ORIGINAL RESEARCH PAPER

Microbiology

KEY WORD:
Chryseobacterium, immunocompromised, nosocomial.

AN ATYPICAL CASE OF EMERGING PATHOGEN IN INTENSIVE CARE UNIT: CHRYSEOBACTERIUM INDOLOGENES

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ABSTRACT

Nosocomial infections and antibiotic resistant pathogens constitute common and serious problems in India. *Chryseobacterium indologenes*, is a non-motile Gram-negative rod. Although it is widely distributed in nature but it is an uncommon human pathogen. It is of common belief that it is an organism of low virulence, but it may cause serious infections, especially among the immunocompromised. A large number of reported cases are nosocomial, often associated with immunosuppression. We came across this case of *Chryseobacterium indologenes* affecting an immunocompromised patient who was hospitalised for a long time. This case study emphasises the importance of diagnosing of this rare potential pathogen early and promotes awareness about Chryseobacterium.

INTRODUCTION

Chryseobacterium indologenes is non fermentive gram-negative bacilli associated with nosocomial infections such as bacteremia, ventilator associated pneumonia, peritonitis, endocarditis, meningitis, indwelling device-associated infection, urinary tract infection, surgical and burn wound infection. *Chryseobacterium indologenes* is a rare human pathogen, formerly known as *Flavobacterium indologenes* belong to family Flavobacteriaceae [(1)]. Members of the family Flavobacteriaceae are ubiquitous in soil and water and are not considered part of the normal human flora often they are found to contaminate hospital equipment hence they are important cause of nosocomial infection. They can be found in municipal water supplies despite adequate chlorination and have been recovered from the hospital environment. Chryseobacterium species are organisms of low virulence, and their presence in clinical specimens usually represents colonization [(2)]. The majority of cases have been nosocomial infections, and the vast majority of patients had undergone invasive procedures. Immunosuppression such as diabetes mellitus, Cancer, steroids therapy, transplantation, long stay in hospital and infused fluids like dialysate, prolonged exposure to broad spectrum of antibiotics and saline irrigations are important risk factors for *Chryseobacterium indologenes*[(3)].

Chryseobacterium causes a wide spectrum of infections especially in the critical care unit and being a multidrug resistant make this organism an ominous emerging pathogen. We report a case of blood stream infection by *Chryseobacterium indologenes* in an immunocompromised patient, history of prolonged exposure to broad spectrum of antibiotics with long duration of stay in hospital. This case study highlights the importance of rare potential pathogen in association with risk factors and promotes awareness about Chryseobacterium.

Case report

A 40 year old male patient with breathing difficulty was referred from a private hospital to our hospital that was diagnosed as atypical pneumonia with ARDS. On examination, bilateral crepitation were present. The patient was a known diabetic with poorly controlled blood sugar of value 230 mg/dl with HB1ac of 10.2. The patient was put on continuous positive airway pressure and empirically started on meropenem and linezolid. On the second day of hospitalization, blood culture and urine culture were sent which came as negative and sputum culture showed the growth of candida albicans. Doxycycline and fluconazole along with methyl prednisolone were also initiated. The serum glucose level -136mg/dl, Serum urea 62mg/dl, Serum creatinine 1mg/dl bilirubin 0.6 mg/dl, SGOT 33 IU/L and SGPT 17 IU/L sodium- 141mmol/L and potassium 3.9mmol/L arterial blood pO2 was 78.6 mmHg and pCO2 34.7mm Hg. On HRCT, bilateral ground glass opacities in the lungs were seen along with parenchymal cysts and mild pleural effusion. On 10th day of admission, the glucose levels had increased to 364mg/dl and serum urea and creatinine had also increased to 105mg/dl and 2.2mg/dl respectively. Hemodialysis was started for the patient. D dimer was also done by automated method in which a very high value of 6336ng/ml was observed (normal <500 ng/ml) PRO BNP cardiac marker had a high value of 4636 ng/ml and procalcitonin was also raised (25.6ng /ml). *Candida albicans* was isolated from urine sample and blood examination showed microcytic hypochromic anemia and neutrophilic leukocytosis along with thrombocytopenia. The patient's condition continued to deteriorate even after the ongoing treatment. Later on at day 20, the blood culture was sent from central line and hemodialysis line was found to be positive for *Chryseobacterium indologens*.

The blood culture which was sent just after the day of admission showed no growth after 48 hours. After 20 days of admission two more blood samples from central line and HD line was sent and which was inoculated on blood agar and Mac Conkey agar. Chryseobacterium was long, thin, filamentous gram negative bacilli on Gram stain. On blood agar, circular, 1-2 mm, dark yellow pigmented colonies were seen. However, on Mac Conkey agar, no growth was observed. The biochemical reaction showed non fermentative, non motile, catalase-positive, oxidase-positive and indole-positive Gram-negative *Bacilli*. Chryseobacterium spp. produces yellow pigment that turns red (figure 1) upon the addition of 20% KOH. The isolate was identified by both conventional biochemical reactions and automated Vitek GNI system (bioMerieux, France) as *C. indologenes*. Both blood samples (central line and hemodialysis line) revealed the same isolate on biochemical and Vitek system.

The Antimicrobial susceptibility testing (AST) was done for both the samples by Kirby–Bauer disc diffusion method and interpreted by CLSI guidelines which showed resistance to piperacillin, ciprofloxacin and piperacillin-tazobactam, gentamicin, cefotaxime, ampicillin, ceftriazone, imipenem, meropenem and ceftazidime. On Vitek system, isolate was found to be susceptible only to trimethoprim-sulfamethoxazole and minocycline.

The above mentioned case of C.indologenes was multidrug resistant. Isolate showed resistance to group of antibiotic like cephalosporins, carbapenems, beta lactam, fluoroquinolones and colistin. Minimum inhibitory concentrations of *Chryseobactrium indologenes* by automated vitek system illustrated in table 1.

Follow up

On second day of admission blood culture was negative after 48 hours of incubation. The next blood culture was send on day twenty of admission, from central line and HD line showed the same isolate of C.indologenes.

Table1. Antimicrobial susceptibility of *Chryseobacterium indologenes* isolated by Vitek system.

S.No	Antimicrobial	MIC	Interpretation
1	Piperacillin/Tazobactem	>=128	R
2	Ceftazidime	>=64	R
3	Cefoperazone/ sulbactam	>=64	R
4	Cefepime	>=64	R
5	Aztreonam	>=64	R
6	Imipenem	>=16	R
7	Meropenem	>=16	R
8	Amikacin	>=64	R
9	Gentamicin	>=16	R
10	Ciprofloxacin	>=4	R
11	Levofloxacin	>=8	R
12	Minocycline	<=1	S
13	Tigecycline	>=8	R
14	Colistin	>=16	R
15	Trimethoprim/sulfamethoxazole	40	S

Table 2: *Chryseobacterium indologenes* cases reported in different study.

S.No	Author	Age /sex	Risk factors	Diagnosis	Treatment	Outcome
1	Khajuria et al., 2014 [4]	77 year, M	Diabetes mellitus	septicemia	Colistin	Survived
2	Baruah M et. Al., 2016 [5]	22 year, F	No underlying illness	Non catheter-associated bacteremia	Ciprofloxacin	Survived
3	Palewar MS et al. 2017 [6]	52 year, M	Diabetes mellitus	Obstructive uropathy	Trimethoprim sulfamethoxazole	Survived
4	Das et al., 2017[7]	10 weeks / F	Congenital heart disease	Pneumonitis	Cefipime	Survived
5	Bhalla GS et al., 2018 [8]	36 year, M	HIV	CAUTI	Cotrimoxazole	Survived
6	Present case	40 year,M	Diabetes mellitus	Atypical pneumonia		Died

DISCUSSION

The pre-eminent role of C.indologenes is due to inherently resistant to a wide range of antibiotics. It has been emerged as a significant pathogen due to its potential to form biofilm, thereby easily colonizing in hospital equipment such as respirators, catheter and endoscope. The C.indologenes found naturally in soil and water. The Chryseobacterium belong to family Flavobacteriaceae, other important species of this family include *C.meningosepticum, C.odoratum, C.gleum.* Chryseobacterium spp. was aerobic, nonfermentative, positive oxidase and catalase reaction, ability to produce indole in tryptophan broth, nonmotile gram negative bacilli that does not grow on MacConkey agar and produce yellow pigment flexirubin hence, was earlier called Flavobacterium indologenes.

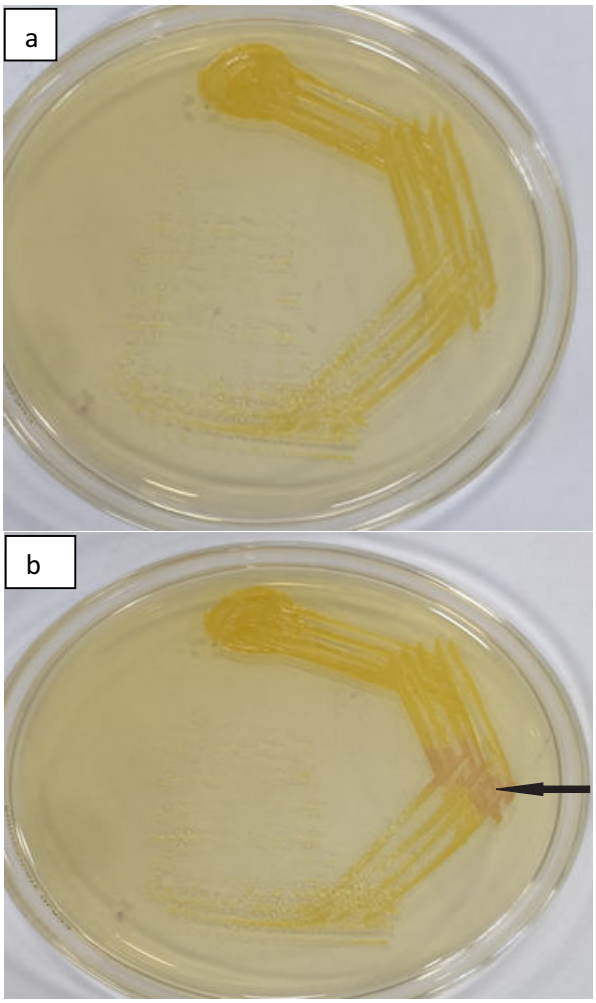

Figure 1: yellow pigmented colony of Chryseobacterium on nutrient agar (a); which turns red (arrow) on addition of 20% KOH (b).

C.indologenes cases in reported in different study (Table 2). There are many cases of *C.indologenes* reported in hospitalized patients with wide spectrum of diseases such as Bacteremia, pneumonia, meningitis and also indwelling device- associated infection such as UTI etc. In 1996, Hsueh et al. found increasing incidence of healthcare associated infection due to Chryseobacterium species [9]. Most cases occurred in immunocompromised patients. The risk factors such as steroids, prolonged exposure to broad-spectrum antibiotic, diabetes mellitus, long hospital stay, use of catheter aggravate *C.indologenes* infection. In our case all these risk factors are involved with limited antibiotic options which worsen the patient condition. In 2018, Bhalla GS *et al.* reported a case of catheter-associated urinary tract infections (CAUTI) in immunocompromised patient by *C.indolens* which matches with our study [8]. The organism showed resistance to wide spectrum of antibiotics and the use of inactive drugs as empirical therapy may contribute to the poor outcome in many infections. Chryseobacterium organisms produce beta-lactamases and are naturally resistant to most beta-lactam drugs, including carbapenems and aztreonam. This resistance in *C.indologenes* has been shown to be due to chromosomally encoded class A extended-spectrum beta-lactamase CIA, in addition to class B metallo-beta-lactamases IND variants (IND-1 to IND-7 and IND-2a).

CONCLUSION:

This case reveals the importance of *C. indologenes* as rare emerging hospital acquired organism. It is multidrug resistant organisms with limited data available that's why it

makes the empirical treatment of *C.indologenes* challenging. While reporting in a microbiology lab, one needs to keep in mind the rare organisms which cause infections so that early diagnosis and treatment can be initiated so as to decrease morbidity and mortality.

Financial support and sponsorship:
Nil

Conflict of interest
There is no conflict of interest.

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