

CASE REPORT

Fatal cervicitis caused by Metallo- β -Lactamase (MBL) strain of *Pseudomonas aeruginosa*

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ABSTRACT

Symptoms suggestive of a lower genital tract infection (LGTI) are common complaints in women who consult gynaecologists. Inflammation of the endocervix (cervicitis) is usually found in those cases, when vaginal speculum examination is being done. Cervicitis is commonly seen in women during their child bearing period. Acute cervicitis is commonly caused by *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis* and is non-fatal. However, rarely cervicitis may be caused by organisms like *Citrobacter* spp, *Enterobacter* spp, and *Pseudomonas* spp. Infections caused by *Pseudomonas aeruginosa* are often hard to treat because of both the intrinsic resistance of the species and its remarkable ability to acquire further resistance mechanisms to multiple groups of antimicrobial agents, including β -lactams, aminoglycosides and fluoroquinolones. In this report, a fatal case of cervicitis caused by metallo- β -lactamase (MBL) strain of *Pseudomonas aeruginosa* in a 35 years old woman is being presented.

Keywords: Cervicitis, MBL strain, *Pseudomonas aeruginosa*

INTRODUCTION

More than half of all women at some point during their adult life are affected by cervicitis. ⁽¹⁾ In a landmark study published in 1984, Brunham et al recognized the clinical syndrome of cervicitis as “the ignored counterpart in women of urethritis in men.” ⁽²⁾ Anatomically the cervix has two parts, ectocervix and endocervix. The ectocervix is lined by squamous epithelium like that of vagina and is susceptible to the infections that cause vaginitis. The endocervix is lined by columnar epithelium and inflammation is known as “endocervicitis” or “mucopurulent cervicitis”. According to the onset it can be either acute or chronic. Acute cervicitis is most often caused by an infection, usually caught during sexual activity. ^(3,4) Common bacterial organisms are *Chlamydia*, *Gonorrhoea*, *Streptococcus*, *E. coli* and *Klebsiella*. Less frequently enterobacteria like *Citrobacter* spp, *Enterobacter* spp, *Pseudomonas* spp, *M. morgani*, and *P. mirabilis* can also cause cervicitis.⁽⁵⁾ The

disease is usually asymptomatic. Vaginal discharge, dysuria and abnormal uterine bleeding are the common symptoms. When the cervix is examined through a vaginal speculum it is seen to be reddened, swollen with edema and a mucopurulent discharge can be seen through the cervical canal. The definitive diagnostic criteria are (a) ectopy of glandular epithelium, (b) friable epithelium, (c) bleeding on touch, (d) gross visualisation of mucopus on cotton swab and (e) ten or more neutrophils on gram-stained smear. ⁽⁶⁾ It can produce ascending infection leading to pelvic inflammatory disease (PID). Though the disease is usually not fatal, there are reported cases of beta haemolytic Group-A streptococcal cervicitis causing disseminated intravascular coagulation, bacteraemic shock, and death. ⁽⁷⁾ We report a case of *Pseudomonas aeruginosa* cervicitis causing death.

THE CASE

This case is of a 35 year old multiparous woman who was first seen in gynecological out patient department (OPD) of a medical college and hospital in Bhubaneswar, Odisha on 9th October

2012. She came with 5 days history of fever, low back pain and purulent foul smelling vaginal discharge. Her menstrual cycles were regular and last menstrual period was 15 days back. She

was using old used clothes as pads during menstruation. On general examination she had fever and tachycardia. Per abdominal examination showed right iliac fossa tenderness without any other specific abnormality. Per speculum examination showed a reddened, slightly thickened cervical opening which was covered by a yellow sticky secretion. There was right forniceal tenderness on bimanual examination.

Routine blood investigations showed total leucocyte count (TLC) 14,000/cu mm with neutrophilia. Haemoglobin level was normal and there was no abnormality in urine examination. Quantitative Buffy Coat (QBC) test for Malaria parasite was negative. Antibody tests for HIV and VDRL infections were negative and the chest x-ray was normal. Pelvic ultrasonography revealed a normal size uterus and bilateral adnexae devoid of masses or collection. Two endocervical swabs were collected, one for microscopic examination and the other for culture and sensitivity testing.

She was provisionally diagnosed as a case of acute cervicitis and prescribed cefuroxime (second generation cephalosporin) tablets, clotrimazole vaginal cream and an anti-inflammatory drug. Despite the treatment for 48 hours, her general condition gradually worsened and she was hospitalized on 11th October 2012. In the hospital she was treated with intravenous ceftriaxone and linezolid injections. She was transferred to the intensive care unit (ICU) on 12th October 2012 as her condition further

deteriorated. Gradually she developed features of septicaemia and inspite of intensive monitoring; she collapsed to death on 13th October 2012.

Gram staining of the swab had revealed plenty of pus cells along with few gram positive cocci and abundant gram negative bacilli. The other swab was plated on Mac Conkey's agar and Blood agar plate. Both plates were incubated at 37°C for overnight. On next day, large, low convex, non lactose fermenting, rough, with typical fruity odour, translucent colonies appeared on Mac Conkey's agar plate. Similar morphotype colonies which were haemolytic appeared on blood agar plate. By further testing of the colonies, it was revealed that the organisms were gram-negative motile rods. They were positive for oxidase and catalase. They produced pigment on Nutrient agar. (Fig. 1) On biochemical reaction the organism was non fermenter, nitrate reduction test and arginine dihydrolase test was positive. From this reaction we identified the organism as *Pseudomonas aeruginosa*.

In antibiotic susceptibility test it was resistant to all commonly used anti-pseudomonal drugs. (Fig. 2) Further testing confirmed the strain to be extended spectrum beta lactamase (ESBL) and MBL positive. (Fig. 3 and 4) For confirmation of identification and antibiotic susceptibility testing the organisms were put on Vitek 2 automated system. From the system it was confirmed as MBL positive strain of *Pseudomonas aeruginosa*. (Fig. 5)

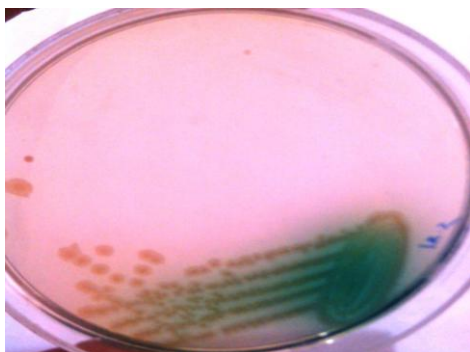


Figure 1: Pigment producing colonies on nutrient agar plate



Figure 2: Antibiotic susceptibility test shows resistant to all commonly used anti-pseudomonal drugs.



Figure 3: Double disc synergy test for ESBL testing using ceftazidime, co-amoxycylav and cefotaxime discs.

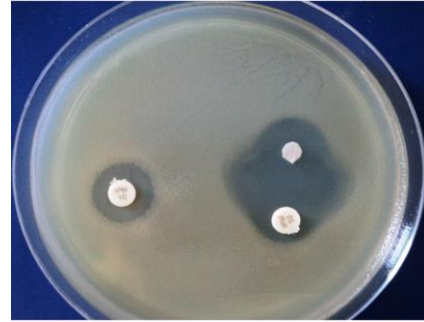


Figure 4: MBL testing using Imipenem and EDTA discs.

DISCUSSION

Pseudomonas is a genus of gram-negative aerobic gammaproteobacteria, belonging to the family Pseudomonadaceae containing 191 validly described species. ⁽⁸⁾ *Pseudomonas aeruginosa* is increasingly recognized as an emerging opportunistic pathogen of clinical relevance. Several different epidemiological studies indicate that antibiotic resistance of *Pseudomonas* is increasing in clinical isolates. ⁽⁹⁾ Being an extremely adaptable organism it can survive and multiply even with minimal nutrients, if moisture is available. *Pseudomonas aeruginosa* is present on the skin of the axilla and perineum in some persons. Though commonly it causes nosocomial infection, it can also infect the community outside the hospital causing infections in ear, joint, vagina and cervix. ⁽¹⁰⁾

Pseudomonas aeruginosa producing Metallo- β -Lactamases (MBLs) was first reported from Japan in 1991 and since then has been described from various parts of the world, including Asia, Europe, Australia, South America, and North America. ⁽¹¹⁻¹³⁾ Metallo- β -lactamases belong to Ambler class B and have the ability to hydrolyze a wide variety of β -lactam agents, such as penicillins, cephalosporins, and carbapenems. ⁽¹⁴⁾ These enzymes require zinc for their catalytic activity and are inhibited by metal chelators, such as ethylene diamine tetra acetic acid (EDTA) and thiol-based compounds. ⁽¹⁴⁾ The genes responsible for the production of MBLs are typically part of an integron structure and are carried on transferable plasmids but can also be part of the chromosome. ⁽¹⁵⁾ Therefore, because of the integron-associated gene cassettes, *P. aeruginosa* isolates producing MBLs are often resistant to different groups of

antimicrobial agents, which can be transferred to various types of bacteria. ⁽¹⁶⁾

Metallo- β -lactamase producing *Pseudomonas aeruginosa* isolates have been responsible for several nosocomial outbreaks in tertiary centers in different parts of the world, illustrating the need for proper infection control practices. ⁽¹⁷⁻²⁰⁾ These isolates have also been responsible for serious infections, such as septicemia and pneumonia, and have been associated with failure of therapy with carbapenems. ⁽¹⁶⁻¹⁷⁾

Cervicitis is caused by varieties of etiology bacterial being more common. Though there are case reports of fatal cervicitis, it is usually a non-fatal disease and can be treated with antibiotics. *Pseudomonas* rarely can cause cervicitis and if it is by a MBL strain then it becomes fatal. In our case the patient mentioned that, she was using cloth pads during her menstrual cycle, which might be the cause of infection. ⁽²¹⁾ Second generation cephalosporin and later third generation cephalosporin was started for treatment with common etiology in mind but the organism was completely resistant to it. The organism was resistant to almost all antibiotics including Piperacillin and Tazobactam. The infection was so fatal that, before the reports of culture and sensitivity were available, she developed septicaemia and died.

Even though the incidence of cervicitis by MBL strain of *Pseudomonas aeruginosa* is very less, it should be suspected in patients not responding to usual treatment and deteriorating quickly. Aggressive treatment in those cases can save the life of patients.

Identification Information					
Pseudomonas aeruginosa					
Entered: Oct 13, 2012 09:54 IST By: labadmin					
Analysis Messages: The following antibiotic(s) are suppressed from analysis: Aztreonam, The following antibiotic(s) are not claimed: ESBL.					
Susceptibility Information					
Card: AST-GN25		Lot Number: 265231210		Expires: Apr 13, 2013 12:00 IST	
Completed: Oct 13, 2012 02:53 IST		Status: Final		Analysis Time: 12.00 hours	
Antimicrobial	MIC	Interpretation	Antimicrobial	MIC	Interpretation
ESBL			Meropenem	>= 16	R
Ampicillin	>= 32	R	Amikacin	>= 64	R
Ampicillin/Sulbactam	>= 32	R	Gentamicin	>= 16	R
Piperacillin/Tazobactam	>= 128	R	Tobramycin	>= 16	R
Cefazolin	>= 64	R	Ciprofloxacin	>= 4	R
Ceftriaxone	>= 64	R	Moxifloxacin	>= 8	R
Cefepime	>= 64	R	Tigecycline	>= 8	R
Aztreonam			Nitrofurantoin	>= 512	R
Ertapenem			Trimethoprim/Sulfamethoxazole	>= 320	R
Imipenem	>= 16	R			

+ = Deduced drug * = AES modified ** = User modified

Figure 5: Report obtained from Vitek 2 automated system.

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