether the appearances will conform to those seen with an infiltrating tumour of the corpus callosum since operation, and post-mortem studies in the former type of tumour show that the anterior cerebral arteries are actually embedded deep in the tumour and are not displaced.

Summary

Two cases of agenesis of the corpus callosum are reported.

The diagnoses were based on the findings fol-

lowing air encephalography. Carotid angiography was also performed, and it is considered that this method of investigation is of value in diagnosis.

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