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REVIEW PAPER

The choroid plexus: a comprehensive review of its history, anatomy, function, histology, embryology, and surgical considerations

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Abstract
Introduction The role of the choroid plexus in cerebrospinal fluid production has been identified for more than a century. Over the years, more intensive studies of this structure has lead to a better understanding of the functions, including brain immunity, protection, absorption, and many others. Here, we review the macro- and microanatomical structure of the choroid plexus in addition to its function and embryology.
Method The literature was searched for articles and textbooks for data related to the history, anatomy, physiology, histology, embryology, potential functions, and surgical implications of the choroid plexus. All were gathered and summarized comprehensively.
Conclusion We summarize the literature regarding the choroid plexus and its surgical implications.

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Introduction

Around the walls of the ventricles, folds of pia mater form vascularized layers named choroid plexus. This vasculature along with the overlying ependymal lining of the ventricles forms the tela choroidea. Sometimes, however, the term choroid plexus is used to describe the entire structure [1]. The narrow cleft, to which the choroids plexus is attached in the ventricles, is defined as the choroidal fissure. [2] The discovery of the choroid plexus is attributed to Herophilus, who named it the choroid mennix. In the first century AD, Rufus of Ephesus used the name *chorioid tunicto* instead. Detailed anatomical descriptions of the lateral ventricles was first made by Vesalius [3] in 1543. Later on, Willis [4] in 1664 and Ridley [5] in 1695 described the choroid plexus of the fourth and third ventricles, respectively. [6]

Anatomy

Choroid plexus of the lateral and third ventricles

In each lateral ventricle, the choroidal fissure represents a C-shaped narrow cleft that extends from the foramen of Monro to the inferior choroidal point behind the uncus and lateral to the lateral geniculate body. Throughout its way, it lies in the medial part of the body, atrium, and temporal horn. It is located between the fornix as an outer margin and the thalamus as an inner margin. The latter forms the core around which the fissure wraps. In the body of the ventricle (the body of the fissure), the body of the fornix lies above the fissure and the superior surface of the

thalamus is below. In the antrum (the antral part of the fissure), the fissure is anterior to the crus of the fornix and posterior to the pulvinar of the thalamus. In the temporal horn (the temporal part of the fissure), the fimbria of the fornix passes below the fissure and the stria terminalis and the lower surface of the thalamus above.

The choroid plexus of each ventricle follows and adheres to the corresponding choroidal fissure. At the level of the foramen of Monro, it becomes continuous with the choroids plexus in the roof of the third ventricle. At the junction of the body and temporal horn in the antral part, the choroid plexus becomes more tortuous and prominent, forming a triangular tuft called the glomus. In addition, at the edges of the fornix and thalamus surrounding the choroidal fissures, small ridges can be found (Figs. 1 and 2). These ridges, called teniae, anchor the choroid plexus to the fornix and thalamus and consist of two layers, ependyma and pia mater. The tenia on the thalamic side is called tenia thalami or tenia choroidea, and on the fornix side, it is called the tenia fornicis except in the temporal part, where it is called the tenia fimbriae [2, 7].

In the third ventricle, the choroid plexus constitutes two parallel strands that run along the midline on the lower layer of the tela choroidea in the roof of the third ventricle and projects into the superior part of the ventricle [2].

Choroid plexus of the fourth ventricle

The choroid plexus of the fourth ventricle is composed of two inverted L-shaped fringes that are located in the ventricle and protrude through its openings. Each one of these strands has two limbs: sagittal and horizontal. The sagittal (longitudinal) limb is located in the roof of the ventricle near the midline and borders the median plane and, thus, is referred to as the medial segment. The medial segment is further divided into two parts:

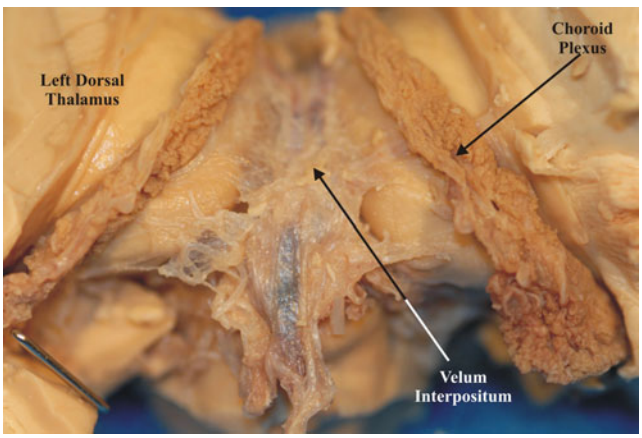

Fig. 1 Cadaveric dissection of the choroid plexus in the lateral ventricles. The choroid plexus of each ventricle follows and adheres to the corresponding choroidal fissure. At the edges of the fornix and thalamus surrounding the choroidal fissures, small ridges, called teniae, anchor the choroid plexus to the fornix and thalamus

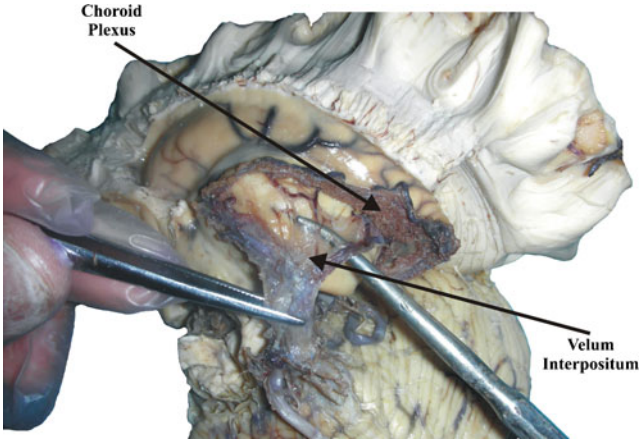

Fig. 2 Cadaveric dissection showing the choroid plexus of the right lateral ventricle with the velum interpositum

rostral and caudal. The caudal part starts between the cerebellar tonsils, climbs over the vermis up to the level of the pyramid bordering the foramen of Magendie. The rostral part extends from the level of the nodule anterior to the tonsils to the level of the foramen of Magendie and parallel to the rhomboid fossa. The horizontal (transverse) limbs arises from the rostral ends of the medial segment where the rostral part is at his widest level and extend through the lateral recesses and the foramina of Luschka into the cerebellopontine angles. These parts are referred to as the lateral segments. The lateral segment is also subdivided into medial and lateral parts. The medial part is attached to the rostral part of the medial segment and is attached to the tela choroidea covering the lateral recess caudal to the cerebellar peduncles. The lateral part continues at the lateral margin of the cerebellar peduncle and protrudes through the foramen of Luschka into the cerebellopontine angle below the flocculus. [8] After entering the foramen of Luschka, the tela choroidea and accompanying choroid plexus rotate and proceed laterally so that what was superior appears lateral [9].

Function of the choroid plexus

CSF production

The choroid plexus has a variety of functions, the most important of which is the production of cerebrospinal fluid (CSF). In 1664, Willis [4] proposed that the choroid plexus works as a secretory gland for the production of CSF. His theory was later supported by Luschka [10] in 1855 after microscopic examination of the plexus. Luschka introduced the theory of secretory globules, which he found in the choroid plexus epithelial cells and frequently on the free surface of the epithelium. This theory became known as the "vesicular theory." His findings were also supported by other authors at that time, including Galeotti [11], Findlay [12], and Studnicka [13]. However, others have

attributed the presence of these globules to nonphysiological conditions, including delay of choroid plexus fixation time or as a result of cellular injury, and denied the secretory function of the choroid plexus. Despite the contradiction, the theory was accepted, and the role of choroid plexus in CSF production became highly recognized and supported by many later experiments. However, the idea of whether the choroid plexus constitutes the main source of CSF production did not persist. Many authors starting with Hassin et al. [14] and including Milhorat et al. [15, 16] thought that most CSF production occurred extrachoroidally, including from the ependyma and brain parenchyma. Nevertheless, the production of CSF remains the most recognized and studied function of the choroid plexus despite the percentage of its contribution [6, 17].

In 1934, Flexner analyzed and compared the chemical components of the blood and CSF in pig embryos and found disparities in distribution. According to him, cerebrospinal fluid contained higher concentrations of chloride and magnesium ions and lower concentrations of proteins, glucose, amino acids, uric acid, phosphate, calcium, and potassium ions than plasma. It also had different types of proteins with the tetrameric human plasma protein transthyretin representing 25 % of these and a higher level of folate than the plasma. These disparities, contradicting other beliefs that the CSF resembles an ultrafitrate or dialysate of the plasma, were supported by later authors, although with some variations in measurements. These findings later lead to the discovery that CSF is produced as a true secretion of the choroid plexus and energy in the form of ATP is consumed for its production. ATPases and other types of ion channels and aquaporins in the apical and basolateral sides of the epithelial cells mediate this active process of secretion. This involves the transportation of sodium, chloride, and bicarbonate from the blood to the ventricles (the bicarbonate can also be synthesized in the epithelial cells, using the carbonic anhydrase enzyme), in a unidirectional fashion, while moving the potassium in an opposite direction. The net movement of ions creates an osmotic gradient that drives the secretion of water molecules toward the ventricles [1, 6, 17–20].

The rate of CSF production was reported by many authors to be constant at 0.37 mL/min or almost 500 mL/day. However, circadian variations influence the rate of production of the CSF as shown by advanced magnetic resonance imaging. In one experiment, the minimum amount of CSF formation was found at 6:00 PM of around 0.2 mL/min, while the maximum amount was at 2:00 AM of about 0.7 mL/min [21]. However, this is a matter of debate [22]. Variations in the rate of production of the CSF have been proposed based on experiments on animal models. This includes increased CSF production and associated ventriculomegaly with long-term use of caffeine in rats [23]. The use of anesthesia, intravenous administration of pilocarpine, and epinephrine in animals has been found to be associated with increased production of CSF [6]. However, the use of halothane was associated with decrease production of CSF [24]. The use of atropine and muscarine was also associated with decreased production [6]. These changes in CSF raised the suspicion of the effects of these drugs on the blood flow to the choroid plexus, which in turn affects CSF production. However, in an experimental study on the effect of acetazolamide on CSF production, the author measured the blood flow to the choroid plexus and found a noticeable decrease in CSF production despite a twofold increase in blood flow [25]. These facts further support the theory that CSF is a true secretion rather than a dialysate of the plasma. The effects of certain diseases like diabetes [26] and acute renal failure [27] have also been studied and have disturbances in the distribution of ion channels and ion gradients across epithelial cells, which may affect CSF production in rats. Based on human experiments, the rate of CSF production in patients with Alzheimer and dementia was also found to decrease to almost half the normal rate [28]. The relationship between body temperature and CSF production has also been studied, and it was found that even slight changes in temperature in either direction can alter the production of CSF [29].

Other functions

The components of the CSF can also be changed in nonphysiological conditions, which give an execratory function to the choroid plexus. For example, in patients with bromide poisoning, continuous lumbar puncture yielded higher concentrations of bromide and gradually lowers concentrations in the plasma. An endocrine function has also been attributed to the choroid plexus, as in experimental studies on animals, the intravenous administration of prepared choroid plexus samples lead to decrease in blood pressure in one and increase in CSF production in others. However, this theory is still not widely accepted [6].

In 1914, Askanazy [30] suggested the absorptive function of the choroid plexus after he noticed the accumulation of hemosiderin in the epithelial cells of patients with intraventricular hemorrhage. His theory was supported by Becht [31] in 1920. Hassin [32–34], who proposed an alternate origin of the cerebrospinal fluid, attributed the role of the choroid plexus to the absorption and removal of waste products from the CSF [6]. Later experimental studies were able to validate these theories using different types of tracers, including horseradish peroxidase. It was found that the choroidal epithelial cells were able to absorb or pinocytose various substances including proteins from the CSF and use active transport for larger molecules. The subsequently formed pinocytotic vesicles and their contents either undergo intracellular digestion or are discharged across the basolateral surface of the epithelial cells to the subcellular connective tissue stroma and blood vessels [35].

Besides its mechanical contribution to the blood–CSF barrier, the choroid plexus also protects the brain from noxious compounds and potentially from damaging cellular invasion using its unique detoxification system. Glutathione, cysteine, and metallothioneine sequester the toxic agents circulating in the CSF. Superoxide dismutase, glutathiones-transferased, glutathione peroxidase, and reductase protect against free-radical oxidative stress. The organic ion transport system and multidrug resistance proteins export noxious compounds from the CSF. Its role in defending against invading organisms derives from recent evidence of the choroid plexus as a coordinator or mediator between the brain and peripheral immune system. These findings include the presence of inducible lymphoid cells within the choroid plexus, the ability to induce proinflammatory cytokines, the expression of MHC molecules and molecules for leukocyte adhesion, and providing a route for activated immune cells to pass [20].

These proven and suggested roles of the choroids plexus, and the changes and dysfunction that occurs during various brain pathological conditions, including trauma, Alzheimer's disease, ischemia, and neurodegenerative diseases, has lead researchers to an idea of choroids plexus transplantation. Whether the transplantation of the choroid plexus will be beneficial in these conditions is not very clear, but current trials show promising results [20].

Histology

The choroid plexus is made of numerous villi, and each choroidal villus is composed of a single layer of cuboidal or columnar epithelial cells that are continuous with the ependymal lining of the ventricles and rest on a basement membrane. Beneath this layer lies connective tissue and a vascular network. On the apical side of the epithelial cells rests variable numbers of microvilli that differ in diameter and shape from slender symmetrical projections to apical bleb formations. These blebs are sometimes thought to be a result of pinocyte secretion, unfolding of the microvilli, or cellular injury. Clusters of cilia with a "9+2" arrangement of microfilaments can also be found in some species on the apical surface of the epithelial cells, and help stirring the CSF flow. Some authors have described a separation of the cellular cytoplasm under normal conditions into an apical clear zone and basal granular zone, although other authors consider this as pathological or postmortem finding. Intracellular pigments and inclusions can also be seen in older adults besides other morphological changes within the cells. These pigments have been divided into three types: large granular, vesicular, and thread-like forms. The inclusions include ring-shaped inclusions that consist of nonhomogeneous filaments. On the lateral surface of the cells, desmosome and tight junctions play the main role in holding the cells together. The tight junctions are concentrated as small strands near the apical end of the cells. It is proposed that they have a significant role in preventing the paracellular passage of molecules and, hence, contributing to the blood–CSF barrier. Thus, at the sites of choroids plexuses, the barrier function shifts from vasculature to epithelial cells. However, the degree of resistance provided by these intercellular adhesions is still a matter of debate. Furthermore, between the lateral walls of the choroid plexus, mainly near the vascular side, complex interdigitations help increase the surface area. The basal surface is unfolded, and extracellular spaces can be noticed. A double-layered nucleus is seen at the center or basal side of the cells housing up to three nucleoli. Other typical cellular organelles can be found inside the cytoplasm, with numerous mitochondria that compensate for the high metabolic needs and energy requirements of the cells. The basement membrane is thin, regular, mildly osmiophilic, and might have a role in the hematoencephalic barrier. Beneath the basement membrane is the connective tissue layer with its collagen fibrils and various types of cells, including pial cells, fibroblasts, macrophages, and others. On the proximal part of the connective tissue, large-caliber, fenestrated capillaries derived from the choroidal arteries are present. The fenestrations allow small hydrophilic molecules to pass easily into the interstitial fluid. Larger arterioles can also be seen on the base of the choroid plexus. At the site of the glomus, the vessels of the choroid plexus have different features and are considered modified veins, as they have no muscular layer in their walls. In this area, large-caliber vessels can be seen anastomosing with very small caliber vessels. Moreover, the endothelium and connective tissue of these vessels are inseparable from the surrounding connective tissue of the choroid plexus. Myelinated and unmyelinated nerve fibers have also been demonstrated in the choroid plexus. The myelinated fibers are regarded as sensory and the unmyelinated fibers as vasomotor. These nerve fibers are mainly derived from the glossopharyngeal and vagus nerves and the sympathetic plexus of the anterior and posterior choroidal arteries. Interepithelial nerve fibers, e.g., pressure receptors have also been identified [6, 20, 36].

Another type of cells, known collectively as intraventricular macrophages, should also be mentioned. This term covers three types of cells that share common, macrophages-like, ultrastructural features, and includes the epiplexus cells, supraependymal cells, and free-floating cells. Epiplexus cells were first described by Kolmer [37] in 1921, and sit on the ventricular surface of the choroids plexus. The supraependymal cells lie on the surface of the ependymal cells facing the ventricular cavity, and the free-floating cells are found inside the ventricles. These cells are monocyte-derived phagocytes that reach the ventricles through the choroids plexus [38].

Embryology

Around the seventh week of gestation, early signs of choroid plexus development can be seen as mesenchymal cells invaginating into the neural tube at the sites of cerebral ventricles formation, starting with the fourth ventricle, then lateral, and last, the third ventricle. The development of the choroid plexus has been divided into phases depending on the morphological and histological changes that occur within the cells. Kappers, in 1958, proposed three stages, while a more detailed study by Netsky and Shuangshoti in 1975 divided this into four stages. Their study mainly focused on the lateral ventricles. The first stage begins at the seventh week of gestation and lasts for 2 weeks. At this stage, the choroid plexus has a minute size compared to the ventricles, and contains tall, pseudostratified epithelial cells with no identifiable villi, and contains central nuclei and no glycogen. The second stage starts at the ninth week and lasts for 8 weeks. The plexus is extremely large compared to the ventricles. It has short columnar cells with sparse primary villi. The cells have apical nuclei and abundant glycogen. The third stage starts at the seventeenth week and lasts for 12 weeks. The plexus size is moderately large compared to the ventricles. They have cuboidal epithelial cells with mostly primary villi. The nuclei are central or apical, and the cells have moderate glycogen. The fourth stage starts at the 29th week and lasts for 11 weeks. The plexus is small compared to the ventricles. The epithelial cells are cuboidal or squamous with central or basal nuclei and no glycogen. Glycogen has also been reported in the third and fourth ventricles but with different timing than the lateral ventricles. The function of the glycogen during development is not clear. Some theories propose that it has a nutritive function; others have suggested that it is involved in the synthesis of certain components of the choroid plexus including mucoproteins of the basement membrane. Mitotic activity in the choroid plexus is very infrequent and, when present, is confined to the base or stalk of the choroid plexus. Carbonic anhydrase can be identified in the choroid plexus of the lateral ventricles as early as the beginning of the second stage. The carbonic anhydrase is a significant factor in the synthesis of the CSF by the formation of bicarbonate ions, which are transported across the apical surface (see above). Also during development, plasma proteins including albumin, fetuin, a-fetoprotein, transthyretin, and transferring can be seen in the epithelial cells of the choroid plexuses in the three ventricles. These proteins are either locally synthesized or transferred from the plasma. Many of these proteins are also found in the immature CSF. This might contradict the fact that the intercellular tight junctions well developed as early as the epithelial cells themselves. However, at the early stages, transcellular transportation of the molecules plays the main role in solving this mystery. In addition, in the immature choroid plexus, the level of permeability was found to be higher for the metabolically important molecules like amino acids than mature plexus. This plays an important role in supplying the developing brain. Additionally to the transepithelial transfer mechanisms, the fetal CSF–brain barrier restricts the entry of proteins from CSF into brain interstitial fluid, explaining a high CSF protein content early in developing brain. The blood flow to the choroid plexuses, mainly of the lateral and fourth ventricles, was noted to increase significantly between the third and fourth week after birth. It stays almost five times or more, per unit weight, more than cerebral blood supply, even during adulthood [39].

Surgical considerations

Pathology involving the choroid plexus is often intertwined with its CSF-producing ability. This is especially prominent in different types of hydrocephalus. Tumors originating from the choroid plexus, besides their neoplastic potential and mass occupying properties, usually have enhanced CSF production as well. Arterial supply to the choroid plexus shares common pathways with arterial supply to many eloquent structures. Hence, special attention needs to be given as occlusion of the arteries supplying the choroid plexus may lead to unintended iatrogenic occlusion of the arterial supply to those eloquent structures supplied by the parental artery. Below, we will discuss major surgical entities where choroid plexus is of major importance.

Choroid plexus neoplasm

The World Health Organization (WHO) has divided choroid plexus neoplasms into three grades: grade I, or benign “fully differentiated” choroid plexus papilloma (CPP); grade II, or “atypical” CPP; and grade III, or choroid plexus carcinoma (CPC). Chromosomal and genetic abnormalities have been linked to all three types [40].

Choroid plexus papilloma

The first description of a case of CPP was made by Guerard [41] in 1833 in an autopsy of a 3-year-old girl. Nevertheless, the first known case of a long-term adult survival postoperatively was made by Perthes [42] in 1919. Surgical treatment of pediatric cases was begun in the late 1920s and early 1930s [40]. CPP is a rare condition that represents only 0.4–1 % of all intracranial tumors. The incidence increases with younger ages, as it represents 1–5 % of intracranial tumors in children and is more common in the first decade of life. It peaks in patients younger than 2 years and represents almost 4–12 % in those younger than 1 year. Full-term and premature neonates may also be affected. Some cases have been reported in siblings, and

in associated with Li-Fraumeni, Aicardi, and Von Hippel-Lindau syndromes [40, 43, 44].

CPP arises from epithelial cells of the choroid plexus and may occur at any location containing plexus. However, age-specific predilection does exist. In adults, with average age of 35.5 years, an infratentorial location is more common, with the fourth ventricle being the most common site. In children, on the other hand, with an average age of 1.5 years, supratentorial location is more common, including the lateral and third ventricles, with the left lateral ventricles being the most common site. Extraventricular locations for CPP, albeit rare, have been described in the literature. The most common site of which is the cerebellopontine angle, which is found mainly in adults and represents the second most common infratentorial location after the fourth ventricle. Other sites may include the sella turcica with suprasellar cistern extension, cistern magna, and medullary cistern. Intraparenchymal extraventricular locations also include the brainstem, cerebellum, and sacral nerve roots. Bilateral CPP of both lateral ventricles and multifocal presentation and the involvement of both intra- and extraventricular locations have also been reported. The mechanism of the extraventricular extension and involvement of unusual locations is controversial, and many theories have been postulated. Of these theories, extension of choroid plexus from the ventricles was considered. This theory, however, proposes that a connection between the extraventricular papillomas and the ventricular choroid plexus should be present, but this is not always the case. Thus, other theories have a risen, including proliferation of ectopic rests of choroid plexus remaining from development, metaplasia of extraventricular ependymal rests, and dissemination through the CSF [45, 46].

The CPP represents a pedunculated mass that resembles a cauliflower macroscopically. It has a grayish-pink color and a soft texture, unless calcification is present, which gives it a gritty quality. It also has an irregular papilliform border. Histological characteristics of the CPP are very similar to the normal choroid plexus, but with occasional variability. The cells are mainly more columnar than cuboidal, the apical surface may or may not show microvilli and cilia, and the basolateral surface usually has numerous interdigitations. Intercellular junctions are also present, which indicates an almost intact blood–CSF barrier function. The number of intracellular organelles and the shape of the nucleus are highly variable as well and with few, if any, mitotic activity. The presence of glycogen- and lipofuscein-containing pigmented granules has been reported. Eosinophilic, onycocytic CPP that contains excessive amount of mitochondria and granular cytoplasm has also been reported. Other variants may include acinar, tubular, adenomatous, and xanthomatous patterns. Argyrophilic nucleolar organizer region count has been found to be significantly different between normal choroid plexus and CPP but similar between CPP and CPC. The presence of secretory vesicles inside the cells along with, although not constant, the presence of the microvilli and cilia indicates an active CSF secretory function of these tumors [40, 43, 47]. The histological difference between WHO grade I and II CPP is where the latter is more cellular with crowding of epithelial cells, varying degrees of anisopoikilokaryosis, increased nuclear to cytoplasmic ratio, and active mitoses. It also has a higher rate of recurrence and, although uncommon, a risk of malignant transformation [43, 44, 48].

Calcification of the CPP has been rarely reported in the literature. Microscopically, these CPP contained many psammoma bodies of various sizes and well-developed mature bone trabeculae with irregular shapes within the stroma. Some of these trabeculae demonstrate bone marrow spaces that contain adipose tissue. These bone tissues were separated from the choroidal epithelium by the intervening connective tissue. The mechanism of this ossification is not well known, but the most accepted theory is the metaplasia of the stromal fibrous connective tissue, induced by the psammoma bodies [49]. Metaplasia with cartilage tissue has also been reported [43].

The age of diagnosis of the CPP varies from a few weeks to more than 70 years of age, and mainly in the first year of life. Symptoms are related to over production of CSF by the tumor cells and the resultant hydrocephalus, which is found in almost 75 % of cases. The hydrocephalus might be due to hypersecretion, obstruction by the tumor itself, or resorptive dysfunction. The latter result from tumor hemorrhage or high protein contents that lead to leptomeningeal fibrosis. Other symptoms due to mass effect of the tumor itself may also present and depends on the tumor location. These lead to a group of nonspecific manifestations including headache, nausea and vomiting, papilledema, cranial nerve palsies, and gait disturbances. In infancy, macrocephaly is a common sign. Unusually, subarachnoid hemorrhage, seizures, titubation, Parinaud's syndrome, endocrine disorders, hearing or visual loss, hemiparesis, and developmental delay may also occur. Interestingly, symptoms of hydrocephalus may not resolve after surgery due to the development of CSF absorption malfunction [40, 50, 51].

Choroid plexus carcinoma

CPCs, or WHO grade III choroid plexus tumors, are uncommon and almost always affects children with a median age of 26 month, and are extremely rare in adults were they account for almost 7 % of the cases of CPC. In the latter, CPC are occasionally misdiagnosed as metastatic adenocarcinoma, which can mimic the same lesion and includes papillary tumors originating in the gastrointestinal tract, kidney, bladder, pancreas, or thyroid gland [52]. It represents 1–20 % of choroid plexus lesions [53] and 20–30 % of choroid plexus tumors [54]. The CPC may be primary or a result of progression

of the WHO grade I and II CPP, with the second being more common. CPC most commonly presents in the lateral ventricles (50 %) followed by the fourth ventricle (40 %), third ventricle (5 %), and multiple ventricles (5 %) [55]. Extraventricular locations of the CPC, although much less common than CPP, have also been reported. These include the cerebellopontine angle, pineal region, and other supratentorial and infratentorial regions [52]. The extraventricular location of the CPC, in either the brain or spinal cord, may be associated with intraventricular lesions [56]. Signs and symptoms of the CPC are very similar to those of CPP.

Differentiation between CPP and CPC is sometimes difficult to make. However, signs of hemorrhage, necroses, and sheet-like growth and brain invasion may be seen [40, 52]. Histologically, the criteria proposed by Lewis or Russell and Rubinstein should be met: (1) transition from normal to abnormal choroid plexus, (2) cellular (or nuclear) atypia, and (3) invasion into the adjacent neural tissue. Cellular atypia may include glandular and acinar structure, solid sheets of anaplastic cells, pleomorphism, necrosis, mitosis, and variation in chromatin content. Loss of the papillary architecture and invasion of the connective tissue stroma may also be seen. This criterion is more important in adults, where differentiation from metastatic adenocarcinoma should be made [54]. Rhabdoid CPC is a rare histological variant of the CPC. It shows solid sheets of undifferentiated cells and papillary features along with rhabdoid cells [57]. Pigmented or melanotic variants of CPC are a very rare form that has also been identified. When the pigmented CPC is encountered, it should be differentiated from similar tumors like pigmented papillary medulloblastoma, cerebellar papillary ependymoma, and metastatic malignant melanoma [58].

Choroid plexus cauterization in treatment of hydrocephalus

The early thought that the choroid plexus is the main site for CSF production led some surgeons to propose that surgical excision of the plexus of the lateral ventricles may help in hydrocephalus patients (Fig. 3). The first known attempt to use this method in nonobstructive (communicating) hydrocephalus was made by Dandy [59] in 1918. At that time, his trial was a failure, three out of four children died. The defect was in the technique he used, as he drained the CSF out of the ventricles before coagulating the choroid plexus, which led to ventricular collapse. Later, Dandy tried endoscopic cauterization treatment of nonobstructive hydrocephalus and described his experiences in the 1920s [60] and 1930s [61]. Other authors also described the mortality of this technique and successful endoscopic cauterization was demonstrated by Putnam [62] in 1934 and Scarff [63] in 1936 again. The basic concept of the method was to destroy the choroid plexus by passing an electrode over the plexus while maintaining the intraventricular pressure by continuous irrigation using Lactated Ringer's solution. In 1943, Putnam reported 42 children they operated upon between 1934 and 1942. In his series, 25 % (11/42) of the patients died immediately after surgery, 33 % (15/42) died later, and 42 % (16/42) survived. In 1952, Scarff [64] reported two case series. The first included 20 infants operated between 1935 and 1941. In this series, 17 patients survived, and only 10 of them showed permanent relief of pressure, but only 6 of them had long-term survival. The second series involved 19 patients treated from 1946 to 1951. In this series, 18 children survived, and 15 of them had permanent relief of symptoms. In 1957, Feld [65] described the use of a slightly modified endoscope and reported endoscopic cauterization of the choroid plexuses in 14 hydrocephalic children. He had no postoperative death and nine children had positive results. In Scarff's [66] description of the procedure, he mentioned that the goal of cauterization was to destroy as much of the plexus of the two lateral ventricles as possible in one surgical session. If this could not be achieved in one session, destruction of the plexuses should be made in one or more secondary operations staged about a week apart, until maximum possible destruction of the plexuses had been accomplished [64, 66].

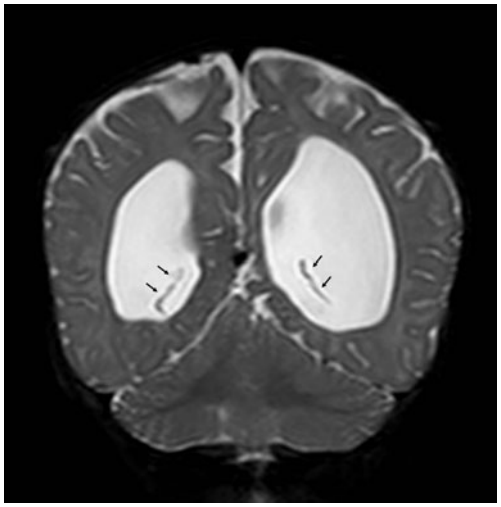

Fig. 3 Magnetic resonance imaging (T2-weighted, coronal view) of a pediatric patient with significant hydrocephalus. *Arrows* indicating the choroid plexus in the lateral ventricles

Combined endoscopic third ventriculostomy with choroid plexus cautherization

In 1922, Dandy [60] initiated the use of third ventriculostomy for the treatment of obstructive hydrocephalus. He soon abandoned the operation before using another approach

to yield more satisfactory results in 1933. In 1936, Stookey and Scarff [67] performed the surgery through puncture of the lamina terminalis and floor of the third ventricle. They reported on six patients upon whom they operated, with four cases of improvement and one death. Later on, the method of third ventriculostomy in treatment of obstructive hydrocephalus became more popular and reports showed significant improvements [68]. The combined use of the endoscopic third ventriculostomy (ETV) and choroid plexus cauterization began to replace the use of conventional CSF shunts, especially in obstructive hydrocephalus patients less than a year of age in developing countries. This combined technique showed superiority over the use of ETV alone in terms of success and over the use of shunts in term of dependency and complications [69, 70]. Choroid plexus cauterization was also shown to be reasonable, effective, and a more economic replacement of CSF shunts in the treatment of patients with hydranencephaly and near hydranencephaly [71].

Eloquent structures sharing a common arterial supply with the choroid plexus

Arterial supply of the choroid plexus in the lateral and third ventricles is derived from the anterior and posterior choroidal arteries. The anterior choroidal artery arises from the internal carotid artery and enters the choroidal fissure in the anterior portion of the inferior (temporal) horn of the lateral ventricle, to reach the choroid plexus. The posterior choroidal arteries (four to five in number) arise from the posterior cerebral artery and reach the choroid plexus through the tela choroidea. The posterior choroidal arteries are divided into two groups: medial and lateral. Each of the choroidal arteries supplies structures along its course. The anterior choroidal artery mostly supplies portions of the temporal and antral parts of the choroids plexus. The lateral posterior choroidal artery supplies portion of the body, antral, and posterior temporal parts. The medial posterior choroidal artery supplies portions in the body in addition to the choroid plexus in the roof of the third ventricle. The lateral and medial posterior arteries may also send branches to supply areas on the contralateral side. The sizes of the areas supplied by the anterior and posterior choroidal arteries are inversely related; so as the area supplied by one artery increases, the area supplied by the other artery decreases. The same relation applies to the lateral and medial posterior arteries. Communications between the anterior and posterior choroidal arteries may be seen in the villous area, tela choroidea, and glomus. Posterior inferior cerebellar artery supplies the choroid plexus of the fourth ventricle.

The choroidal arteries communicate with the choroidal veins through arterioles and capillaries or arteriovenous shunts. The veins draining the choroid plexus are located in the walls of the lateral ventricles, roof of the third ventricle, and the basal cisterns bordering the tentorial incisura. These veins of the lateral ventricles arise in the deep white and gray mater, and depending on their location related to the choroidal fissures, the ventricular veins are divided into medial and lateral veins. The medial choroidal veins pass through the outer or forniceal side, and the lateral passes through the inner thalamic side. Both medial and lateral veins join before entering the choroidal fissure. After entering the fissure, the choroidal veins course in the roof of the third ventricle and basal cisterns and empty into the internal cerebral, basal, and great vein of Galen [6, 7].

Arterial supply of the lateral horizontal segment is mainly derived from the anterior inferior cerebellar artery, while the posterior inferior cerebellar artery is the main supply of all the other segments in most cases. After arising from its main trunk, the choroidal arteries reach the choroid plexus from the cerebellomedullary fissure or through the foramina of the fourth ventricle [8].

Besides supplying the choroid plexus, the choroidal arteries also supply other important structures within the brain. The most constant extrachoroidal structures supplied by the anterior choroidal artery are the optic tract, the posterior half of the posterior limb of the internal capsule, and the middle third of the cerebral peduncle. Other structure may include the lateral geniculate body, the medial segments of the globus pallidus, uncus, piriform cortex, posteromedial half of the amygdala, the anterior hippocampus, dentate gyrus, the substantia nigra, red nucleus, subthalamus, ventral anterior, ventral lateral, pulvinar, reticular nuclei of the thalamus, the tail of the caudate nucleus, and the retrolenticular fibers of the capsule, including the geniculocalcarine tract and some of the auditory radiations emanating from the medial geniculate body [72–74].

The lateral posterior choroidal artery also supplies the pulvinar, the posterior part of the dorsolateral nucleus, the lateral geniculate body, the posterior part of the caudate nucleus, and sometimes the hippocampus and the mesial temporal lobe [75]. The medial posterior choroidal artery supplies the pineal body, tegmentum of the midbrain, and posterior border of the thalamus. It may also supply the superomedial aspect of the pulvinar and parts of the nucleus medialis [76].

Besides giving branches to the choroid plexus of the fourth ventricle, the anterior inferior cerebellar artery also supplies the anteroinferior part of cerebellum, middle cerebellar peduncle, inferolateral parts of the pons, and the upper part of the medulla oblongata [77, 78]. The posterior inferior cerebellar gives branches to the inferior surface of the vermis, the central nuclei of the cerebellum, the undersurface of cerebellar hemisphere, and the medulla oblongata [78].

These extensive territories of the choroidal arteries and their main trunks indicate that accidental traumatic manipulation or

cauterization during surgery, which may affect the main stem, can lead to ischemic effects on the other neural structures sharing the same blood supply, which in turn may result in motor or sensory disturbances.

Conclusion

A comprehensive knowledge of the choroid plexus is important to the clinician who interprets imaging of this structure and to the neurosurgeon who performs intraventricular procedures.

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