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ORIGINAL ARTICLE

Interhypothalamic adhesions in endoscopic third ventriculostomy

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Abstract

Introduction An interhypothalamic adhesion (IHA) is a gray mater–like band of tissue traversing across the third ventricle anterior to the mammillary bodies and is similar but distinct from an interthalamic adhesion. These rare anatomic anomalies can be detected with magnetic resonance imaging or, incidentally, during endoscopic ventricular surgery.

Methods All cases of interhypothalamic adhesions visualized during endoscopic third ventriculotomy (ETV), outside of the myelomeningocele setting, were identified from two institutions. Retrospective chart and imaging reviews were conducted and compared to intraoperative videos and photos for all cases. IHA variables collected included the following size, location, multiplicity, and associated anatomic anomalies.

Results Four cases of interhypothalamic adhesions were identified during ETV—all of which, either partially or completely, obscured access to the third ventricular floor. The IHAs in our cohort were duplicated in two patients, large (> 3 mm and severely obstructing access to the third ventricular floor) in three patients, and adherent to the floor of the third ventricle in three patients. All four patients had primary absence of the septum pellucidum. Previous reports found associations of IHAs with other congenital, particularly midline, abnormalities. The IHAs in our cohort affected the surgery in three of four cases including misdirecting the ventriculostomy and requiring retraction or division of the IHA. In no case was postoperative pituitary or hypothalamic dysfunction observed.

Conclusions Although interhypothalamic adhesions are rare, these anomalies must be recognized as they may hinder access to the third ventricular floor. IHAs may be large, multiple, or adherent to adjacent ventricular structures, they can misdirect or occlude the ventriculostomy or impart risk of bleeding and hypothalamic injury. Techniques for management of IHA include aborting the attempt, re-siting the ventriculostomy, or retracting or dividing the IHA, which enabled technically successful ETV in three of four patients in this series.

Keywords Hypothalamic adhesion · Intrahypothalamic adhesion · Primary agenesis of the septum pellucidum · Third ventricle anatomy

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Introduction

Interhypothalamic adhesions (IHA) can obstruct access to the third ventricular floor during an endoscopic third ventriculostomy (ETV). These horizontally oriented bands of tissue have been described variably in the literature in the past, and as such, are incompletely understood. Initially described in 1937 as the dorsal supra-optic decussation (Ganser's commissure) [1] and later rediscovered in the MRI era and named hypothalamic adhesions [2] and interhypothalamic adhesions [3]. IHAs are smooth, symmetric structures with gray mater characteristics connected to the hypothalami (i.e., ventral to the thalami) on MRI, autopsy, and endoscopy. As humans only have one hypothalamus already connected by the tuber cinereum and third ventricular floor, the term interhypothalamic adhesion may not be technically accurate, yet evokes multiple similarities to the more commonly seen

Table 1 Case series of interhypothalamic adhesion during endoscopic third ventriculostomy

Case	Patient history	Visible on MRI	Management during ETV	Follow-up	Interhypothalamic adhesion (IHA) description
1	11-month-old male with congenital hydrocephalus (elevated HC between 7 and 11 months)	Yes	Ostomy into pituitary infundibulum then immediately shunted	Shunted	2 IHAs, one large, adherent to floor of third ventricle, second thin, and ventral
2	7-month-old male with septo-optic dysplasia, cysts in lateral ventricle and temporal lobe, seizures and aqueductal stenosis. Had cysto-peritoneal shunt inserted with one revision before 1mo, then surgical cyst decompression at 7 months. Presented with hydrocephalus.	Yes	ETV between IHA and mammillary body followed by cyst fenestration.	ETV failed, ventriculo-peritoneal shunt inserted 4wks later	2 IHAs arranged vertically, one large and one small, adherent to floor near mammillary bodies
3	35-year-old female with Chiari malformation, history of headaches, memory issues, and elevated head circumference.	Limited imaging available prior to surgery.	IHA retracted ventrally, ETV placed between IHA, and mammillary bodies.	ETV successful, symptoms incompletely resolved	Solitary thick IHA, adherent to floor of third ventricle
4	25-year-old female, developmentally normal with ventriculo-peritoneal shunt since 3 months of age (revised 6 times before 19 years). Presented with shunt failure.	Yes	ETV, divided IHA, removal shunt	ETV successful	Solitary IHA, isolated in third ventricle.

interthalamic adhesions or massa intermedia. As such, they likely represent gray mater *choristomas* or normal tissue in an abnormal location. They can be isolated findings or associated with other abnormalities. Only four reports of IHAs discovered endoscopically have been described previously (two misattributing them as interthalamic adhesions or "thickened bands") [4–7] outside of the myelomeningocele population [5, 8], to which we add four new variations of IHAs.

Methods

A retrospective case series was collected by the senior author of interhypothalamic adhesions identified during endoscopic ventricular surgery (ETV) at two centers. Patients with myelomeningocele were excluded from this series due to the expectation of ventricular abnormalities in this cohort. Retrospective chart reviews were conducted for each case to obtain the following variables: age at ETV, presenting symptoms, underlying hydrocephalus etiology, intraoperative description and management associated with the IHAs, and the success of the ETV itself. Recorded endoscopic videos and photos were examined and videos reviewed by two authors (DP and VM) for each case to corroborate the intraoperative findings and management. Preoperative MRI imaging was reviewed retrospectively for the presence of IHA. Institutional research ethics approval for this case series was obtained from the University of Alberta.

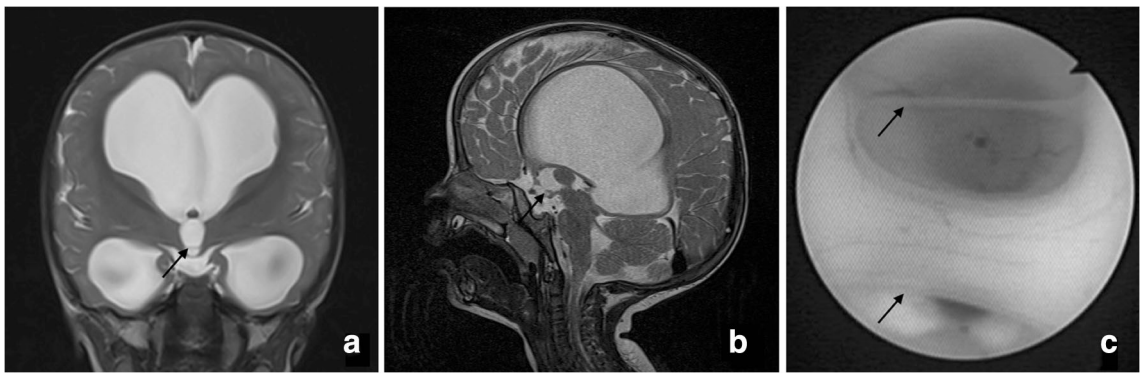

Fig. 1 **a** Coronal and **b** sagittal T2-weighted images of the interhypothalamic adhesions (IHA, arrows) and absent septum pellucidum in an 11-month-old patient with congenital hydrocephalus. **c** Two IHAs were discovered on endoscopy, one large and adherent to the floor of third ventricle, and the second thin and ventral. The IHA obstructed access to the planned stoma site and thus a ventriculo-peritoneal shunt was placed

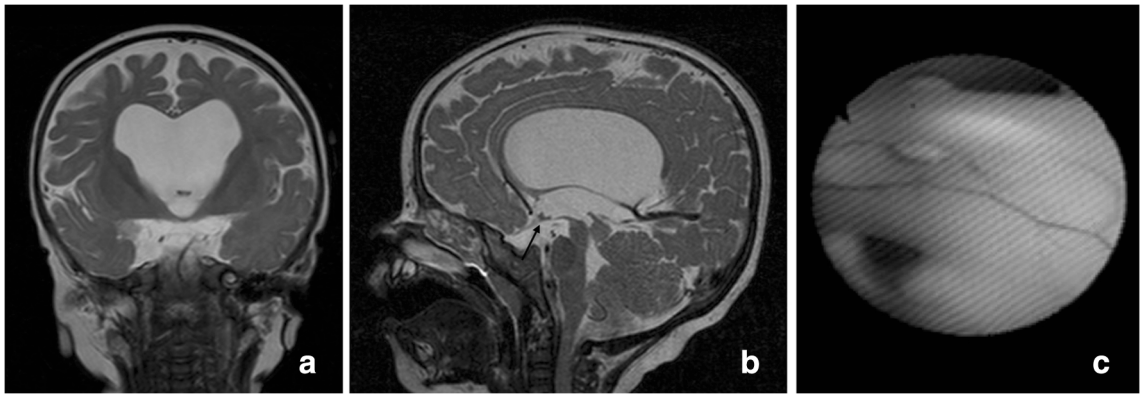

Fig. 2 **a** Coronal and **b** sagittal T2-weighted image of a 7 month male with septo-optic dysplasia, ventricular cysts, seizures, and aqueductal stenosis with a large interhypothalamic adhesion (IHA, arrow) attached to the third ventricular floor. **c** On endoscopy, two IHAs were arranged vertically, one large and one small, adherent to floor near mammillary bodies, allowing a small access point for a ventriculostomy

Results

Four cases of IHA encountered during ETV were identified (Table 1). None of the patients had a history of myelomeningocele. In all cases, the IHA was not appreciated on preoperative MRI (either due to limitations in preoperative imaging or due to surgeon and radiologist not recognizing its presence) (Figs. 1, 2, 3, and 4).

Each patient had comorbid primary agenesis of the septum pellucidum, defined as a large, near-complete absence of this structure. One patient had septo-optic dysplasia with a cyst in the temporal lobe, and one had Chiari I malformation. Two patients previously had ventriculo-peritoneal shunts.

Regarding the anatomy of the IHAs, two patients had dual IHAs of different sizes, one pair arranged vertically and one anteriorly-posteriorly. The IHA was connected to the third ventricular floor in three patients and was unattached in one case. Three patients had large IHAs (> 3 mm and severely obstructing access to the floor), while one was smaller and non-obstructing.

Surgical implications

Surgery was modified from our usual pattern due to the presence of an IHA in three cases. In one case, an attempted third ventriculostomy ventral to the IHA resulted in perforation of the tuber cinereum into the pituitary infundibulum, thus leading to an aborted ETV attempt. A second case required retraction of the IHA to access the preferred ventriculostomy site. In the third case, the IHA was divided endoscopically using electrocautery after performance of an ETV as it was intermittently occluding the stoma. ETV provided shunt freedom in two patients. No postoperative pituitary or hypothalamic dysfunction was observed in any of the four cases.

Discussion

IHAs were first described in 1937 by Vonderahe in eight of 371 autopsies (2.2%). Vonderahe felt it was a fusion of the paraventricular nuclei with some interspersed paraventricular

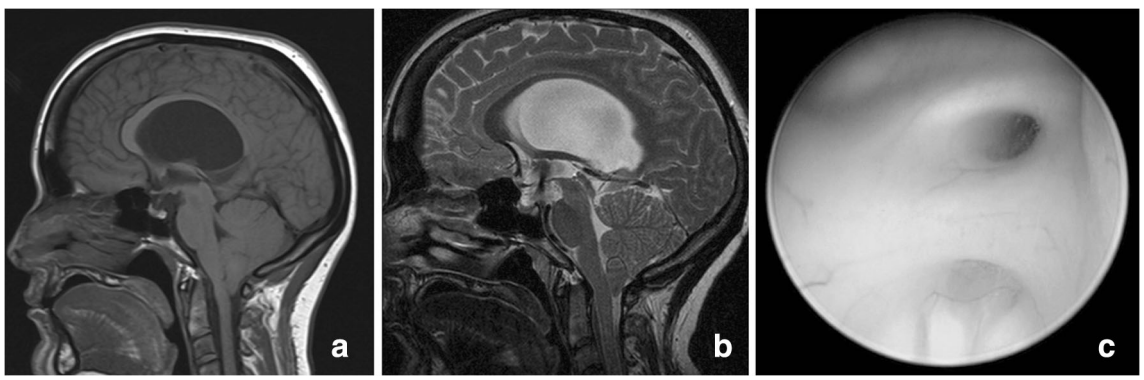

Fig. 3 Sagittal T1-weighted image **a** of a 35-year-old female with Chiari malformation, history of headaches, memory issues, and elevated head circumference, harboring primary agenesis of the septum pellucidum (PAS, not shown) and a solitary, large interhypothalamic adhesion (IHA) attached to the third ventricular floor (limited preoperative imaging is available). The IHA was retracted ventrally and an ostomy was ultimately placed ventral to the mammillary bodies. **b** The postoperative flow-void is visible in the sagittal T2-weighted image. **c** The anatomy of the third ventricular floor pre-ventriculostomy, including the targeted ventriculostomy site between mammillary bodies and IHA

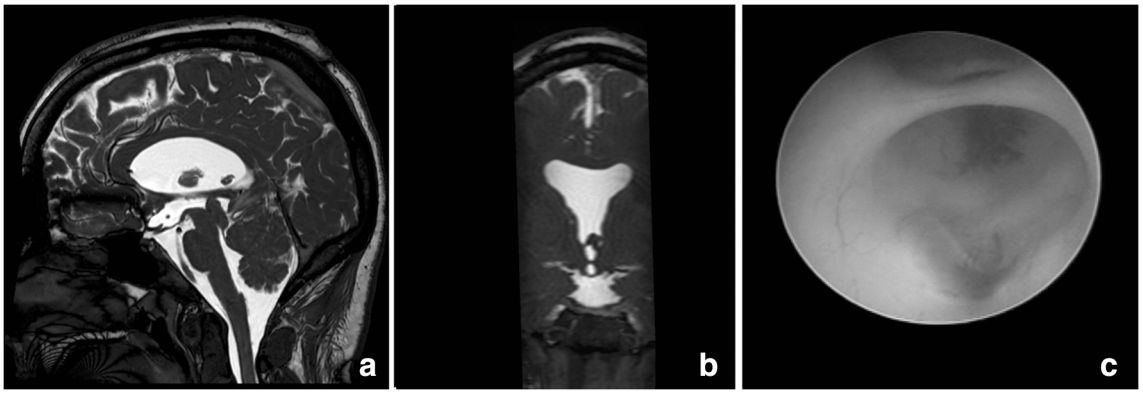

Fig. 4 **a** Sagittal T2-weighted image and **b** coronal reconstruction of a 25-year-old female, developmentally normal with congenital hydrocephalus and a solitary, unattached, interhypothalamic adhesion (IHA) in the anterior third ventricle. **c** The IHA was divided and a stoma was fashioned in the exposed third ventricular floor

Table 2 Literature review of interhypothalamic adhesions

Author and year	No. cases with IHA	Relevant associations with interhypothalamic adhesions (IHA)
Vonderahe 1937	8	IHAs were observed in 8 of 371 autopsy specimens. Vonderahe did not comment on additional intracranial anomalies.
Simon et al. 2000	56	Fused, partial, or minimal hypothalamic non-cleavage was found in all patients with holoprosencephaly, however, these findings may be distinct from the IHAs described herein.
Warf 2005	5	In five patients out of 27 (19%) with myelomeningocele undergoing ETV, "variable degrees of interhypothalamic adhesion, traversing the third ventricle and interconnecting its lateral walls, hampered access to the floor (of the third ventricle)."
Miller et al. 2008	36	Thirty-six of 74 patients with Chiari II malformation had an IHA. Other diencephalic, interhemispheric, and white matter/cortical abnormalities were also noted.
Whitehead and Vezina 2014	13	Associated abnormalities were found in 12 of 13 patients with IHA found by MRI; midline abnormalities were found in 12 patients and pituitary hypoplasia was present in one patient.
Vossough and Nabavizadeh 2016	36	An MRI study revealed 36 cases with IHA. Associated findings were sparse, comprising 2 callosal abnormalities and 3 nodular heterotypias. IHAs were felt to be incidental findings, unrelated to clinical indications for MRI (5 cases had conditions with a potential relationship to an IHA).
Ahmed, Stence and Mirsky 2016	57	MRI study finding 23 patients with gray matter heterotopia, four with septo-optic dysplasia, two with Chiari I malformation, one with Chiari II malformation, and 18 had otherwise normal examinations. The same group later found 72 additional patients.
Mirsky, Ahmed and Stence 2016	72	Four patients (all symptomatic) had additional midline abnormalities. Fifty of the patients were asymptomatic, likely incidental findings.
Severino et al. 2016	3	In a study of 445 patients with diencephalic-mesencephalic junction abnormalities, 3/5 patients with type B abnormalities had IHAs. The adhesion was attached to the lower portion of the lamina terminalis in two patients or to the tuber cinereum in one.
Etus, Morali Guler and Karabagli 2017	68	Of 455 patients with myelomeningocele, 187 (41.1%) had abnormalities of the floor of the third ventricle and 68 (14.9%) had interhypothalamic adhesion. Two or more abnormalities "were documented in most of the cases."
Mirone et al. 2019	1	Case report of ETV attempt in one 3-year-old boy with interhypothalamic adhesion, medulloblastoma and no hypothalamic symptoms. Endoscopic third ventriculostomy aborted due to "a very thick IHA that prevented approach to the floor of the third ventricle."

Table 3 Abnormalities associated with interhypothalamic adhesions and primary agenesis of the septum pellucidum

Abnormalities associated with interhypothalamic adhesions	Abnormalities associated with primary agenesis of the septum pellucidum
Midline abnormalities, including septum pellucidum abnormalities, and callosal abnormalities	Inferior vermian hypoplasia
Pituitary hypoplasia	Agenesis of the corpus callosum
Diencephalic-mesencephalic junction abnormalities	Septo-optic dysplasia
Gray matter heterotypias and migrational disorders	Chiari malformation
Septo-optic dysplasia	Holoprosencephaly
Chiari I or II malformations	
Holoprosencephaly	

cells found on an illustrative specimen. He found a number of fish species with similar anatomy. In one of the eight original cases, the IHA was duplicated [1]. A dearth of literature exists until the 2000s when an MRI study of patients with Chiari II malformations used the term hypothalamic adhesion for a finding in 36 of 74 patients (49%) [2]. Debates about the origin and association of IHAs ensued, fueled by their association with other abnormalities (Table 2). The MRI characteristics of IHAs are isointense to gray matter on all sequences, and non-gadolinium enhancing. Similarly, the IHAs in our series were all uniform, smooth tissue with similar MRI and endoscopic appearance to gray mater.

In one study, IHAs were separate from adjacent structures in 10/13 and adherent in the remaining patients to the fornices, third ventricular floor, tuber cinereum, mammillary bodies, optic chiasm, anterior commissure, and/or lamina terminalis [3]. In myelomeningoceles, IHAs are often attached to the lower portion of the lamina terminalis [2]. In three of our four cases, the IHA was adherent to the third ventricular floor or lamina terminalis. A fifth patient whose MRI was shared with the authors harbored a large IHA that was adherent to the lamina terminalis as opposed to the third ventricular floor (personal communication from Dr. Abhaya Kulkarni). The size of the IHA in our series also varied and they were duplicated in two cases.

IHAs may be associated with other intracranial abnormalities (Table 3), though the incidence is highly variable (14–93%) [3, 5, 8–13]. Interestingly, all the patients in our study had primary agenesis of the septum pellucidum (rather than other injury or atrophy). Other experienced endoscopists have identified IHAs during ETV with choroid plexus coagulation for patients with myelomeningocele (personal communication with Dr. Jay Riva-Cambrin), a group of patients who were not included in this report due to the expectation of third ventricular abnormalities in this patient population (41%, including 15% with IHA) [8]. The prevalence of multiple abnormalities seen in our patients (absent septum pellucidum, septo-optic dysplasia, and Chiari I malformation) is a notable association, a finding expected more often in MMCs than in general population undergoing ETVs.

Ultimately, as IHAs resemble normal gray mater, they are likely choristomas (collections of normal tissues in an abnormal location). IHAs share other features with interthalamic adhesions: they may also be multiple or absent and are commonly enlarged in Chiari II malformations [14]. As such, they are unlikely to be commissures or hamartomas. Origin theories include "incomplete hypothalamic cleavage, failed apoptosis, or abnormal neuronal migration" [10], late hypothalamic fusion [1] or a *forme fruste* of holoprosencephaly [3, 13].

IHAs have only recently been reported during endoscopic surgery, though two previous articles identified them as either interthalamic adhesions, a septum, or thickened bands of tissue [4–8]. Interestingly, one of these reports also describes comorbid absence of the septum pellucidum [4]. Small, non-impeding abnormalities may be under-reported in ETV studies, thus the true prevalence of IHA during ETV is unknown. Warf, in his seminal paper about the management of hydrocephalus in Uganda, found 5/27 (19%) patients with MMC who had an IHA that "hampered access" to the third ventricular floor, none causing him to abort the ETV [5]. Etus et al. similarly found IHAs in 68/455 (15%) of patients with MMC, without comment on surgical impact [8]. The most recent case report of an IHA resulted in an aborted ETV attempt due to the obstructing IHA and two episodes of supraventricular tachycardia (one at skin incision) [7].

Similarly, we aborted the ETV attempt in one case, modified the surgery in two others (retracting or dividing the IHA), and ultimately had to shunt two patients. ETV success rate is affected by prognostic factors beyond an IHA [15], such as other third ventricular anomalies [16], ostomy size, and visualization of a naked basilar artery [17]. A thick IHA with broad adherence to the floor of the third ventricle could necessitate the decision to abort the ETV attempt as in one case in this series. With early identification of IHA, possibly signaled by the presence of a comorbid PAS, a surgeon may be better prepared for managing this unusual finding.

In addition to elucidating the nature of an IHA for the neurosurgeon, there are a few options for the management of an interhypothalamic adhesion. Firstly, obtaining high-resolution MRI of the third ventricle (e.g., thin-slice multi-planar imaging

with CISS or FIESTA sequences) was not standard practice in the author's institutions prior to these cases. The authors have since updated their imaging protocols prior to ETV and now consider IHAs in addition to other 3rd ventricular abnormalities in the surgical planning. Intraoperative navigation can also be helpful in planning trajectory, entry into the ventricle and identification of anatomical structures. As the IHA may hinder access to the ventricular floor, the surgeon may choose to navigate around the IHA, retract or divide the IHA, make the stoma in the lamina terminalis, or abort the ETV attempt and place a shunt. The thickness and adherence of the IHA are factors to consider. Manipulating an IHA carries the risk of causing bleeding or hypothalamic and pituitary injury. Though not generalizable to all IHAs, manipulation or division of three of the four IHAs in this small cohort enabled technically successful ETV with no cases of postoperative hypothalamic or pituitary dysfunction.

Conclusions

Endoscopic third ventriculostomies are elegant procedures affected by alterations in ventricular anatomy, including the rare entity of an interhypothalamic adhesion. As evidenced by our cases, the IHA can be of varying size, multiplicity, and can be adherent to the third ventricular floor, lamina terminalis, fornices, or mammillary bodies. IHAs may be isolated findings or associated with other comorbidities, such as primary agenesis of the septum pellucidum. However, successful ETVs can be accomplished safely with avoidance, manipulation, or division of the IHAs themselves. As Mixter opined in his initial ETV case report, we hope that this added information about IHA will make ETV "easier and that it will prove more satisfactory… though time alone will tell." [18]

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Compliance with ethical standards

Conflict of interest The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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