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PRACTICE FORUM

Prompt control of outbreak of potentially fatal iatrogenic encephalitis due to intrinsically contaminated intrathecal anaesthetic agent by ESBL producing *Klebsiella pneumoniae*

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Abstract

Iatrogenic meningitis is a serious complication of anaesthesia with an estimated mortality of 35%. The Department of Anaesthesia reported 8 postoperative patients of encephalitis over a period of two weeks. All had received subarachnoid block with 0.5% bupivacaine and within 2-6 hours presented with a typical clinical picture of severe headache and high grade fever. The cerebrospinal fluid (CSF) of three patients was collected by lumbar puncture and sent for culture and sensitivity. The hospital infection control team was notified about these patients. Apart from extensive personal and environmental surveillance, culture of intravenous solutions (5% dextrose and Normal Saline), blood bags and finger tip cultures of doctors and nurses was done. Several vials of 0.5% bupivacaine injections (Injection A and Injection B) of two companies were also collected and processed. Injection B revealed growth of Extended spectrum beta lactamase (ESBL) producing *Klebsiella pneumoniae*. This isolate was similar to *Klebsiella pneumoniae* isolated from the CSF of one of the patients in biochemical reactions, antibiotic sensitivity testing and ESBL production. Results were immediately conveyed to Department of Anaesthesia for stopping the use of Injection B. We want to highlight that with proper microbiological surveillance and intervention by hospital infection control team we could save precious lives of patients.

Keywords: Iatrogenic diseases; Meningitis, bacterial; *Klebsiella pneumoniae*; Postoperative complications; Bupivacaine and adverse effects

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Introduction

Iatrogenic meningitis and encephalitis is a serious complication of spinal intrathecal and epidural anaesthesia. It carries an estimated mortality of 35%. Bacterial infections after spinal and epidural anesthesia are uncommon events, with a reported incidence of less than 1 for every 53,000 procedures.[1] *Streptococcus, Staphylococcus, Enterococcus*, and *Acinetobacter* are the bacteria most c ommonly involved.[2] In this study we present a series of patients who acquired encephalitis due to a intrinsically contaminated intrathecal anaesthetic agent by *Klebsiella pneumoniae*. The hospital infection control team was notified of the above findings. Suspecting the possibility of an outbreak, inspection of the postoperative wards and operation theatre was undertaken to identify the source of infection. We want to highlight that with proper microbiological surveillance and intervention lives of patients can be saved as we did in this case.

Materials and methods

In May 2013, the anaesthesia department of our 569 bedded rural medical college noted similar features of severe headache and high grade fever in eight postoperative cases over a period of two weeks. Five of the patients belonged to Department of Obstetrics and Gynaecology and 3 patients belonged to Department of Orthopaedics. The patients were operated uneventfully with no immediate postoperative complications and were kept in postoperative room under strict supervision. All of them had received subarachnoid block with 0.5% heavy bupivacaine and within 2-6 hrs of giving subarachnoid block the patients presented with a typical clinical picture complaining of severe headache followed by high grade fever. One of the patients of the Department of Obstetrics and Gynaecology in addition presented with altered sensorium and signs of meningism. Consultation from Department of Medicine was sought and clinical diagnosis of encephalitis was kept. The case series is summarized in table I and Figure 1 gives the epi-curve of the patients.

The cerebrospinal fluid (CSF) of three patients was collected by lumbar puncture and sent for culture and sensitivity. Empirical postoperative treatment with ceftriaxone for orthopaedics patients and amoxyclav (amoxicillin and clavulanate) for Gynaecology patients was started.

The hospital infection control team was notified of the above findings. Suspecting the possibility of an outbreak, inspection of the postoperative wards and operation theatre was undertaken to identify the source of infection. Extensive personal and environmental surveillance was undertaken. Surface swabs pre-moistened with sterile normal saline were collected from various sites including stethoscopes of doctors, operation tables, dressing trolley, air conditioner, floor, walls, oxygen cylinder, tap, suction apparatus and door knobs. Within one hour, taking all aseptic precautions these were inoculated on sheep Blood agar and MacConkey agar plates in Department of Microbiology. The plates were incubated overnight at 37°C.

Further to investigate the source, finger tip culture of all the doctors and nurses of suspected outbreak ward

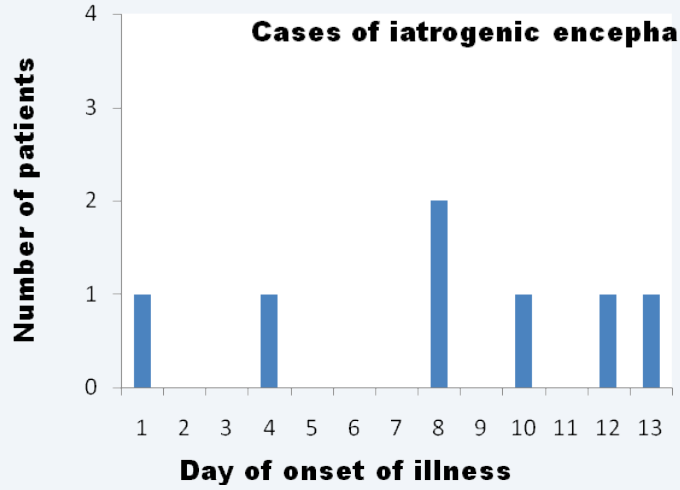

Figure 1. Cases of iatrogenic encephalitis along with their onset of illness

Table I. Clinical details of the patients suffering from iatrogenic encephalitis

S No.	Age (years)	Surgery	Anaesthetic Technique	Onset of Symptoms (days)	Symptoms	Perioperative Blood Transfusion	Recovery (Days)
1	42	TAH	SAB	2	Headache	No	1
2	28	Unruptured ectopic pregnancy	SAB	4	Headache, Dizziness, Fever, neck stiffness	No	7
3	62	ORIF for fracture femur	SAB	3	Headache	Yes	1
4	60	ORIF for fracture tibia	SAB	6	Headache	Yes	1
5	50	TAH	SAB	3	Headache, Fever, Shivering	Yes	2
6	63	ORIF for fracture femur	SAB	5	Headache, neck stiffness, dizziness	No	2
7	27	LSCS	SAB	4	Headache, neck stiffness, Nausea, Fever	No	5
8	25	LSCS	SAB	3	Headache	No	1

TAH-Total abdominal hysterectomy; LSCS- Lower segment caesarean section; ORIF-Open reduction and internal fixation; SAB- Subarachnoid block

and operation theatre was also done and the plates incubated overnight at 37°C. In addition, samples of commonly used intravenous solutions namely 5% Dextrose and Normal Saline were collected and tested by sterility test using casein digest broth. Since three of the patients had received blood transfusion the possibility of blood transfusion reactions was kept in mind. The repeat crossmatch of respective donor and recipient blood in all the 3 cases did not show any mismatch of blood. The blood bags which were obtained from the patients were sent for culture. In addition the Elseviers solution used in blood bag was also aspirated aseptically and cultured. After much pondering, another common factor noticed was the administration of intrathecal subarachnoid block of 0.5% bupivacaine from two different companies (Injection A and injection B). Several of these vials were sent to the Department of Microbiology for sterility testing, where their manufacturing dates, expiry date and batch number were noted. Both were subjected to various microbiological investigations namely direct gram staining, aerobic culture and fungal culture. The media used for aerobic culture was Blood and MacConkey agar and the inoculated plates were kept at 37°C for two days. The fluids from both injections were added to bottles containing Brain heart

infusion broth for enrichment and incubated at 37°C for two days. Then, subcultures were made to Blood and MacConkey agar to see for presence of growth. For fungal culture the material from both vials was inoculated on tubes with Sabourauds Dextrose Agar (SDA) with and without antibiotics and were kept at 37°C and 25°C for at least 3 weeks.

Results

No growth was seen in aerobic bacterial and fungal culture media from the various samples taken for extensive personal and environmental surveillance. Similarly samples from finger tip culture, blood bags and intravenous solutions namely 5% dextrose and normal saline did not reveal any results. One of the CSF culture reports of the three patients showed growth of *Klebsiella pneumoniae* (patient 2; Table I) and the other two were sterile (patients 6 and 7; Table I).

Injection A did not reveal any microorganisms in direct gram staining. There was no growth in aerobic culture media (direct as well as after enrichment with Brain heart infusion broth). On the other hand, Injection B showed quite different results. No microorganisms were seen in direct gram staining and there was no growth in direct aerobic media after 2 days of incubation. However, turbidity was seen after overnight incubation in Brain Heart Infusion Broth. Subculture on MacConkey agar showed growth of pink, lactose fermenting colonies which were identified as Klebsiella pneumoniae by standard microbiological techniques.[3] The results were immediately conveyed to Head of Department of Anaesthesia for stopping the total use of injection B. Retrospective analysis showed that all the patients had indeed received injection B. Further, antibiotic susceptibility testing (AST) was performed on Mueller Hinton agar (MHA) by Kirby Bauer technique.[4] The results of AST showed that the microorganism was resistant to ceftazidime, ciprofloxacin, amoxyclav and cephalothin and it was sensitive to gentamicin and imipenem. Screening for Extended spectrum beta lactamase (ESBL) production was done as per criteria recommended by Clinical Laboratory Standards Institute (CLSI) by using ceftazidime (30 µg) disc in each case.[5] An inhibition zone of ≤ 22mm for ceftazidime indicated probable ESBL production. This was confirmed by Double disc synergy test (DDST) using ceftazidime (30 µg) disc and a co-amoxiclav (20 µg of amoxicillin and 10 µg of clavulanic acid) disc. The zone of inhibition around the ceftazidime disc showed an extension towards the co-amoxiclav disc showing it to be an ESBL producer.

The above findings were reconfirmed by testing several vials of the same batch number of injection B which gave consistent results. No growth was obtained in fungal culture media (Injection A and B) despite of incubation for three weeks.

So based on our study, we concluded that the source for this outbreak was the intrathecal injection B and the pathogen present in it was ESBL producing *Klebsiella pneumoniae*. This isolate was similar to the *Klebsiella pneumoniae* isolated from the CSF of one of the patients in biochemical reactions, antibiotic sensitivity testing and ESBL production. The results were conveyed to the concerned physicians so that appropriate antibiotic therapy could be given to the affected patients. Luckily, all patients improved with therapy and there was no complications in any of them.

Discussion

Several diagnostic and therapeutic procedures like lumbar puncture, myelography and spinal anaethesia gain entry into the intrathecal space. Agents used for intrathecal injections can be contaminated either intrinsically or extrinsically. Various viruses and bacteria have been previously associated with extrinsic contamination of intravenous agents.[6,7,8] The possibility of introducing infection into subarachnoid space by spinal tap has been recognized from the time when lumbar puncture was first performed. Babcock first reviewed the cause of death after spinal in 1932 and found that though post spinal meningitis is a rare occurrence yet it is a dreaded complication.[9] Baer has reported 179 cases of post spinal meningitis worldwide during a span of more than 50 years (1952-2005).[10] Recently, there has been a similar outbreak of fungal meningitis caused by contaminated methylprednisolone used for epidural injections and more than 200 patients were suspected to be involved.[11] Propofol related outbreaks have been reported to cause surgical wound infections or blood stream infections.[12,13]

Post spinal procedure meningitis leads to grave consequences and can cause mortality in one third of the cases.

Bupivacaine is a sterile anaesthetic agent used for local anaesthesia including infiltration, nerve block, epidural and intrathecal anaesthesia. Eldor *et al.* have elicited bactericidal and fungicidal properties of Bupivacaine in addition to its anaesthetic effects.[14] In our case, the drug used must have been contaminated with *Klebsiella pneumoniae* to an extent that in spite of its bactericidal property it supported the growth of the bacteria.

The prompt personal and extensive environmental surveillance of the affected areas and early identification of the source of infection gave valuable guidance to the treating physicians which led to the survival of all the six patients. We recommend that every postoperative infection should be taken seriously and investigated to know the probable source of infection. Apart from good infection control practices, use of Bupivacaine with a preservative should be there. In addition, we recommend that all anaesthilogists should practice the use of standard work precautions, proper aseptic techniques, safe injection practices and hand hygiene. One should also avoid prolonged epidural catheterization in immunocompromised patients to avoid infections. By following these guidelines for asepsis in giving central neuraxial blocks, many serious complications can be avoided. In addition, to rule out the possibility of contamination in intravenous and regional anaesthetic drugs, they should be sent for frequent culture to avoid similar life threatening complications.

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