

## Study design

This study is a multicenter retrospective cohort study. We included data from IPSFC and IPSE children under one year of age who underwent surgical treatment at the Nanhu Campus of Shengjing Hospital Affiliated to China Medical University and the Huaxiang Campus of the Second Affiliated Hospital of China Medical University between 2010 and 2024. The data included: basic patient information, present and past medical history, imaging materials, laboratory results, medical orders, surgical records, and complete 1-year follow-up data. The objectives of this study were to investigate the association between different surgical intervention timings and the non-cure rate of IPSSL, compare the efficacy differences between BHID and neuroendoscopic technique combined with Ommaya reservoir implantation in treating IPSSL, and analyze the high-risk factors for Stage III IPSFC progression to IPSE. In this study, legal guardians of all child patients provided written informed consent. This protocol was approved by the Ethics Review Committee of China Medical University. This study conformed to the Helsinki Declaration, and all child patient information was de-identified.

All child patients had undergone at least three weeks of standardized anti-infection therapy before inclusion in this study, including antibiotics (empirical or based on antibiotic susceptibility results) and appropriate dexamethasone administered intrathecally after lumbar puncture or intravenously. During conservative treatment, vital signs and neurological signs were closely monitored, with regular imaging reviews to assess changes in fluid collection thickness and the development of empyema. Cranial ultrasound was the primary modality, performed at intervals of no more than 3 days, while cranial computed tomography (CT) and MRI were conducted no more than once weekly.

By integrating imaging findings and clinical manifestations, the inclusion criteria for this study were determined. Children undergoing surgical treatment should meet at least one imaging criterion (persistent short-term widening of the subdural space or compression of lateral ventricles; unilateral fluid collection thickness  $>1$  cm for two consecutive weeks; formation of empyema abscess wall or mature empyema) and at least two clinical criteria (head circumference growth rate exceeding normal range or increased fontanelle tension; worsening IPSSL symptoms or persistent poor infection control; manifestations of intracranial hypertension such as repeated vomiting or lethargy; frequent neurological abnormalities like epileptic seizures; asymptomatic cases with fluid/empyema thickness  $>1$  cm for  $>2$  weeks). All IPSFC children undergoing surgical intervention should have a unilateral fluid collection thickness of at least 1 cm. Asymptomatic IPSSL children should be primarily managed with non-surgical treatment and under close monitoring of their condition. The surgical protocols and indications were approved by a dedicated review committee.

To investigate the association between different surgical timings and the non-cure rate of IPSSL, all IPSSL children who underwent the same surgical procedure were divided into an acute group ( $<14$  days), a subacute group (14 to 28 days), and a delayed intervention group ( $>28$  days). The grouping was based on the duration from the time of initial detection of subdural fluid collection formation to the day of surgery. The onset of fluid collection is defined as a thickness of  $>3$  mm in IPSFC children. Cure was defined as complete resolution of clinical symptoms (fever, headache,

etc.), absence of seizures, normal activity and feeding, normal CSF white blood cell (WBC) count, protein, and glucose levels with negative pathogen detection, age-appropriate neurological function at 1 year, sustained stability allowing normal social participation at 2 years, Bayley Scales of Infant and Toddler Development III score >85 during follow-up, cranial imaging showing no brain parenchyma compression or new lesions, and no secondary surgical treatment. Enrolled children not meeting all criteria were defined as non-cured.

To investigate the risk factors for Stage III IPSFC progression to IPSE formation, this study enrolled not only all IPSE children who underwent surgical treatment but also all children whose disease had progressed to Stage III IPSFC. The number of days from the first observation of Stage III IPSFC to IPSE formation was calculated. Potential risk factors considered primarily included: presence of immunodeficiency, timeliness of treatment, prematurity, days from IBM diagnosis to progression to Stage III IPSFC, days from Stage I to Stage III IPSFC progression, and pathogenic agents.

Major exclusion criteria included: subdural fluid collections secondary to viral meningitis; secondary subdural fluid collections with a confirmed history of craniocerebral trauma; diagnosis of tuberculous subdural effusion; and presence of intracranial space-occupying lesions.

#### Study endpoint

To compare the imaging changes between different surgical procedures, we calculated the thickness of fluid collection or empyema on the day before surgery and seven days after surgery. The thickest section of the subdural lesion was selected for measurement in CT or MRI. As far as we know, there is currently a lack of scoring scales for IPSSL-related disease assessment in both the field of pediatric neurosurgery and pediatric intensive care. To visually demonstrate the symptomatic improvement in children before and after surgery, we developed a scoring scale specific to this study (IPSSL-score) to evaluate the severity of IPSSL and the efficacy of surgical treatment. This scoring scale incorporates the Hines neurological score for infants, intracranial pressure assessment parameters, inflammatory control status, and neurological function evaluation. The Hines Neurological Score for Infants is a neurofunctional assessment tool for neonates to 2-year-old infants, adjusted for infant neurological developmental characteristics based on the traditional Hines Score. It is used to monitor neurological injury, developmental abnormalities, or postoperative neurological status, demonstrating high practical value in perioperative and intensive care settings. The specific scoring criteria for IPSSL-score are presented in **Figure 1**. The total score is 20 points, where a lower preoperative score indicates more severe symptoms and a higher postoperative score suggests better therapeutic efficacy. We collected IPSSL-score data for all children before surgery and during follow-up at 3 months, 6 months, and 12 months postoperatively. The diagnostic criteria for IPSFC, IPSE, and IBM are presented in **Supplementary 1**.

#### Surgical procedure and treatment process

After successful general anesthesia, the child was placed in the supine position with the head

turned approximately 30 degrees to the opposite side of the surgical site and fixed with a head ring. A 4-cm curved incision was marked on the forehead. Routine disinfection was performed with povidone-iodine, followed by draping with sterile towels. After incising the scalp along the marked line, a scalp retractor was used to retract the scalp, and subcutaneous soft tissues were dissected to expose the skull. A burr hole was drilled on the skull surface, which was expanded into an oval shape. The dura mater was suspended outside the bone window. A cruciate incision of the dura mater revealed subdural lesions (effusion or pus). A drainage tube was carefully inserted into the subdural space to aspirate approximately 20 ml of fluid. A neuroendoscope was introduced to remove palpable FIPLs (jelly-like purulent exudate, fibrous cord-like tissues, inflammatory pseudomembranes, septa, and blood clots) within the abscess cavity. The cavity was irrigated repeatedly with saline until the effluent became clear. A Medtronic Ommaya reservoir was connected to the distal drainage tube, inserted approximately 3 cm into the subdural space, and the reservoir was fixed subcutaneously. Patency was tested. The surgical field was carefully hemostatic, irrigated with hydrogen peroxide and saline, and the subcutaneous tissue and scalp were closed in layers. Instruments, gauzes, and cotton pads were counted without discrepancy. The operation proceeded smoothly. Blood transfusion was administered as indicated by intraoperative blood gas analysis, and the child was transferred to the pediatric intensive care unit postoperatively.

The drainage volume for each Ommaya reservoir puncture is controlled within the weight-based safety range (typically  $<5$  ml/kg) to avoid brain shift caused by rapid decompression. For IPSFC children, puncture aspiration was performed once daily during the postoperative initial period. After 7 consecutive days of puncture drainage, whether to continue was assessed based on disease progression. For IPSE children, twice-daily puncture aspiration was performed initially, accompanied by specimen testing. This continued until the puncture specimens showed clear transparency for three consecutive days with normal test results, after which the aspiration frequency was reduced gradually until discontinuation. Strict aseptic technique must be performed before each aspiration: local skin disinfection should cover an area with a diameter of  $\geq 5$  cm. A 22-gauge scalp needle is used to puncture the reservoir vertically, avoiding oblique puncture to prevent reservoir damage. The aspiration process should be performed slowly and stopped immediately when increased resistance is encountered during retraction, to prevent excessive negative pressure from damaging brain tissue.

For IPSSL children with unidentified pathogens, empirical intra-reservoir injection of vancomycin in combination with carbapenems via the Ommaya reservoir is initially recommended. Following bacterial culture and susceptibility testing, sensitive antibiotics should be added based on the results. For children within 6 months of age, administration is typically once every 24 hours, while infants older than 6 months may receive the drug once every 12 hours. Adjustments should be made by referring to the serum drug concentration in puncture drainage specimens and monitoring based on the drug half-life. The drug should be diluted with normal saline and slowly instilled into the Ommaya reservoir over more than 5 minutes. After instillation, the catheter should be clamped for 30 minutes to ensure adequate drug diffusion. Specimens of CSF should be obtained via the Ommaya reservoir at intervals of no more than 3 days for routine, biochemical, and culture examinations. IPSFC treatment courses should last at least 1 week, while IPSE treatment courses

should last at least 2 weeks. Treatment may only be considered for discontinuation when CSF tests are normal and CSF culture is negative for two consecutive times.

#### Statistical analysis

Continuous variables were presented as mean  $\pm$  standard error. Repeated measures ANOVA was used to analyze continuous variables between baseline and outcome, as well as to perform intergroup comparisons across different groups. Mauchly's test of sphericity was used to determine whether the sphericity assumption was met across repeated measurements, and the Bonferroni correction was applied to test for intergroup effects. Multivariate binary logistic regression analysis was used to analyze the association between different surgical timings and the probability of non-cure. Multivariate Cox regression analysis was performed to identify the primary risk factors for progression from stage III IPSFC to IPSE. Statistical significance was defined as  $p < 0.05$ . Statistical analyses were performed using SPSS 27.0 software (developed by IBM, Armonk, NY, USA). Data visualizations were performed using Graphpad Prism (Version 10.1.2).