

The Probst bundle associated with anomalies of the precommissural separated fornix in an acallosal brain

Behpour Yousefi¹, Parviz Kokhaei²

1- Department of Anatomical Sciences, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran

2- Department of Immunology, School of Medicine, Semnan University of Medical Sciences, Semnan, Iran

SUMMARY

Dissection of the brain disclosed a unique form of the Probst bundle and a rare variation of the precommissural fornix. The latter showed an unusual size, branches and path on the medial surface of hemisphere. Its posterior branch continued to curve parallel with the posterior commissural fornix to follow an abnormal path and end in the hypothalamus. The Probst bundle was intermingled with the separated fornix in an anteroposterior direction as well as in the anterior and posterior parts in an atypical way. Focusing on such morphological abnormalities may help to gain a better understanding of the pathophysiology of brain disorders.

Key words: Agenesis – Corpus callosum – Fornix – Lateral ventricle – Septum pellucidum

INTRODUCTION

The corpus callosum develops embryologically in intimate relationship to the hippocampal formation, fornix, septum pellucidum, and cingulate gyrus (Swayze et al., 1990). The Probst bundle is known to be

a typical sign of agenesis of the corpus callosum (ACC) and consists of heterotopic myelinated callosal fibers. This is also a result of a migration disorder of callosal fibers (Lee et al., 2004).

The fornix is a large fiber bundle connecting the hippocampal formation to the mammillary body. The fibers of the fimbria arc posterosuperiorly and medially to form the crus. Anteriorly, the crura meet to form the body of the fornix, under the corpus callosum (Atlas et al., 1986). Above the interventricular foramina, the body of the fornix diverges into right and left fascicles, which split into a precommissural fornix (PF) and a posterior commissural fornix (PCF) (the columns of the fornix) near the anterior commissure (Williams et al., 1989). The columns bend ventrally in front of the interventricular foramina and caudal to the anterior commissure, to join the anterior thalamus and hypothalamus (Atlas et al., 1986). Although there have been reports indicating that in individuals with callosal agenesis abnormalities also occur in the development of the limbic structures (Swayze et al., 1990; Atlas et al., 1986) to varying extents (Atlas et al., 1986), this type of the Probst bundle and malformations of the fornix have not been described so far.

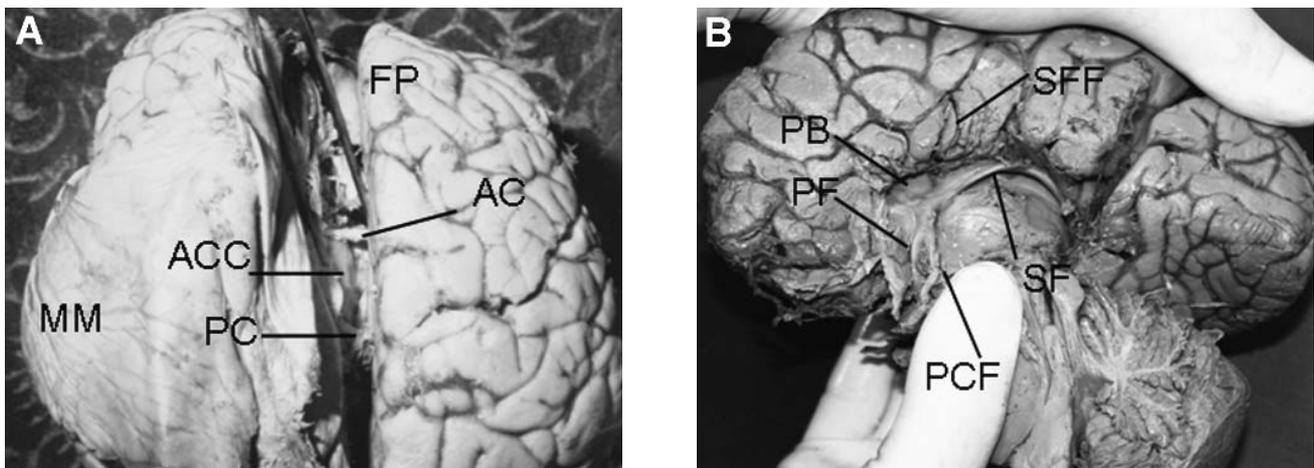


Fig. 1. Photographs of the brain from the superior view (A) and on the midsagittal plane (B) showing the absence of the corpus callosum (ACC), septum pellucidum, cingulate sulcus, interthalamic adhesion and hippocampal commissure. The sulci of the medial surface of the hemisphere radiate in a fan-like fashion (SFF) towards to third ventricular roof. The anterior (AC) and posterior commissure (PC) are seen within the hemispheres. Other abbreviations in this figure: FP, frontal pole; MM, meningeal membrane; SF, separated fornix; PF, precommissural fornix; PCF, postcommissural fornix; PB, Probst bundle.

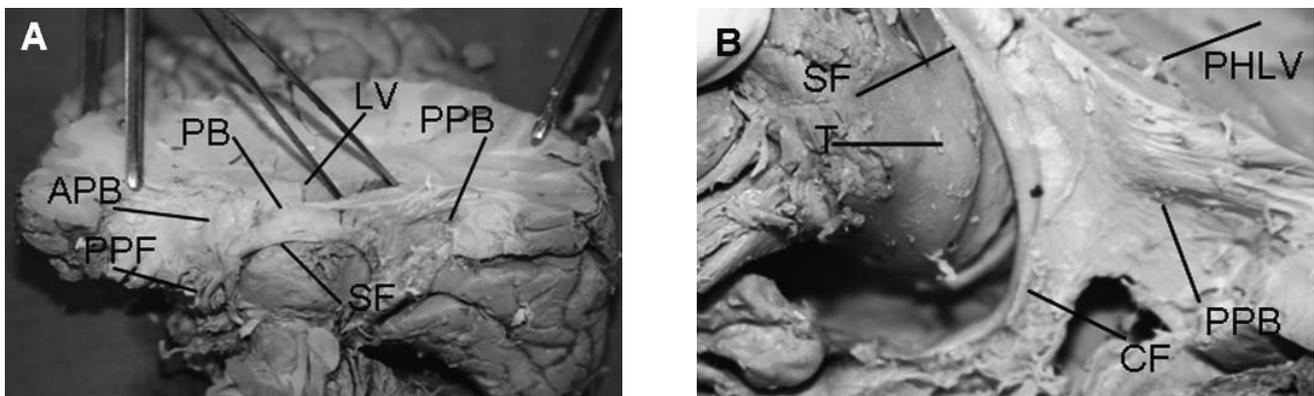


Fig. 2. Medial aspect of the frontal and occipital lobes (A, B) showing the Probst bundle (PB) and the lower area of the anterior (APB) and posterior parts of the Probst bundle (PPB). Other abbreviations in this figure: PPF, posterior branch of the precommissural fornix; SF, separated fornix; CF, crus of fornix; T, thalamus; LV, lateral ventricle; PHLV, posterior horn of the lateral ventricle.

CASE STUDY

During gross anatomy dissection of the brain for medical students, developmental abnormalities were found in a 32-year old male cadaver with an unknown previous medical history. There were no signs of an intracranial operation on his head or brain. The brain weighed 1320 g. The findings were photographed and documented during the dissection. We observed a spectrum of associated malformations together with ACC, such as completely separated fornices (SF), an absence of the septum pellucidum, cingulate sulcus, interthalamic adhesion, hippocampal commissure, and longitudinal striae (Fig. 1). The anterior commissure was slightly thickened, but the size of the posterior commissure was normal (Fig. 1A).

The Probst bundle in the hemisphere was well developed and intermingled with the

superior lip of the lateral border of the fornix. It extended towards the frontal, parietal, and occipital lobes of the brain as the roof and medial wall of the lateral ventricle, producing a thick septum. The lower component of the anterior portion of the Probst bundle extended inferoposteriorly toward the PF, showing a close connection with the PF. The nerve fibers of the lower part of the posterior portion of the Probst bundle continue and attach to crus of the fornix (CF) (Fig. 2).

Additionally, the separated fornix (SF) curved ventrally towards the anterior commissure divided into the PF and PCF. There was a variation in the pattern of distribution of the PF in comparison with the normal status and distribution. The PF was divided into more than three branches on the medial surface of the frontal lobe (Fig. 3). One of the PF branches was thickened and continued to curve inferiorly and posteriorly parallel with

the PCF, first on the medial surface of the third ventricle, then sinking into the corresponding hypothalamus and could be visualized without dissection (Fig. 3B).

The sulci of the medial surface of the hemisphere radiated in a fan-like fashion towards the lateral wall of the third ventricle, without a visible callosomarginal and cingulate sulcation. The parieto-occipital and calcarine sulci

crossed in the medial surface and entered toward the lateral ventricle (Fig. 1).

The anterior horn of the lateral ventricle (AHLV) curved anteromedially from the body of the lateral ventricle into the frontal lobe. Its roof and medial wall were formed by the fibers of the Probst bundle (Fig. 4). The other regions of the brain were normal.

DISCUSSION

Many studies have described a long list of abnormalities, including the hypogenesis of corpus callosum, gray matter heterotopia, polymicrogyria (Hetts et al., 2006), an absence of the posterior commissure, a hypoplastic anterior commissure (Meyer and Röricht, 1998), a large midline cyst, or lipoma and everted (unrotated) cingulated gyri (Sztrihá, 2005) intrinsic to ACC (Atlas et al., 1986), with clinical manifestations ranging from mild to devastating forms (Richards et al., 2004). However the type, number, and severity of associated anomalies differ (Hetts et al., 2006). This report has shown a rare morphological feature of the Probst bundle and an abnormal, localisation, distribution and paths of the PF along with a medial curvature of the AHLV.

This brain had a well-developed Probst bundle, suggesting a failure of the axons to cross the midline, rather than defective axon growth. According to previous reports, the Probst bundle runs anteroposteriorly (Lee et al., 2004; Hetts et al., 2006; Meyer and Röricht, 1998) and is intermingled with upper border of the SF (Hetts et al., 2006; Meyer and Röricht, 1998). Frontally, it was comma shaped; and posteriorly it formed a thin layer on the upper medial wall of the lat-

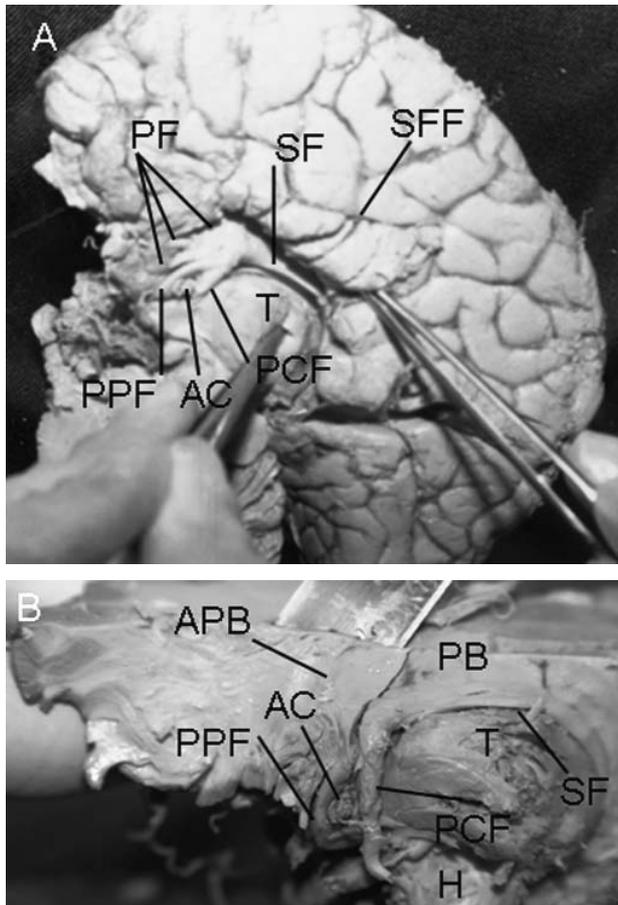


Fig. 3. The brain on the midsagittal plane (A), and medial aspect of the frontal lobe (B) showing the separated fornix (SF) and associated branches. The precommissural fornix (PF) is abnormal. Other abbreviations in this figure: PCF, postcommissural fornix; AC, anterior commissure; PB, Probst bundle; SFF, sulci as fan-like fashion.

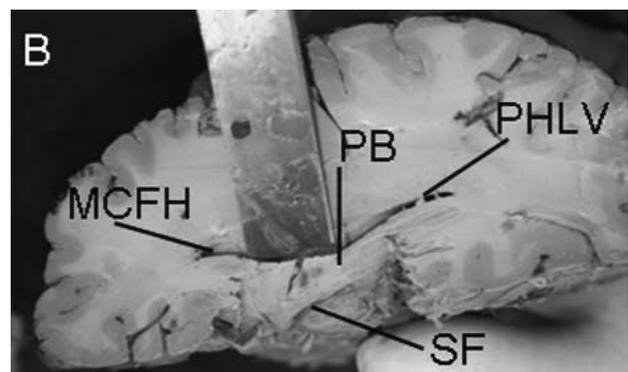
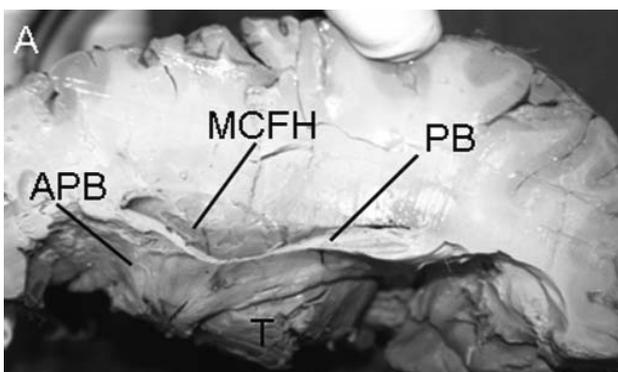


Fig. 4. Transverse sections of the cerebral hemisphere (A, B) showing the Probst bundle (PB) and medially concave frontal horn (MCFH). APB, anterior part of the Probst bundle; T, thalamus; SF, separated fornix; PHLV, posterior horn of the lateral ventricle.

eral ventricles (Meyer and Rörich, 1998). In mice, it has been shown that fibers leaving from the anterior part of Probst bundle make a U-shaped turn and the fibers that arise from the posterior portion of it accumulate as an anomalous fascicle below the cingulum (Ozaki et al., 1987). Although the position of these parts was similar to the case in our study, their attachments to the fornix were different, so that the lower area of the anterior and posterior portions (radiated fibers) of the Probst bundle were attached to the ventral branches of the PF and the CF at the beginning of the fimbria, respectively.

Most patients with complete agenesis without telencephalic dysgenesis or syndromic features typically have Probst's bundles (Sztriha, 2005). The etiology of ACC is heterogeneous, including cytogenetic abnormalities, metabolic disorders and genetic syndromes (Dobyns, 1996). At the molecular level, the process of development of the corpus callosum is complex. These processes rely on intricate cell-to-cell signaling mechanisms. Disruption or desynchronization of these mechanisms could lead to partial or complete callosal agenesis (Prasad et al., 2007). During embryogenesis, the fibers are thought to arrive at the mid-plane, where they are hindered in their further migration across the midline and then change their direction of growth to an anteroposterior direction, which leads to the formation of Probst's bundles in each hemisphere (Rosenthal-Wisskirchen, 1967). In humans, ACC is always associated with four syndromes: the Aicardi, acrocallosal, Andermann and Shapiro syndromes (Jeret et al., 1987).

The varieties reported by Meyer and Rörich (1998), Atlas et al. (1986) and Scott et al. (1993) on congenital morphologic abnormalities of the fornix were also found in the present case. However, these authors have not described the abnormal size, distribution and course of the PF, in that it was divided into a number of branches (up to three) superficial to the medial surface of the hemisphere. Also, its posterior branch appeared as a single thick midline cord and an unusual long arch and ran parallel to PCF on the medial surface of the third ventricle into the corresponding hypothalamus.

In the normal brain, the fornix is a large fiber bundle connecting the hippocampal formations to mamillary body. The body arcs over the thalamus to split into two anterior bundles (Atlas et al., 1986). On each side the

PCF contains the majority of the fornical fibers that project predominantly to the mamillary body. The PF contains the remaining portion of the fornical fibers arising from the cornu ammonis and some of the fibers from the subiculum and terminates exclusively in the septal nuclei (Meibach and Siegel, 1977). However, our finding shows a clear deviation from the normal status, as described above. It has been suggested that focusing on fornix abnormalities and their association with hippocampal abnormalities might be important for our understanding of the pathophysiology of schizophrenia (Kuroki et al., 2006). Since the medical history of the present case was not available, it was not possible to investigate the precise outcome of these anomalies, and therefore future studies are needed to find possible correlations.

Our observation of AHLV curvature was consistent with a previous study by Atlas et al. (1986), which explained a secondary deformity of the anterior horn.

Furthermore, the agenesis of the septum pellucidum observed in our study was similar to other reports (Lee et al., 2004; Meyer and Rörich, 1998; Scott et al., 1993). Abnormalities of the septum pellucidum have a higher incidence in women (Scott et al., 1993). During caudal development of the corpus callosum and fornix, as their courses diverge, the intervening commissural plate stretches to form the leaves of the septum pellucidum (Guibert-Tranier et al., 1982).

Similar to previous observations, the convolutional pattern on the medial surface of the hemisphere was abnormal and the gyri radiated in a fan-like fashion (Meyer and Rörich 1998; Sztriha, 2005) towards the lateral wall of the third ventricle (Sztriha, 2005) without a visible callosomarginal (Meyer and Rörich, 1998) and cingulate sulci (Sztriha, 2005). The parietooccipital and calcarine sulci converged into the lateral ventricle and a lack of a well-defined cingulum was observed (Atlas et al., 1986).

The white matter has been postulated to contribute to normal sulcation. Abnormalities of sulcation may be possibly associated with a decreased volume of white matter, as found by Hetts et al. (2006). Considering the brain weight in this case, it is unlikely that the volume of white matter had been decreased.

Finally, we believe that these abnormalities might have developed as a result of an early and abnormal embryological growth and

development. Although some of these anomalies were quite small, they may be important for radiologists, neurologists and neurosurgeons in clinics and are noticed clearly in dissection.

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