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Clostridium novyi type A infantile meningitis; A Case report.

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ผู้ป่วยเป็นเด็กหญิงไทย อายุ 2 เดือน มาโรงพยาบาลด้วยอาการไข้สูง มีอุจจาระร่วง
เรื้อรัง และต้องอยู่โรงพยาบาลมาแล้ว 2 ครั้ง

ได้รับตัวผู้ป่วยไว้รักษาในโรงพยาบาล นอกจากอุจจาระร่วงเรื้อรัง, ยังพบอาการปอด
บวมและเยื่อหุ้มสมองอักเสบ เพาะเชื้อจากอุจจาระ พบสัลโมเนลล่า สปีดิส และแยก
วิเคราะห์ได้จุลินทรีย์ คลอสทริเดียม โนวี จากน้ำไขสันหลังรวม 2 ครั้ง สันนิษฐานว่า
ผู้ป่วยอาจได้เชื้อผ่านทางขูดนมหรือการผสมน้ำนมที่ไม่ถูกสุขลักษณะ หรือโดยการให้
น้ำเกลือหรือเจาะไขสันหลัง ผู้ป่วยรายนี้เป็นรายแรกที่พบคลอสทริเดียม โนวี ในน้ำ
ไขสันหลังในประเทศไทย.

Introduction

In man, *C. novyi* is of importance only as an agent of wound infections. It had been isolated from about 6 per cent of cases of anaerobic cellulitis.⁽⁵⁾

In infant, the anaerobes were isolated from conjunctiva, and the related

clostridia were isolated from septic arthritis, brain abscess, peritonitis, septicemia, wound infection impetigo, and conjunctivitis.^(4,8,9)

Up to the present time, none of meningeal infection by the *C. novyi* has

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been reported in the literature. The present report described one case in which the organism was isolated from the specimens of cerebrospinal fluid (CSF). This may be the first reported case in Thailand.

Case report

A 59 day old Thai female infant was admitted to the infectious unit of Pediatric Department, of Chulalongkorn Hospital, on June 24 1980, because of chronic recurrent diarrhea, severe dehydration and acidosis. She had been admitted 2 times previously with severe gastroenteritis at the age of 10 and 49 days old. On the second admission, *Salmonella krefeld* (1,3,19:y:1,w) was cultured from her stool. She was discharged after 10 days in the hospital (from June 9 to June 19). When discharged, her weight was 2990 grams.

At home after discharge she was given humanized milk formula in an unsterilized bottle about 4-5 times/day. Her diarrhea continued. The stools were yellowish watery about 10 times per day. Vomiting, high fever, restlessness, coughing, weakness, and dyspnea were reported. Physical finding on admission revealed a chronically ill looking infant with severe prostration, drowsy, pale, dehydrated and dyspnoeic. The body temperature was 39° C, pulse rate 200/min, respiratory rate 36/min, head circumference 35 cm. and weight 2700 gms. Course crepitations were heard all over the lungfields. The anterior fontanel was slightly bulging and measured 4×4 cm. The posterior fontanel was still open with 1×1 cm. in

size. Other neurological signs were negative.

Laboratory investigations: blood; hemoglobin, 11.1 gm.%, white blood cell count, 15400/cu mm.; neutrophils, 60%; lymphocytes, 35%; atypical lymphocytes, 2%; monocytes, 3%.

The urine on June, 25, 1980, had trace albumin, no sugar, 0-4 red blood cells/H.D., 0-4 white blood cells/H.D., negative for bile, 1 Ehrlich Unit of urobilinogen/100 ml. of urine. The microscopic urine examination showed few cocci with 0-2/H.D. of tubular cells.

The blood chemistry were: blood sugar, 137; mg % Na⁺, 148 mEq/L; K⁺, 9 mEq/L (hemolysed blood), HCO₃⁻, 9 mEq/L.

Chest x-ray showed minimal infiltration in the right upper lung field. Multiple specimens including blood, stool and CSF were sent for analysis and cultures.

Out of 7 stool specimens for culture, *Salmonella* type E 4 was isolated from specimen on the first day of admission. The blood obtained for culture also on the first day of admission was negative.

The initial lumbar puncture showed clear CSF, a microscopic traumatic tap as shown in Table 1. The cerebrospinal fluids were aerobically and anaerobically cultured routinely on fresh blood trypticase soy agars, and cooked meat media.⁽⁷⁾

The microscopic morphology revealed Gram positive rods (Fig. 1). Further study showed that the anaerobes could ferment glycerol, dextrose, maltose but not sucrose and lactose.

However, the anaerobes had no capsule, were motile with slight proteolysis. The anaerobes grew also in the presence of even traces of oxygen. Deep agar colonies had the appearance of bursting grenades (Fig. 2). After 48 hours in the tube of cooked meat medium containing 0.2-0.5 per-cent starch, the oval subterminal spores were easily seen by Gram's stain. These characters suggested anaerobic *Clostridium novyi*,

type A.⁽⁸⁾ The anaerobe identification was also confirmed by the special Anaerobic Unit of Virginia Polytechnic Institutes of Anaerobes, U.S.A.

The anaerobic susceptibility test of the *C. novyi* by broth discs showed that the anaerobes resisted to all aminoglycosides, was slightly sensitive to erythromycin, tetracyclines and lincomycin but was sensitive to penicillin, clindamycin, metronidazole and chloramphenicol.

*Table I showing the result
of CSF analysis and culture*

Days after hospitalization	White blood cell/cu.mm.		Pandy's test	Protein (mg %)	CSP Sugar/ blood sugar (mg %)	Culture— result
	number	types				
1	400 (traumatic puncture)	—	trace	—	64/137	NG
2	18	L = 98 % N = 2 %	⁺ 1 — 2 ⁺	—	66/90	C. novyi A
9	116	N = 50 % L = 40 % M = 10 %	0	—	—	C. novyi A
15	200	—	0	108	66/94	NG
20	50	—	⁺ 1	268	38/72	NG
28	0	—	0	—	53	NG

NG = no growth

L = lymphocytes

N = neutrophil

M = monocytes

Table 2 The result of CSF culture

Day of hospitalization	Colonial growths in blood agars.		Colonial character
	aerobes	anaerobes	
1	NG	NG	--
2	NG	G (11 colonies)	irregular round colonies.
9	NG	G (2 colonies)	translucent with a pattern of ground glass appearance.
15	NG	NG	—
20	NG	NG	—
28	NG	NG	—

NG = growth

G = growth

Treatment and progress

Due to first traumatic tap and meningitis was highly suspected because of the child's serious condition, a second spinal tap was done on the next day and for the first time was positive for the *Clostridium novyi*. The treatment received were correction of acidosis and dehydration. The antibiotics used were gentamycin 7.5 mg/kg/day and ampicillin 200/mg/kg/day intravenously. She became afebrile after 10 days of treatment, started to gain weight very gradually despite her frequent stools. The cerebrospinal fluid culture was negative on the 15 th hospital day. Her diarrhea responded to colimycin orally and sulfa-trimethoprim compound.

She was discharged after 17 days in the hospital. The discharge weight was 3550 gms.

Discussion

Infection due to Anaerobic *Clostridium novyi* appears to be rare. *Clostridium novyi* has been known since 1894, when it was first isolated by Novyi from guinea pigs he had injected with casein.⁽¹⁾ He described this organism under the name of *Bacillus oedematis*. Similar organisms were isolated by Weinberg and Seguin from cases of gas gangrene in battle casualties of World War I.⁽²⁾ Scott, Turner, and Vawter suggested that these Clostridia be called *Clostridium novyi*.⁽¹³⁾

C. novyi occurs as part of the microbial flora of the soil and sea sediments. It has been isolated from 25-64 per cent of the specimens of soil that have been investigated by different workers.

The *C. novyi*-toxin is highly active (200-8000 MLD) and possesses complex structure, such as; the lethal factor, necrotizing lecithinase, oxygen-labile hemolysin, oxygen-stable hemolysin, non-necrotizing lecithinase and the factor responsible for the pearly zone. At least

two toxic and two non toxic types are known⁽¹⁾ (Table III). Types A and B release many toxins while Type D of *C. novyi* is probably called *C. histolyticum*. (Table 3).^{11,12}

Almost all the strains that have been isolated from the specimens belonged to type A.⁽⁸⁾ Actually type A and B of *C. novyi* are the causative agents of toxic gas gangrene in men, hepatic necrosis in sheep (black disease), and human being.⁽¹⁾

Table III Toxins produced by *Clostridium novyi*.

Toxin	Activity	Produced by types			
		A	B	C	D
Alpha	Necrotising, lethal.	++	++	-	-
Beta	Necrotising, lethal, lecithinolytic, hemolytic.	-	+	-	++
Gamma	Necrotising hemolytic lecithinolytic.	+	-	-	-
Delta	Oxygen-labile hemolysin.	+	-	-	-
Epsilon	Lipolytic ; produces pearly layer.	+	-	-	-
Zeta	Hemolytic.	-	+	-	-
Ets	Tropomyosinase.	-	+	-	+
Theta	Lipase.	-	tr.	-	+

Note : + = produced ; ++ produced in lethal amount ;

- = not produced.

tr. = traced amount.

Table. IV

*Morphological and Biochemical Characteristics
 of the Important Pathogenic Clostridia.*

Clostridia	Spores	Capsule	Motility	Proteolysis	Fermentations			Exotoxin
					Dextrose	Lactose	Sucrose	
<i>C. tetani</i>	Spherical terminal	—	+	—	—	—	—	++++
<i>C. septicum</i>	oval sub-terminal	—	+	+ sl*	+	+	—	++
<i>C. welchii</i>	„	+	—	+ sl*	+	+	+	++
<i>C. novyi</i>	„	—	+	+ sl*	+	—	—	+++
<i>C. histolyticum</i>	„	—	+	+	a +	—	—	+
<i>C. sporogenes</i>	„	—	+	+	—	—	—	—
<i>C. chauvei</i>	„	—	+	+ sl	+	+	+	++
<i>C. botulinum</i>	„	—	+	±	+	±	—	+++

* sl : relatively slight ; a + : acid ; + strong, moderate, and weak.

As mentioned before, *C. novyi* occurs as part of the microbial flora of the soil. Almost all of the strains that have been isolated from soil are type A. In this case there were three possible routes the anaerobic may contaminate :

First, The family lived in very low socioeconomic background and poor sanitation. The infant owned only one milk bottle and were not properly sterilized before each feeding. *C. novyi* could easily contaminate the milk-bottle because

the anaerobes could withstand boiling for thirty minutes or more.⁽¹⁰⁾ But we failed to demonstrate this bacteria in the stool specimen culture.

Moreover the prolonged and chronic diarrhea, either from the Salmonella E 4 or from oral route contamination, failure to thrive, deminished the infant's resistance to infection. Usually anaerobic sepsis was serious infection in new born infant and anaerobic bacteremia were

also found more often than older children.⁽⁴⁾ But the patient received ampicillin for treatment of pneumonia *C. novyi* was sensitive to all penicillin-like compounds, so the anaerobes could not be isolated from the infant's blood.

The second mode of contamination could be from unsterilized lumbar puncture needle or procedure, because the first CSF culture specimen was negative for *C. novyi* and unfortunately, a traumatic tap. Cell identification to confirm the diagnosis of meningitis was missing. Therefore the preexisting meningitis or the superimposed infection could not be verified.

Another mode of contamination could be from scalp vein needles. The needles used were bathed in benzalkonium chloride (Zephrol)^(R) 1 : 100 solution for 24 hours which theoretically could not disinfect *Clostridium novyi* spores. But proof again was lack in the case, for culture of the scalp vein needle, and the bathing solution were not done, and no other occurrence of the same type of infection reported in other patients admitted and received intravenous therapy at the same time. However, the possibility of iatrogenic induction of infection should be kept in mind and great precaution should be operated to prevent this serious infection.

The non suppurative meningitis is caused by organisms which under ordinary condition are in the soil.

To prevent this totally unnecessary disease, strict asepsis should be practised. All disposable set-for scalp vein puncture should be sterile, and discarded after uses. Strict aseptic and antiseptic precaution should also be performed on the skin where there might be contamination before veinipuncture, lumbar puncture and vensection.

The appropriate choice of antibiotic treatment for anaerobic infection should ideally be based upon accurate sensitivity data as well as the urgent and reliable report of anaerobic culture.

Anaerobic microorganisms may act alone or synergistic with aerobes.⁽⁴⁾ In this report only *C. novyi* was isolated from the CSF. However, consideration should be given to providing with antibiotics which would be effective in treating all organisms in a seriously ill child such as our case report.

Conclusion

Anaerobic *Clostridium novyi* type A was isolated from the cerebrospinal fluid of a 2 month-old infant who entered the hospital severely ill from chronic diarrhea, high fever, acidosis and bulging fontanels. The anaerobes may be contaminated via milk bottle or scalp vein set for fluid replacement or lumbar puncture procedure. This may be the first clinical and laboratory report in Thailand.

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