

## Short Communication

# Unexpected Ventriculitis Complication of Neonatal Meningitis Caused by *Streptococcus gallolyticus* Subsp. *pasteurianus*: a Case Report

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**SUMMARY:** *Streptococcus gallolyticus* subsp. *pasteurianus*, previously recognized as *S. bovis* biotype II/2, is an uncommon yet important cause of invasive infection in young infants. Here, we report the first case of ventriculitis that was unexpectedly diagnosed in the course of neonatal meningitis due to *S. gallolyticus* subsp. *pasteurianus*, and we review the relevant literature. A 28-day-old male infant from Japan presented with fever, lethargy, and irritability. *S. bovis* was isolated from blood and the cerebrospinal fluid culture and was then identified as *S. gallolyticus* subsp. *pasteurianus*. Intravenous antibiotic therapy was initiated, which helped improve the clinical course of the disease; however, the patient presented ventriculitis-related complications diagnosed using follow-up magnetic resonance imaging (MRI) on day 12 of hospitalization. Ampicillin was administered for 21 days and discontinued after the patient showed improvement, according to MRI findings. The patient was discharged without sequelae. Ventriculitis is a rare complication of childhood meningitis due to *S. gallolyticus* subsp. *pasteurianus*. However, it may have been underdiagnosed, especially in cases with no specific manifestations similar to the present case. We suggest that MRI should be performed to screen for ventriculitis in the course of meningitis to avoid failure in treatment.

*Streptococcus gallolyticus* subsp. *pasteurianus*, previously known as *S. bovis* biotype II/2, belongs to the *S. bovis* group and is an uncommon cause of neonatal bacterial meningitis (1). Over the last 2 decades, this pathogen is increasingly recognized as a cause of meningitis and bacteremia in young infants; however, its clinical significance has not been well established. Here, we report a case of neonatal meningitis that was unexpectedly complicated by ventriculitis due to this pathogen and review the relevant literature.

A male infant was born by spontaneous vaginal delivery at term, weighing 3,680 g. Pregnancy and labor were uneventful. The patient developed fever (39°C) when he was 27 days old. Next day, he was admitted to the hospital with peripheral coldness, tachycardia, facial pallor, lethargy, and irritability. His anterior fontanel was not distended. Blood examination showed the following results: leukocyte count 17,380/mm<sup>3</sup> (64.5% segmented neutrophils, 18% bands); C-reactive protein 7.86 mg/dL; procalcitonin 23.32 ng/mL. The cerebrospinal fluid (CSF) was cloudy with leukocyte count at 7,909/mm<sup>3</sup> (97% polymorphonuclear cells), protein levels at 214 mg/dL, and glucose levels at 1 mg/dL (blood glucose 112 mg/dL). Latex antigen tests were negative for *Haemophilus influenzae* type b, *Neisseria meningitidis*, *Escherichia coli*, group B *Streptococcus* (GBS) and

*Streptococcus pneumoniae* (Pastorex Meningitis; Bio-Rad, Tokyo, Japan). The patient was treated empirically with intravenous administration of dexamethasone (DX) 0.6 mg/kg/day, cefotaxime (CTX) 300 mg/kg/day and ampicillin (ABPC) 300 mg/kg/day. When gram-positive cocci in chains were detected with CSF Gram stain, DX was discontinued. The isolates from both the CSF and blood cultures were initially reported as *S. bovis*, which was susceptible to  $\beta$ -lactams. CTX was discontinued while treatment with ABPC alone was continued. Head computed tomography, performed during day 2 of hospitalization, showed no abnormal findings. On day 5, patient's fever subsided. A repeat CSF culture after 7 days of antibiotic treatment was negative. ABPC was scheduled to continue for a total of 14 days. However, ventriculitis was unexpectedly diagnosed using head magnetic resonance imaging (MRI) that was performed to evaluate brain damage caused by severe inflammation in CSF and by this unusual pathogen on day 12 of hospitalization (Fig. 1). Therefore, ABPC was continued until day 22, when the ventriculitis was successfully treated with complete resolution confirmed by MRI (Fig. 2). Hearing test and neurological examination at discharge were normal and the patient was discharged without sequelae. Additional blood and CSF cultures identified *S. gallolyticus* subsp. *pasteurianus* isolates, defined according to API 20 Strep (Sysmex bioMérieux, Kobe, Japan) and the isolate's 16S rRNA sequence.

The majority of *S. bovis* meningitis cases in children is caused by the subspecies, *S. bovis* biotype II/2, now recognized as *S. gallolyticus* subsp. *pasteurianus*. However, as the current classification system for *S. bovis* species is not yet fully embraced, there have not been many reports that have appropriately identified the *S. bovis* isolates to the subspecies level in childhood men-

Received February 7, 2017. Accepted September 5, 2017.  
J-STAGE Advance Publication December 26, 2017.

DOI: 10.7883/yoken.JJID.2017.053

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ingitis. A review of the English literature revealed that only 13 previously reported cases of childhood meningitis were due to *S. gallolyticus* subsp. *pasteurianus* and no prior case of ventriculitis has been reported (Table 1) (2–11). Clinical presentation and examination findings were similar to those caused by GBS. Seven out of 14 cases were early onset ( $\leq 6$  days of life) and the oldest patient among late onset cases was 6 weeks old. Eleven out of 14 cases had meningitis with concurrent bacteremia. Most of the isolates in the literature were sensitive to  $\beta$ -lactams and most cases were treated with a 14–16-day course of penicillin (PC) and a few cases with CTX. In 2 cases, which were treated with CTX or PC and gentamicin, isolates had intermediate resistance to PC (4,6). A few patients showed neurological complications including seizure, intraventricular hemorrhage, or subdural effusion with no neurologic sequelae. As all the reported patients survived, meningitis caused by this pathogen in infants appears to have a relatively good prognosis. The pathogenesis of invasive *S. gallolyticus* subsp. *pasteurianus* infection in infants is unclear. Similar to patterns of GBS meningitis, most authors have proposed that this infection occurs via horizontal transmission or vertical contagion (10). In an early-onset case report, a similar sensitivity pattern was identified both from the isolate of *S. gallolyticus* subsp. *partetrianus* detected in the patient's CSF and the isolate of *Streptococcus* group D detected in the urine of the patient's mother (5). The late-onset case report from Takahashi et al. demon-

strated that identical isolates of *S. gallolyticus* subsp. *pasteurianus* were isolated from blood, CSF, and stool in a 50-day-old-girl with meningitis, suggesting that the gastrointestinal tract may be a possible source (9). The source of the organism in the present case was not further investigated.

Ventriculitis is uncommon in adults, while it has been reported as a frequent complication of bacterial meningitis in neonates with greater morbidity and mortality rates (12,13). Thus, early and accurate diagnosis is necessary. Berman et al. performed a pathological study at autopsy following neonatal bacterial meningitis and revealed that 21 of 25 neonates had ventriculitis (12). Lee et al. reported that meningitis in all of the 16 newborns examined was accompanied by ventriculitis at the time of the initial ventricular puncture (13). Ventriculitis is usually considered when bacterial meningitis shows poor response to appropriate antibiotics, or when hydrocephalus is diagnosed using brain imaging. Nevertheless, it is difficult to predict the presence of ventriculitis if there is no specific manifestation as seen in the present case. MRI is more specific and more sensitive than CT for diagnosis (14). Treatment of ventriculitis complicating bacterial meningitis is pursuant to bacterial meningitis treatment, which requires prompt and adequate antibiotic administration; however, the duration of antibiotic treatment has not been clearly determined and treatment occasionally requires intraventricular chemotherapy (13). The present case was successfully treated

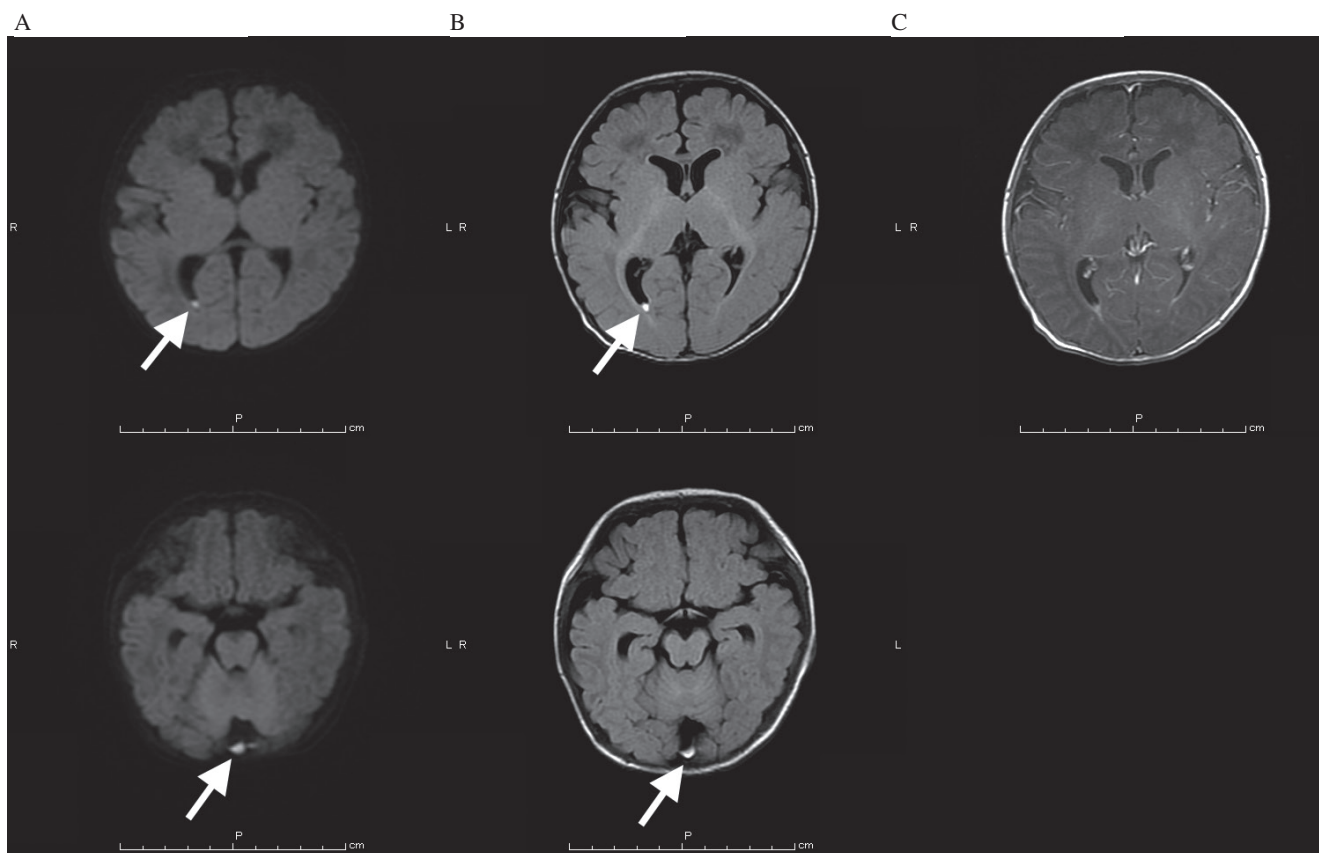


Fig. 1. Head magnetic resonance imaging (MRI) on admission day 12. (A) Diffusion-weighted imaging. (B) Fluid Attenuated Inversion Recovery (FLAIR) imaging. (C) Gadolinium (Gd)-enhanced T1 weighted image. Diffusion-weighted imaging and FLAIR imaging showed hyperintense debris in occipital horn of the right lateral ventricle and the subarachnoid space of dorsal posterior cranial fossa. Gd-enhanced T1 weighted image showed surface of brain, fissure of brain, and ependyma enhancement with contrast.

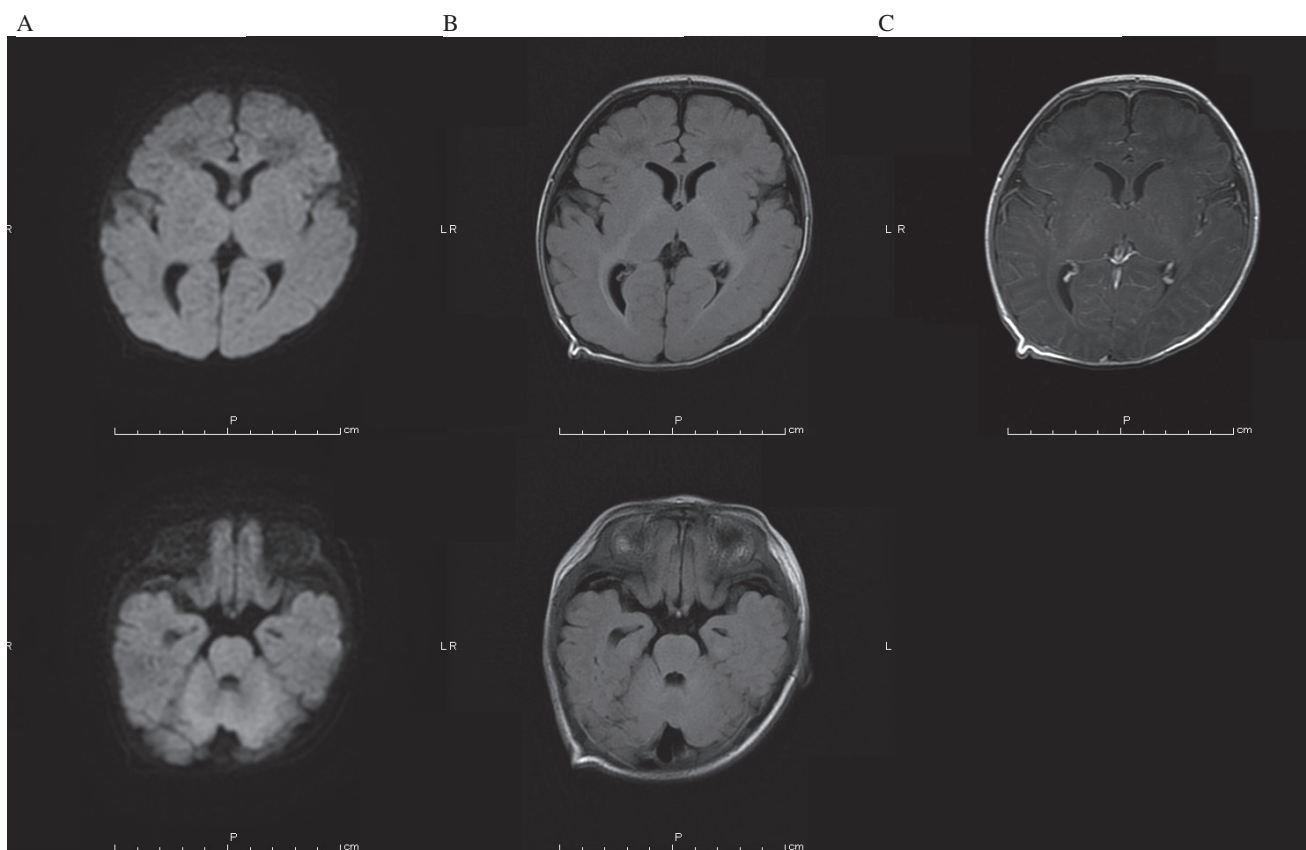


Fig. 2. Head MRI on admission day22. (A) Diffusion-weighted imaging. (B) FLAIR imaging. (C) Gd-enhanced T1 weighted image. Abnormalities detected on MRI completely disappeared on admission day 22.

Table 1. Clinical presentation of childhood meningitis caused by *S. gallolyticus* subsp. *pasteurianus*

	Gavin et al, 2003	Onoyama et al, 2009	Khan, 2009	Thatrimontrichai et al, 2012	Case1	Klatte et al, 2012 Case2	Case3	Case4	Nagamatsu et al, 2012	Punpanich et al, 2012	Takahashi et al, 2014	Hede et al, 2015	Park et al, 2015	This case
Onset of symptoms	3days	4days	3days	3days	13days	5days	2days	5days	8days	6weeks	5weeks	24days	28days	27days
Sex	Male	Female	NR	Male	Male	Female	Male	Male	Male	Male	Male	Male	Male	Male
Gestational age	Term	Term	NR	Term	Term	Term	Term	Post-term	Term	Term	Term	Preterm (32w)	Term	Term
Birth weight (grams)	3925	3192	NR	3,188	NR	NR	NR	NR	3,092	3,600	NR	2,120	3,600	3,680
Premature rupture of membrane	None	None	NR	None	NR	NR	NR	Positive	NR	NR	NR	None	NR	None
Clinical signs	Fever, seizure	Fever, poor activity	Apnea, lethargy	Fever, lethargy, poor feeding	Lethargy, increased work of breathing	Fever, seizure	Poor feeding, lethargy, seizure	Fever, rhinorrhea, fussiness	Eye deviation, fever, irritability	Fever, generalized tonic-clonic convulsion	Diarrhea, fever, irritability	Pale color, loose stool, hypoxemia	Fever, lethargy, grunting	Fever, lethargy, irritability
Complete blood count														
Leukocytes (/mm <sup>3</sup> )	3,400	13,900	2,800	2,500	6,570	3,490	7,000	25,740	NR	28,400	1,600	1,310	5,120	17,380
C-reactive protein (mg/dL)	NR	6.5	2.2	9.6	NR	4.1	NR	NR	NR	NR	NR	3.9	13.48	7.86
Blood culture	Positive	Positive	Positive	Negative	Negative	Positive	Positive	Positive	NR	Positive	Positive	Positive	Positive	Positive
Cerebrospinal fluid														
Leukocyte (/mm <sup>3</sup> )	2,100	12,971	4,500	190	13	1,340	4,470	2,000	8,752	1,910	3,016	61	4,000	7,909
Neutrophils (%)	80	98.7	98	90	NR	NR	NR	NR	73.3	96	> 50	NR	78	97
Glucose (mg/dL)	4	21	NR	26	35	< 20	65	< 20	NR	93	36	< 20	4	1
Protein (mg/dL)	600	3,320	NR	192.6	60	NR	NR	234	1352.5	351	305	404	319	214
Final antimicrobial therapy	PCG (50,000 U/kg every 8h for 14days)	CTX (200MKD for 14days)	Penicillin (120MKD) + GM (4MKD) for 12days	CTX (250MKD for 14days)	CTX (300MKD for 16days)	ABPC (300MKD for 14days)	ABPC (300MKD for 16days)	CTX (300MKD for 14days)	ABPC (210MKD) + PAMP/BP (100MKD) for 20days	VCM + PCG (14days)	ABPC + CTRX (14days)	ABPC (300MKD for 14days)	ABPC (300MKD) + CTX (200MKD) for 21days	ABPC (300MKD for 21days)
Complication	None	None	None	Right IVH grade1	None	None	None	None	None	None	None	IVH grade3	Subdural effusion	Ventriculitis
Prognosis	Survived	Survived	Survived	Survived	Survived	Survived	Survived	Survived	Survived	Survived	Survived	Survived	Survived	Survived

NR, not recorded; PCG, penicillinG; CTX, cefotaxime; MKD, milligrams per kilograms per day; GM, gentamicin; ABPC, ampicillin; PAMP/BP, panipenem/betamipron; IVH, intraventricular hemorrhage.

by extending the period of antibiotic administration for 21 days, until patient's improvement was determined using both CSF findings and MRI imaging. However, recurrence of meningitis was reported in a case of adult meningococcal meningitis complicated by ventriculitis even after adequate treatment of antibiotics with complete improvement according to CSF and MRI findings, indicating the current challenges in sufficient treatment of ventriculitis complicating meningitis (15). Therefore, it is important to evaluate ventriculitis in the course of bacterial meningitis regardless of the presence of symptoms, because delayed or inadequate treatment causes serious neurological sequelae and may account for the high mortality in neonatal ventriculitis. Moreover, screening for ventriculitis in meningitis is likely to provide information regarding accurate prevalence of the disease, adequate duration of antibiotic treatment and prognosis of the disease.

In conclusion, the present case illustrates that uncommon organisms such as *S. gallolyticus* subsp. *pasteurianus* do occasionally cause meningitis and ventriculitis, and highlights the importance of a thorough evaluation of central nervous system complications, including ventriculitis, by MRI, regardless of the presence of symptoms.

Informed consent was obtained from the patient's parents for inclusion in and publication of this case report.

**Conflict of interest** None to declare.

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