

# Six cases of sepsis caused by *Pantoea agglomerans* in a teaching hospital

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## SUMMARY

*Pantoea agglomerans* is an environmental organism which may seldom cause opportunistic infections. Here we report on a 6 case outbreak in a teaching hospital. Within three months *P. agglomerans* was isolated from blood cultures of 5 patients from oncology and 1 patient from ICU departments. *P. agglomerans* was in pure culture in 5 cases, while in the last one *Rahnella aquatilis* and *Candida famata* were also isolated. Therefore, *P. agglomerans* is able to produce nosocomial infections in patients with primary pathology often associated with immune suppression.

**KEY WORDS:** Pantoea, Sepsis, Outbreak

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In recent years a significant increase in nosocomial infections has been reported especially in Intensive Care Units (ICU) and Oncology Departments. Sepsis is a complex, multifactorial syndrome that can develop into conditions of different severity, described as severe sepsis or septic shock. Cancer chemotherapy or intravenous catheterization can be predisposing factors to cases of bacteraemia due to unusual organisms (Beebe *et al.*, 1995), including *Listeria*, *Salmonella* and *Campylobacter*. Clinical signs are often misleading and, in some circumstances, it may be difficult or even impossible to identify the source of the infection (Gullo *et al.*, 2005).

*Pantoea agglomerans* is member of Enterobacteriaceae that inhabits plants, soil, water and such species includes bacteria reported as both commensal and pathogen of animals and humans

(Gavini *et al.*, 1989). The most common infection caused by *P. agglomerans* is septic arthritis or synovitis (Kratz *et al.*, 2003), but *Pantoea* has been also involved in nationwide epidemic of septicaemia due to contaminated intravenous products (Mackel *et al.*, 1975), an outbreak secondary to contaminated parental nutrition (Habsah H *et al.*, 2005), osteitis (Laporte *et al.*, 2002), colelithiasis (Flores *et al.*, 2003), occupational respiratory infections and skin allergy (Milanowski *et al.*, 2003), blood stream infection in an elderly person (De Baere *et al.*, 2004) and peritonitis (Lim *et al.*, 2006). *Pantoea* spp are clearly opportunistic pathogens and rarely cause disease in the otherwise healthy individuals (Sanders and Sanders, 1997).

Infections by *P. agglomerans* are usually associated with an identifiable exogenous source (Matsaniotis *et al.*, 1984; Stenhouse, 1992; Ferguson *et al.*, 1993; Wagner *et al.*, 1994; Bennet *et al.*, 1995). This organism grows well at 4°C, is often associated with plants, and can be readily recovered from cotton (Ferguson *et al.*, 1993; Lindh *et al.*, 1991). Therefore *Pantoea* spp are often associated with outbreaks due to contaminated intravenous solutions and stored blood

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products as well as "cotton fever" in intravenous drug abusers (Matsaniotis *et al.*, 1984; Stenhouse, 1992; Ferguson *et al.*, 1993; Wagner *et al.*, 1994; Bennet *et al.*, 1995).

Here we report an outbreak caused by *P. agglomerans* among oncological patients of a teaching hospital.

Case 1 was a 75-year-old man, who underwent a total gastrectomy for a poorly differentiated adenocarcinoma with serosal and lymphonodal involvement. One month later he had received the first of eight cycles of chemotherapy through a central venous catheter (CVC) within five months. During his hospital stay for the 8<sup>th</sup> chemotherapy cycle he had chills followed by an increase in body temperature (38.4°C). However he had a normal chest radiograph and a sterile urine culture. Due to his low peripheral white blood cell count ( $0.655 \times 10^9/L$ ) chemotherapy was stopped. Blood samples from CVC and from a peripheral vein, as well as CVC tip were sent immediately to our microbiology laboratory. The patient was started empirically on teicoplanin and imipenem. Three days later the treatment was modified and teicoplanin was withdrawn according to antimicrobial susceptibility test. The clinical condition of the patient improved and he was discharged with an antibacterial therapy per os (ciprofloxacin, 500 mg, bid).

Case 2 was a 29-year-old male with a 2-year history of surgery, radiotherapy and chemotherapy for osteosarcoma with lung involvement. A CVC was used for chemotherapy administration. However the patient developed chills followed by fever (40.0°C). Laboratory investigation revealed a leukocytosis of  $10.9 \times 10^9/L$ , with 84% neutrophils and a sterile urine culture. Blood samples from a peripheral vein, from the CVC as well as the CVC itself were sent to our microbiology laboratory. The empirical treatment was started with teicoplanin plus imipenem that was changed to imipenem only until discharge, when amoxicillin/clavulanic acid was started for one week, with progressive improvement of clinical conditions.

Case 3 was a 45-year-old woman with a two year history of sigma adenocarcinoma and previous surgery on a metastatic liver as well as lymphonodal invasion. In addition the primary cancer at the left colon was surgically resected. The patient underwent several radiotherapy and chemother-

apy cycles, until a CVC was implanted for a further chemotherapy administration. Two months later chills and fever suggested a septic complication. The white blood cells were  $6.1 \times 10^9/L$  with 72.7% neutrophils. A peripheral vein and a CVC blood sample were submitted to microbiology laboratory. An empirical treatment with teicoplanin plus imipenem was started, but after the antimicrobial susceptibility test results, only imipenem was continued for seven days. The CVC was removed later on and *Pantoea* isolated from the catheter tip.

Case 4 was a 47-year-old man with pancreas cancer and liver and lymphonodal involvement who underwent surgery and chemotherapy. Again a CVC was used for the administration of chemotherapy, however after less than two months the patient exhibited chills and fever with a white blood cell count of  $13.9 \times 10^9/L$  and 85% of neutrophils. After a teicoplanin plus meropenem antibiotic association the body temperature became normal. The samples of blood from a peripheral vein and from CVC showed a *Pantoea* isolate sensitive to meropenem.

Case 5 was a 49-year-old male with a two year history of pancreas cancer with liver involvement. After 8 cycles of chemotherapy a CVC for both parenteral nutrition and further chemotherapy was inserted. However after one month and half he appeared ill and mildly febrile. Therefore empirical antibiotic therapy with imipenem was started and led to an improved condition. From peripheral venous blood and CVC *P. agglomerans* was isolated.

Case 6 was a 78-year-old male hospitalized in the Intensive Care Unit (ICU) and exhibiting fever and other septic features. The samples of blood from a peripheral vein and from CVC showed a *P. agglomerans* isolate sensitive to meropenem, which was used as antimicrobial therapy.

Therefore within a three month time-span, *P. agglomerans* was isolated in a series of blood cultures carried out on samples from both central and/or peripheral venous catheter of six patients with different malignancies, in particular 5 patients from oncology and 1 patient from ICU departments (Table 1). Every time a blood sample drawn from a peripheral vein was also examined. *P. agglomerans* grew in pure culture from blood of 5 patients. However from the sixth patient a strain of *P. agglomerans* associated with

*Rahnella aquatilis* and *Candida famata* was isolated. Blood samples drawn from a peripheral vein gave the same results, therefore a contamination of blood by the catheter should be ruled out. Blood samples were drawn into aerobic and anaerobic blood culture bottles (BacT/Alert FA; BioMerieux, Mercy l'Etoile, France). After a period of 1-3 days of incubation (incubator BacT/Alert/3D; BioMerieux, Mercy l'Etoile, France), aliquots of broth were routinely subcultured into 5% sheep blood agar and McConkey agar. Identification was carried out by GN card (bioMérieux, Marcy-l'Etoile, France), resulting in *P. agglomerans*, although with a different percentage of identification probability. In addition to fermentation of sorbitol that has been reported as variable for *P. agglomerans* (Sanders and

Sanders, 1997), as well as D-cellobiose and sodium citrate percentage variability in cases 1 and 3 reflect the results of trivial identification test, due to instrument failure of NAGA or GGT measurement respectively. This mistake dramatically decreased the identification probability to 50.26%. Therefore identification test was repeated in different sessions and higher percentages similar to the other strains (95%) were consistently obtained (Table1).

On blood agar plates yellow, pinpoint-sized and smooth-surface colonies were observed. All six isolates were consistently sensitive to ampicillin/sulbactam, cefepime, cefixime, cefotaxime, ceftazidime, cefuroxime, quinolones, gentamicin, imipenem, meropenem, mezlocillin, piperacillin, piperacillin-tazobactam, tetracycline, cotrimox-

TABLE 1 - Summary of clinical and microbiological features of cases.

Case	Sex/Age (years)	Department	Antecedent disease	Positivation time	Bacterial isolate/ percentage of identification	Other isolates	Resistance pattern	Test used to differentiate <i>Pantoea agglomerans</i> recovered from clinical specimens (blood)
1	M/75	Oncology	Gastric Cancer	3 days	<i>Pantoea agglomerans</i> /95%*		Ampicillin: I Cefazoline: I	dSOR: + ODC: - LDC: -
2	M/29	Oncology	Osteosarcoma	2 days	<i>Pantoea agglomerans</i> /95%		Ampicillin: I Cefazoline: I	dSOR: + ODC: - LDC: -
3	F/45	Oncology	Colon cancer	2 days	<i>Pantoea agglomerans</i> /95%*		Ampicillin: I Cefazoline: R	dSOR: + ODC: - LDC: -
4	M/47	Oncology	Pancreatic cancer	1 day	<i>Pantoea agglomerans</i> /95%		Ampicillin: I Cafazoline: I	dSOR: + ODC: - LDC: -
5	M/49	Oncology	Pancreatic cancer	2 days	<i>Pantoea agglomerans</i> /95%	<i>Rahnella aquatilis</i> <i>Candida famata</i>	Ampicillin: I Cefazoline: R	dSOR: - ODC: - LDC: -
6	M/78	ICU		18 hours	<i>Pantoea agglomerans</i> /95%		Ampicillin: I Cefazoline: R	dSOR: - ODC: - LDC: -

LDC: Lysine decarboxylase; ODC: Ornithine decarboxylase; dSOR: Fermentation of D-sorbitol. R: Resistant; I: Intermediate. \*Identification test was repeated and higher percentages, similar to the other strains, were obtained with respect to previous values (50.26%).

azol while they were resistant/intermediate to ampicillin and cefazolin (Vitek, BioMerieux, Mercy l'Etoile, France).

In order to identify the source of the present outbreak, environmental screening cultures were carried out by means of blood culture bottle (Bact/Alert FA) on the same batches used for patients therapy of the following medications: saline, glucose 5% and 33% solution, solamin forte 7.5 gr/100 ml 500 ml bottle i.v., INTRALIPID, EPSOCLAR sodium heparin. No positivity was found among such environmental samples. In addition, the tip of the peripheral venous catheter was cultured.

A culture of stools was not performed, because the physicians who sent those samples for blood culture to our lab did not also submit stool samples. Moreover outbreak of the same organism without other enterobacteria, in a short timespan, within two clinical units of the same hospital, would suggest a source of infection other from translocation.

From our results we conclude that *P. agglomerans* is able to start hospital outbreak, although the source of these *Pantoea* infections remains to be investigated. *Pantoea* spp have been reportedly found in samples obtained from cotton swabs, intra-arterial devices, as well as plants and plant materials (Sanders and Sanders, 1997). Cotton pledgets are continuously used by nurses and physicians in hospital and can be contaminated in many ways. Furthermore one of our patients was bearing an intra-arterial device. Moreover bunches of flowers are sometimes used as gifts for patients, and although plants and flowers are not allowed in the patient rooms, sometimes they are left in the corridors or close to the windows. The intrinsic capability of *Pantoea* to remain viable and grow luxuriously at 25°C (room temperature) may contribute to such outbreak (Mackel *et al.*, 1975). *P. agglomerans* has been reported to survive some steps of the autoclaving process (Mackel *et al.*, 1975). However *P. agglomerans*, which is ubiquitous in nature, is not a frequent cause of endogenous nosocomial infections. Intrinsic *P. agglomerans* susceptibility to beta-lactam antibiotics (Sanders and Sanders, 1997), that is consistent with our present data on resistance patterns, might account for the limited number of reports on *Pantoea* outbreaks. On the contrary, *Pseudomonas* spp. and other noso-

comial Gram negative infectious agents with environment survival capability might have a different behaviour from *Pantoea* for the dramatic resistance patterns to antibiotics.

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