Supplemental Table S1. The PPVs and sensitivities of different search strategies in the FUTURE database

Search strategies	No. of patients in the FUTURE database*	No. of confirmed BA in the FUTURE database*	PPV (%)	Sensitivity** (%)
(1) BA diagnosis in primary diagnosis, secondary diagnosis, and supplementary diagnosis	141	123	87.2	96.1
(2) BA diagnosis in primary diagnosis	68	67	98.5	52.3
(3) BA diagnosis in the secondary or supplementary diagnosis	73	56	76.7	43.8
(4) BA diagnosis in the secondary diagnosis	38	30	78.9	23.4
(5) BA diagnosis in the supplementary diagnosis	35	26	74.3	20.3
(6) BA diagnosis in the supplementary diagnosis and CNS infection*** in the primary diagnosis	38	32	84.2	25.0
(7) BA diagnosis in the supplementary diagnosis and pathogen confirmed BI or IE	17	16	94.1	12.5
(8) BA diagnosis in the supplementary diagnosis and any known predisposing factors	31	25	80.6	19.5
(9) BA diagnosis in the supplementary diagnosis and neurosurgeries about BA	3	3	100.0	2.3
(10)=(4)+(6)+(7)+(8)+(9)	69	56	81.2	43.8
(11)=(2)+(10)****	137	123	89.8	96.1
(12)=(6)+(7)+(8)+(9)	62	51	82.3	39.8
(13)=(2)+(12)	130	118	90.8	92.2

*Including BA patients admitted to Beijing Children's Hospital from 2016 to 2023 in the FUTURE database
**The number of confirmed BA in the Medical Record System of Beijing Children's Hospital was 128
***Excluding viral CNS infections
****The strategy that was used to identify all patients with a BA diagnosis admitted to 33 hospitals in the entire FUTURE database
PPV: positive predictive value; FUTURE database: FuTang Update Medical Records database; BA: brain abscess; CNS: central nervous system

Supplemental Table S2 The specific criteria for brain abscess

Categories	Details
Definite BA	Meet (1) or (2) (1) A brain abscess confirmed by aspiration of pus or histologic examination (2) For patients not undergoing neurosurgery, a BA was diagnosed via imaging findings*, with pathogen evidence from one or more of the following: positive culture (blood, CSF, or extracranial abscess pus), positive Gram stain (CSF or extracranial pus), or positive mNGS** testing (CSF or extracranial abscess pus)
Probable BA	Patients presented clinical manifestations of BA (such as fever, seizures, headache, local neurologic deficits, or decreased consciousness), imaging findings consistent with BA, a good treatment response (BA improved after antibiotic treatments) and no causative pathogens were identified
Possible BA	Patients presented clinical manifestations of BA, imaging findings consistent with BA, known predisposing factors, but there was not enough time to observe a favorable response to antibiotics due to the progressive development of the disease
Not BA	Did not fulfill the criteria described above or had proven alternative diagnosis

*Imaging findings comprised findings from brain MRI (including DWI/ADC maps, and T1-weighted sequences), or contrast-enhanced CT (Bodilsen, J, QG D'Alessandris, H Humphreys, MA Iro, M Klein, K Last, et al. 2024. Clin Microbiol Infect 30:66-89.)

**The results of mNGS were confirmed by the infectious disease specialists

ADC: apparent diffusion coefficient; BA: brain abscess; CSF: cerebrospinal fluid; CT: computed tomography; ADC: apparent diffusion coefficient; mNGS: metagenomic next-generation sequencing; MRI: Magnetic Resonance Imaging;

Supplemental Table S3. The details of confirmed BA in the MRS of BCH

No. of Patients	**Sex**	Age	**Categories of BA**	**Details**
2	Male	2 years	Definite BA	Surgery proven and pathogen positive
3	Male	7 years	Definite BA	Surgery proven but pathogen negative
4	Male	8 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
6	Male	1 year	Definite BA	Surgery proven and pathogen positive
8	Female	7 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
12	Female	4 years	Definite BA	Surgery proven and pathogen positive
14	Male	2 years	Definite BA	Surgery proven but pathogen negative
15	Female	1 year	Definite BA	Surgery proven but pathogen negative
16	Female	0 years	Definite BA	Surgery proven and pathogen positive
18	Male	13 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
20	Male	11 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
22	Male	1 year	Definite BA	Surgery proven and pathogen positive
29	Male	1 year	Definite BA	Surgery proven and pathogen positive
30	Female	5 years	Definite BA	Surgery proven but pathogen negative
33	Male	1 year	Definite BA	Surgery proven and pathogen positive
35	Female	4 months	Definite BA	Surgery proven and pathogen positive
39	Female	4 years	Definite BA	Surgery proven but pathogen negative
43	Male	6 years	Definite BA	Surgery proven but pathogen negative
44	Female	3 years	Definite BA	Surgery proven but pathogen negative
45	Male	13 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
48	Male	3 months	Definite BA	Surgery proven and pathogen positive
55	Male	12 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
56	Male	1 month	Definite BA	Surgery proven but pathogen negative
57	Male	8 years	Definite BA	Surgery proven and pathogen positive

59	Female	12 years	Definite BA	Surgery proven but pathogen negative
61	Male	3 years	Definite BA	Surgery proven but pathogen negative
62	Male	6 years	Definite BA	Surgery proven and pathogen positive
63	Male	3 months	Definite BA	Patients without neurosurgery but with a positive pathogen result
65	Female	11 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
66	Male	2 months	Definite BA	Surgery proven and pathogen positive
67	Male	1 year	Definite BA	Surgery proven and pathogen positive
69	Male	5 years	Definite BA	Surgery proven and pathogen positive
70	Male	10 years	Definite BA	Surgery proven and pathogen positive
73	Male	10 years	Definite BA	Surgery proven and pathogen positive
74	Male	2 years	Definite BA	Surgery proven but pathogen negative
75	Male	1 year	Definite BA	Surgery proven and pathogen positive
76	Female	2 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
77	Male	13 years	Definite BA	Surgery proven but pathogen negative
81	Female	11 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
87	Female	9 days	Definite BA	Surgery proven and pathogen positive
88	Male	12 years	Definite BA	Surgery proven but pathogen negative
89	Female	4 years	Definite BA	Surgery proven and pathogen positive
90	Male	2 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
91	Male	1 year	Definite BA	Surgery proven but pathogen negative
92	Female	4 years	Definite BA	Surgery proven and pathogen positive
95	Male	4 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
98	Female	7 days	Definite BA	Patients without neurosurgery but with a positive pathogen result
101	Male	8 years	Definite BA	Surgery proven and pathogen positive
102	Female	7 years	Definite BA	Surgery proven and pathogen positive
104	Male	6 months	Definite BA	Surgery proven and pathogen positive

105	Male	10 years	Definite BA	Surgery proven and pathogen positive
106	Male	4 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
107	Female	1 year	Definite BA	Patients without neurosurgery but with a positive pathogen result
108	Male	3 years	Definite BA	Surgery proven and pathogen positive
109	Female	7 years	Definite BA	Surgery proven and pathogen positive
110	Male	9 months	Definite BA	Surgery proven and pathogen positive
112	Male	4 years	Definite BA	Surgery proven and pathogen positive
113	Male	9 years	Definite BA	Surgery proven and pathogen positive
114	Male	12 days	Definite BA	Patients without neurosurgery but with a positive pathogen result
115	Male	9 years	Definite BA	Surgery proven and pathogen positive
116	Female	7 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
117	Male	6 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
118	Male	2 years	Definite BA	Surgery proven and pathogen positive
119	Male	9 years	Definite BA	Surgery proven and pathogen positive
120	Female	8 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
122	Female	2 years	Definite BA	Surgery proven and pathogen positive
123	Male	12 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
126	Female	4 years	Definite BA	Surgery proven but pathogen negative
127	Male	11 years	Definite BA	Surgery proven and pathogen positive
129	Female	12 years	Definite BA	Surgery proven and pathogen positive
130	Female	12 years	Definite BA	Surgery proven and pathogen positive
131	Male	2 months	Definite BA	Patients without neurosurgery but with a positive pathogen result
132	Female	5 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
133	Male	10 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
134	Male	3 years	Definite BA	Surgery proven and pathogen positive
136	Female	4 years	Definite BA	Patients without neurosurgery but with a positive pathogen result

138	Male	10 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
139	Female	4 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
140	Male	13 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
141	Male	8 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
143	Female	14 years	Definite BA	Surgery proven and pathogen positive
144	Male	8 years	Definite BA	Surgery proven and pathogen positive
145	Male	11 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
146	Male	11 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
147	Male	13 years	Definite BA	Surgery proven and pathogen positive
149	Female	1 year	Definite BA	Surgery proven and pathogen positive
150	Male	8 years	Definite BA	Surgery proven and pathogen positive
151	Male	1 year	Definite BA	Surgery proven and pathogen positive
152	Male	10 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
153	Female	15 years	Definite BA	Surgery proven and pathogen positive
154	Male	7 years	Definite BA	Surgery proven and pathogen positive
155	Male	12 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
156	Male	10 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
157	Male	7 months	Definite BA	Patients without neurosurgery but with a positive pathogen result
158	Female	7 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
159	Male	10 years	Definite BA	Surgery proven and pathogen positive
160	Male	14 days	Definite BA	Patients without neurosurgery but with a positive pathogen result
161	Male	7 years	Definite BA	Patients without neurosurgery but with a positive pathogen result
162	Male	7 years	Definite BA	Surgery proven and pathogen positive
163	Female	5 months	Definite BA	Patients without neurosurgery but with a positive pathogen result
164	Male	9 years	Definite BA	Surgery proven but pathogen negative
17	Female	1 month	Probable BA	Improve after antibiotic treatments

38	Male	1 year	Probable BA	Improve after antibiotic treatments
41	Female	7 years	Probable BA	Improve after antibiotic treatments
50	Male	10 years	Probable BA	Improve after antibiotic treatments
51	Male	5 years	Probable BA	Improve after antibiotic treatments
64	Male	22 days	Probable BA	Improve after antibiotic treatments
68	Female	5 years	Probable BA	Improve after antibiotic treatments
72	Female	1 month	Probable BA	Improve after antibiotic treatments
78	Male	2 years	Probable BA	Improve after antibiotic treatments
83	Male	11 years	Probable BA	Improve after antibiotic treatments
94	Female	10 years	Probable BA	Improve after antibiotic treatments
99	Female	2 years	Probable BA	Improve after antibiotic treatments
103	Female	3 years	Probable BA	Improve after antibiotic treatments
111	Female	8 days	Probable BA	Improve after antibiotic treatments
125	Male	4 years	Probable BA	Improve after antibiotic treatments
137	Male	8 years	Probable BA	Improve after antibiotic treatments
53	Male	10 years	Possible BA	The patient presented with fever and seizures. A significant predisposing factor was a recent neurosurgery. During the initial management, the patient received a 4-day course of antibiotics and was subsequently transferred to the local hospital. No follow-up information regarding the patient's outcome is available.
54	Male	4 months	Possible BA	The patient presented with fever and seizures, with a significant predisposing factor of bacterial meningitis. His parents discontinued the treatment and withdrew him from the hospital after only one day of admission.
60	Female	4 years	Possible BA	The patient presented with fever and unconsciousness. Tetralogy of Fallot was a significant predisposing factor. The patient's condition deteriorated rapidly, and he succumbed after one day of hospitalization
71	Female	11 years	Possible BA	The patient presented with a fever. A prior history of neurosurgery was a predisposing factor. After completing a 20-day course of antibiotic treatment, she was subsequently transferred to local hospital. No repeat brain imaging was performed during her stay, and no follow-up information is available thereafter.

79	Female	7 years	Possible BA	The patient presented with fever, seizure, and unconsciousness. Pulmonary artery venous fistula and persistent cyanosis were the predisposing factors. Her condition progressed rapidly, and she succumbed within 24 hours of admission.
80	Male	3 years	Possible BA	The patient presented with fever, limb hypertonia, and positive meningeal signs. He had an underlying condition of severe combined immunodeficiency. After a 19-day course of treatment, he was transferred to the local hospital. During his stay, no repeat brain imaging was performed. No follow-up information was available thereafter
82	Female	1 year	Possible BA	The patient presented with fever, seizures, and unconsciousness. The cerebrospinal fluid findings indicated a purulent infection. Her condition deteriorated rapidly, and she succumbed one day after hospitalization.
84	Female	5 months	Possible BA	The patient presented with poor feeding. She had an underlying condition of meningocele and had undergone neurosurgery within the past 3 months. In addition to a brain abscess, a spinal abscess was found on her spinal MRI. After a 14-day course of antibiotics, her parents discontinued treatment and discharged her against medical advice. No follow-up information was available.
85	Female	11 years	Possible BA	The patient presented with fever and had an underlying cyanotic congenital heart disease. After a 17-day course of antibiotics, her clinical condition improved; however, the brain abscess showed no significant reduction in size. Subsequently, she was transferred to a local hospital by her parents for further management. No follow-up information is available.
128	Female	7 years	Possible BA	The patients presented with headaches and had an underlying cavernous transformation of the portal vein. After receiving a 10-day course of antibiotics, she was transferred to the local hospital. No follow-up information was available.
142	Female	13 years	Possible BA	The patients presented with fever, seizures, and an alert mental status. She had an underlying condition of infectious endocarditis. Her condition deteriorated rapidly, and she succumbed after 3 days of hospitalization.

BCH: Beijing Children's Hospital
MRS: Medical Record System

Supplementary Table S4 The distribution of hospitalized children and confirmed BA among different years

Years	No. of hospitalized patients	No. of confirmed BA	Percentage (%)
2016	1244114	105	8.44
2017	1382111	105	7.60
2018	1461394	104	7.12
2019	1584608	135	8.52
2020	1192987	105	8.80
2021	1394197	110	7.89
2022	1238673	98	7.91
2023	1472763	111	7.54

BA: brain abscess

Supplementary Table S5: The proportion of patients undergoing neurosurgical intervention among those with different predisposing factors

	Total cases	Number of cases	Proportion(%)
BA with unknown origin	338	118	34.9
Meningitis	138	10	7.2
Contiguous infections*	107	24	22.4
CHD	126	38	30.2
Incomplete skull**	59	15	25.4
Immunocompromise	24	8	33.3
Bloodstream infection	51	9	17.6
Pulmonary artery fistula	4	2	50.0
Dental infection	4	2	50.0
Previous neurological surgery	6	3	50.0
Other underlying disease***	16	4	25.0
Total	873	233	26.7

BA: brain abscess; CHD: congenital heart disease
* including infections such as otitis media, sinusitis, and periorbital cellulitis, which are adjacent to the brain
** including cerebrospinal fluid leak, open skull fracture and basilar skull fracture
*** Four of the five patients with Down syndrome were also diagnosed with congenital heart disease

Supplementary Table S6 Neurosurgical intervention among patients with different predisposing factors

Predisposing factors	2020-2023(%)	2016-2019(%)	P-value
BA with unknown origin	66(44.6)	52(27.4)	0.001
Meningitis	2(3.7)	8(9.5)	0.342
Contiguous infections*	19(28.8)	5(12.2)	0.045
CHD	19(30.2)	19(30.2)	1.000
Incomplete skull**	6(21.4)	3(13.0)	0.680
Immunocompromise	8(25.0)	7(25.9)	0.935
Bloodstream infection	2(15.4)	6(54.5)	0.082
Pulmonary artery fistula	2(66.7)	0	N/A
Dental infection	2(50.0)	2(50.0)	N/A
Previous neurological surgery	1(33.3)	2(66.7)	1.000
Other underlying disease***	2(16.7)	2(50.0)	0.245

BA: brain abscess; CHD: congenital heart disease
* including infections such as otitis media, sinusitis, and periorbital cellulitis, which are adjacent to the brain
** including cerebrospinal fluid leak, open skull fracture and basilar skull fracture
*** Four of the five patients with Down syndrome were also diagnosed with congenital heart disease
N/A Not applicable

Supplementary Table S7 The proportion of patients with complications among those with different predisposing factors

	Total cases	Number of cases	Proportion(%)
BA with unknown origin	338	111	32.8
Meningitis	138	62	44.9
Contiguous infections*	107	32	29.9
CHD	126	41	32.5
Incomplete skull**	59	13	54.2
Immunocompromise	24	16	31.4
Bloodstream infection	51	30	50.8
Pulmonary artery fistula	4	3	75.0
Dental infection	4	2	50.0
Previous neurological surgery	6	2	33.3
Other underlying disease***	16	6	37.5
Total	873	318	36.4

BA: brain abscess; CHD: congenital heart disease; CHD: congenital heart disease;
* including infections such as otitis media, sinusitis, and periorbital cellulitis, which are adjacent to the brain
** including cerebrospinal fluid leak, open skull fracture and basilar skull fracture
*** Four of the five patients with Down syndrome were also diagnosed with congenital heart disease

Supplementary Table S8 Complications among patients with different predisposing factors

Predisposing factors	2020-2023(%)	2016-2019(%)	P-value
BA with unknown origin	55(37.2)	56(29.5)	0.135
Meningitis	33(61.1)	29(34.5)	0.002
Contiguous infections*	27(40.9)	5(12.2)	0.002
CHD	27(42.9)	14(22.2)	0.013
Incomplete skull**	6(54.5)	7(53.8)	1.000
Immunocompromise	7(25.0)	10(43.5)	0.164
Bloodstream infection	19(59.4)	11(40.7)	0.154
Pulmonary artery fistula	2(66.7)	1(100)	N/A
Dental infection	2(50)	0	N/A
Previous neurological surgery	2(66.7)	0(0%)	N/A
Other underlying disease***	4(33.3)	2(50.0)	0.064

BA: brain abscess; CHD: congenital heart disease
* including infections such as otitis media, sinusitis, and periorbital cellulitis, which are adjacent to the brain
** including cerebrospinal fluid leak, open skull fracture and basilar skull fracture
*** Four of the five patients with Down syndrome were also diagnosed with congenital heart disease
N/A Not applicable