

## Case Report

# Neurologic complication after intrathecal injection of polygeline: a case report

Lan Wu<sup>1,2</sup>, Linli Luo<sup>1,2</sup>, Dong Luo<sup>1,2</sup>

<sup>1</sup>West China Second University Hospital, Chengdu, Sichuan, China; <sup>2</sup>Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, Chengdu, Sichuan, China

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**Abstract:** Post dural puncture headache (PDPH) is a common complication of neuraxial anesthesia. The strategies to manage PDPH are various, including conservative methods, drug therapy, epidural blood patch, epidural injection of colloid solution, etc. A 31-year-old woman who had undergone emergency Cesarean section due to vaginal bleeding and fetal asphyxia was analyzed. Epidural anesthesia was performed with accidental dural puncture and 20 ml polygeline was misused intrathecally in an attempt to augment cerebrospinal fluid (CSF) volume and prevent PDPH. Unfortunately, adverse complications, numbness, and paresthesia on anterior and lateral aspects of left thigh and seizures, occurred in the following days after injecting of polygeline into the subarachnoid. Epidural injection of colloid solution has been proposed to replace the blood patch for management of PDPH and the animal experiment showed its safety, with success in 31 French cases. It is believed that such solutions have negligible toxicity and side effects. However, this case reflects the neurotoxicity associated with the specific route, subarachnoid, administration polygeline, which indicate further investigations should be done in humans to evaluate the safety of this treatment.

**Keywords:** Postdural puncture headache, neurologic complication, seizure

### Introduction

Post-dural puncture headache (spinal headache, PDPH) is the most common serious complication resulting from epidural or spinal anesthetics in pregnant women. These headaches can be severe and debilitating, preventing ambulation and limiting interaction between mother and baby during the postpartum period, in addition to prolonging hospitalization and increasing health care costs. A possible pathophysiologic mechanism is thought to be CSF flow into the epidural space through the dural hole and result in intracranial hypotension, which could cause increased cerebral blood flow and vascular dilation. According to the nature of the defect (needle size suspected of making the puncture) and presence and severity of symptoms, the time and ways of interventions differ. Epidural blood patch (EBP) as a gold standard for the treatment of PDPH is often used in severe and persistent cases [1], to “patch” the meningeal leak.

Epidural injection of colloid solution (e.g. modified fluid gelatin, hydroxyethylstarch) instead of autologous blood is another option to replace blood patch for the management of PDPH. Because of its viscosity, re-absorption of the colloid from the epidural space is delayed, leading to a greater and longer compression, enabling closure of the dural tap [2]. Although a French retrospective [3] study indicated the efficacy of colloid injection without neurotoxicity and dextran 40 and polygeline were injected in rats intrathecally failed to show neurotoxicity [4] in another report, the safety still needed to be validated further. Here, we report a case of paresthesia and seizure after polygeline (modified fluid gelatin) misused into the subarachnoid space to prevent PDPH. Written consent was obtained from the patient for the publication of this case.

### Case report

A 31-year-old woman, 34 weeks and 3 days gestation, was admitted to the hospital emer-

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gency due to vaginal bleeding (approximately 100 ml). An ultrasound examination indicated central placenta praevia. Bolus magnesium sulfate (4 g) was used to inhibit uterus contraction and to prevent preterm delivery. The bleeding decreased and completely stopped on the 3rd day. Additionally, 10 mg dexamethasone was injected per day for three days intramuscularly to promote the lung maturation of the fetus. She was discharged on the 4th day, but re-admitted 10 days later for vaginal bleeding (450 ml) with abdominal pain. A non-stress test revealed fetal no response. An urgent cesarean section was scheduled under epidural anesthesia. Dura mater was accidentally punctured at L2-3 at the depth of 4-cm using an 18 G Tuohy epidural needle. As a result, 20 ml polygeline (Wuhan Hualong Bio-pharmaceutical) was misused intrathecally to augment CSF volume and to prevent PDPH. The patient did not complain of any discomfort and the vital signs remained stable. An epidural catheter was placed at lumbar 1-2 space for lidocaine anesthesia (2%; initial dose of 60 mg without epinephrine. A total of 200 mg lidocaine was used). The cesarean section was uneventful. The patient gave birth to a healthy infant weighing 2980 g. Apgar scores were 9 at both 1 and 5 minutes. On completion of the surgery, pethidine (30 mg) was administered intravenously, and the patient was transferred back to the OBGYN ward. On the third postoperative day, the patient complained numbness and paresthesia on the anterior and lateral aspects of left thigh without the abnormal changes in ultrasound. Motor function (5/5 in strength), urinary and fecal continence were not affected. The patient could even walk under the support of one's hand, without complain of headache. On the tenth postoperative day, a generalized seizure (with loss of consciousness) occurred and lasted for approximately 1-2 min. Seizure dissipated without specific treatment. Cranial and spinal MRI was conducted but did not reveal any abnormality. Vitamin B<sub>12</sub> (500 µg per day) and dexamethasone (10 mg per day) were injected till the 14th day when she was discharged.

One month later, the patient visited our hospital, complaining of pain and edema in the left thigh. Ultrasound examination revealed a thrombus in the deep femoral vein. Nadroparin calcium was given subcutaneously at 4100 anti-factor Xa IU/0.4 mL twice daily for five days.

Pain and edema alleviated and the patient was discharged after five days. Warfarin was given 2.5 mg/d for 3 days and was adjusted to regular international normalized ratio (INR) until stable warfarin maintenance dose. It was used for 3-month course under INR monitoring. The ultrasound examination revealed normal blood flow in the left leg without any symptoms and cranial MRI was unremarkable in the following three months. The patient has now been followed-up for nine years, without severe relevant conditions.

### Discussion

Over the past 2 decades, with the introduction of pencil-point spinal needles for spinal anesthesia in pregnant women, the problem of PDPH in obstetrics has been more associated with accidental dural puncture (ADP) during attempted epidural procedures. The overall incidence of epidural needles accidental entry into the subarachnoid when attempting epidural procedures with 16-18 gauge epidural needles is 0.5-4%, with a resulting headache rate of 45-80% [5]. In many cases, the headache is mild in intensity and brief in duration, without significant sequelae. However, PDPH is occasionally severe enough to last months or even years [6]. In the OBGYN setting, the ability to care for the new born by the mothers could be compromised. PDPH could prolong hospital stay for both the mother and child [7]. Optimal management of PDPH is thus particularly important for delivering mothers.

For severe and persistent cases, treatment strategies to prevent PDPH typically aim at expanding/maintaining CSF volume, such as epidural blood patch [1], passing an epidural catheter through the dural hole, and injecting saline into the subarachnoid space through the intrathecal catheter, and so on. Pterygopalatine ganglion block is another novel invasive effective therapy for PDPH [8]. The new technology for optimum treatment is, however, still a matter for debate [9].

Colloidal solutions (e.g., polygeline) have been proposed to replace blood patch for epidural injection in dilemma situation such as HIV patient [10] and safety and effectiveness have been proven [11]. Re-absorption of the colloid from the epidural space is delayed because of its viscosity, leading to a greater and longer-

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lasting compression [12], which was the main mechanism of treatment PDPH by epidural injection of colloid. Injection colloid into the subarachnoid space to preventing PDPH was not used in the past in humans, in spite of intrathecally injected dextran 40 and polygeline in rats not indicating neurotoxicity [4]. After injecting polygeline into the subarachnoid space in this case, the mother developed paresthesia and seizure. We speculate that the adverse effects are associated with the specific administration of polygeline.

In this case, it is impossible to conclude whether the absence of PDPH was due to polygeline treatment or not. The colloid injected into the subarachnoid space may have helped to maintain the osmotic pressure of CSF and cranial pressure. Redundant polygeline may leak into the epidural space to play the same role as Salvador [12] described, which means: 1) as epidural saline infusion, the injection of colloid increases the epidural pressure and immediately relieves headache; 2) the existence of colloids in epidural space lead to a greater and longer-lasting compression; 3) enabled closure of the dural tap.

Seizure has been associated with dural puncture [13]. Seizure typically starts within one week after the dural puncture, but was reported as long as three weeks after the dural puncture [13]. The etiology of the seizure is likely multi-factorial, such as disturbances of the cerebral vascular circulation. Caffeine has been implicated in seizure after dural puncture [14], but the patients in this case did not use any beverage/food containing caffeine. The colloids injected into the CSF may penetrate the brain-blood barrier and be metabolized slowly, causing the brain environment to become soaked and unusual, which triggers the seizure.

Epidural and spinal anesthesia is commonly associated with paresthesia, but permanent trauma to the spinal cord or nerve roots is rare. In a review of more than 10,000 patients receiving spinal anesthesia, minor nerve root damage with symptoms lasting up to 1 year was noted in 17 cases [15]. Needle trauma and local anesthetic neurotoxicity are the most common causes of neurologic complications related to neuraxial anesthesia. Paresthesia during needle insertion or injection of drug and multiple attempts to perform a block were

major factors associated with lumbosacral nerve root injuries. Paresthesia at the site of needle insertion indicates contact with either the spinal cord or the nerve roots of the cauda equina, and has been shown to increase the likelihood of subsequent neurological deficit. In a prospective study [16], two thirds of patients with neurologic complications experienced pain during needle placement or injection of local anesthesia. But in this case, no discomfort occurred during the process of needle insertion and injection of polygeline and lidocaine. Also, the two epidural puncture processes were successfully performed without multiple attempts. In this case, paresthesia may not be caused by the puncture process.

The patient suffered edema and pain caused by deep femoral thrombosis in one month later with the same location of paresthesia. Did paresthesia cause by the deep vein thrombosis? The symptoms of deep vein thrombosis (DVT) includes: edema, warmth, pain, tenderness, and redness, except paresthesia. In addition, although pregnancy and bed rest are risk factors of DVT, the ultrasound images did not indicate that. Paresthesia is an isolated symptom from the DVT.

Since paresthesia and seizure presented on the initial following days of intrathecally injection of polygeline, both of them were thought to be the neurotoxicity of the polygeline. Although the cranial and spinal MRI did not show any remarkable change, the histologic or ion channel changes could not be confirmed in this patient. As the safety of epidural injection of polygeline was confirmed by the early study, the mechanism of the neurotoxicity of polygeline can be inferred in this case may including 1) the severity of neurotoxicity is depended on the duration when neuron contacted with polygeline. Epidural injections will be absorbed by the vein in the epidural space, and be metabolized quickly. In contrast, intrathecal polygeline could not be metabolized immediately due to the blood-brain barrier. 2) injury is reversible and the symptoms may causing by the changes of ion channel or concentration of some ion.

Intrathecally injection of any substance clearly carries significant risk. It should be cautioned that any substance attempted to be injected into the subarachnoid space in humans must be confirm for safety by large research studies.

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However, it could be used into the epidural space.

### Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Dong Luo, West China Second University Hospital, No. 20, Section 3, South Renmin Road, Chengdu, Sichuan, China; Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, No. 20, Section 3, South Renmin Road, Chengdu, Sichuan, China. Tel: +86-28-85503752; 8613880039933; Fax: +86-28-8550-3752; E-mail: luodong8706@163.com

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