

# An unusual pathogen in a typical clinical scenario: *Pseudomonas oryzae* urosepsis in a patient with Myelodysplastic syndrome

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### SUMMARY

Neutropenia is a common clinical occurrence in the background of malignancies, either as a direct result of defective haematopoiesis due to the illness or as a result of antineoplastic therapies. Opportunistic infections with low-virulence organisms are not uncommon among immunocompromised patients. Within this patient subset, opportunistic infections with *Pseudomonas oryzae* (*P. oryzae*) are considered rare. In this first reported case of *P. oryzae* infection in Malaysia, we describe its clinical presentation in a susceptible patient, the management, and its subsequent clinical course. Comparing against a brief overview of the literature, we explore the mechanisms driving immunosuppression, leading to susceptibility of opportunistic infections among patients with myelodysplastic syndrome. We also feature the use of matrix-assisted laser desorption-ionisation time of flight mass spectrometry (MALDI-TOF MS) as a promising platform to revolutionize microorganism identification and diagnosis.

### INTRODUCTION

*Pseudomonas oryzae* (formerly known as *Flavimonas oryzae*) is a gram-negative rod-shaped aerobic bacillus, an uncommon pathogen which acts as an opportunistic pathogen in immunocompromised patients.<sup>1</sup> It has been reported in both humans and as a zoonotic pathogen.<sup>2</sup> In this case, we detected this relatively unusual pathogen in a patient with a background of myelodysplastic syndrome (MDS) and numerous other chronic co-morbidities.

### CASE REPORT

A 73-year-old female with a recent diagnosis of myelodysplastic syndrome presented with an acute episode of dysuria following 3 days' duration of abdominal distension and suprapubic discomfort. She denied having fever, hematuria, difficulty in breathing, or gastrointestinal losses. She has multiple co-morbidities, including type 2 diabetes, hypertension, dyslipidemia, and neurogenic bladder due to T12-spinal cord injury following a motor vehicle accident more than two decades ago.

She was bed bound and highly dependent on her daughter on most daily activities. Further medical history reveals a recent diagnosis of myelodysplastic syndrome 4 months prior to her current admission, where her bone marrow aspiration and trephine biopsy (BMAT) reported hypercellular marrow with trilineage myelodysplasia. Whilst awaiting cytogenetic study results, management for her myelodysplastic syndrome has been largely supportive, where blood products transfusions were arranged to address her anaemia and thrombocytopenia.

Upon examination, she appeared alert but pale, with no apparent signs of respiratory distress. She was afebrile but tachycardic, with a heart rate of 117. Her blood pressure reading and oxygen saturation under room air were otherwise normal. An indwelling urinary catheter with the attached urine bag contained heavily sedimented urine, with no evidence of gross hematuria. A physical examination revealed a soft abdomen with mild tenderness over the suprapubic region, with no masses palpable. Cardiovascular and respiratory examinations were unremarkable.

Investigations revealed pancytopenia, with a haemoglobin reading of 6.7g/dL (normochromic, normocytic picture), absolute neutrophils count (ANC) of 270 cells/mm<sup>3</sup>, and platelet count of 23 x10<sup>9</sup>/L. Urinalysis showed a positive leucocyte and nitrite picture. Renal profile and liver function tests were normal. Ultrasound of kidney, ureter, bladder (KUB) identified bilateral renal parenchymal disease, with no features of hydronephrosis or pyelonephritis. Inflammation was evidenced by an elevated C-reactive protein reading of 53 mg/L.

She was empirically treated with intravenous ceftriaxone 2g daily for the urinary tract infection. The initial urine culture on admission showed mixed growth due to contamination. On day two of admission, her blood culture yielded *P. oryzae* that was sensitive to piperacillin-tazobactam, imipenem, and meropenem; but with intermediate sensitivity to cefepime and resistant to ceftazidime. Based on the working diagnosis of *P. oryzae* blood stream infection secondary to urinary tract infection, her intravenous antibiotics was switched to a 6-hourly regime of 4.5g intravenous piperacillin-tazobactam.

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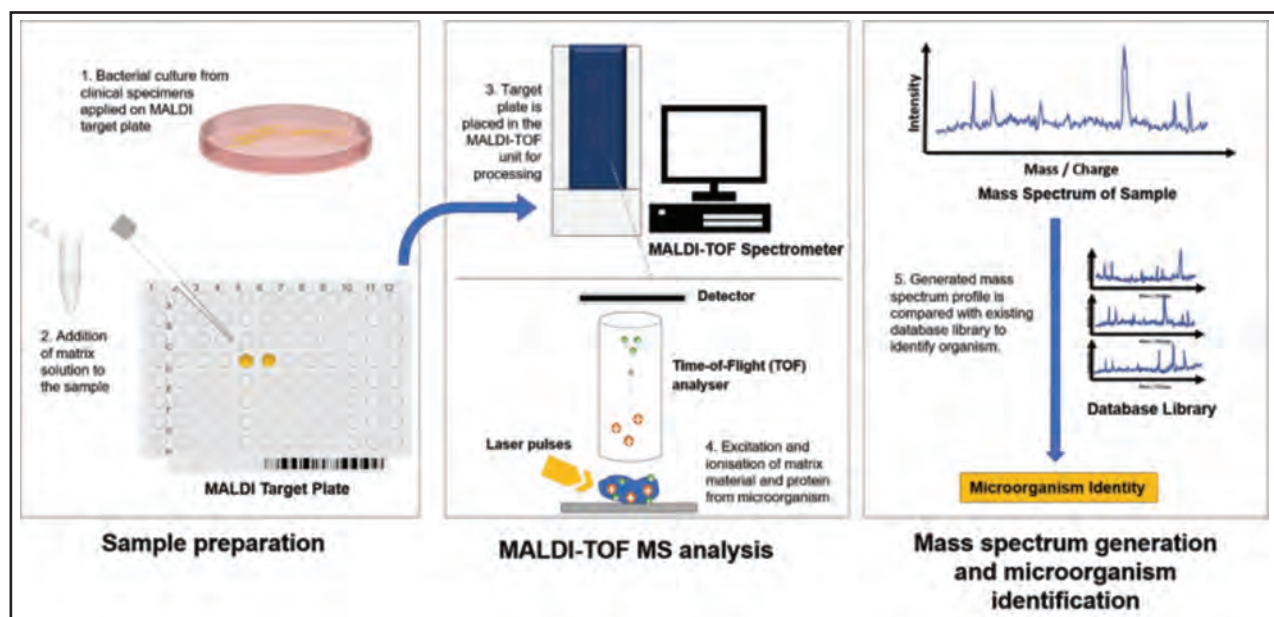


Fig. 1: Workflow of the matrix-assisted laser desorption-ionisation time-of-flight mass spectrometry (MALDI-TOF MS) in microorganism identification

Throughout admission, she remained afebrile, but the neutropenia persisted. Haematology team initiated a course of oral danazol 200mg twice daily as a therapy for her persistent pancytopenia. Patient also received one unit of packed cell transfusion on day 6 of admission to address her symptomatic anaemia. Following completion of the 2-week antibiotic regime, with the absence of fever, suppression of inflammatory markers, and no further isolation of *P. oryzihabitans*, patient was discharged home.

## DISCUSSION

*P. oryzihabitans* is a yellow-pigmented, aerobic, non-fermenting, gram-negative organism.<sup>1</sup> Indigenous to rice paddies, it is commonly found as a soil and saprophytic organism that thrives in damp environments.<sup>1</sup> Since its discovery in the 1980s, *P. oryzihabitans* have been increasingly implicated as a causative organism in bacteremia, septicemia, and peritonitis; among individuals who are immunocompromised, particularly in haematological malignancies, acquired immunodeficiency syndrome, or individuals on steroid treatment.<sup>3,4</sup> There were also reports of *P. oryzihabitans* infection causing peritonitis and septicemia among individuals on peritoneal dialysis with long-term indwelling catheters.<sup>3</sup> Several *P. oryzihabitans* outbreaks in the hospital setting have also been reported in the literature, noting that *P. Oryzihabitans* was frequently isolated in various sites, such as sink drains, respiratory therapy equipments, and containers of saline gauzes.<sup>5</sup>

MDS is a group of heterogenous clonal disorder of the haematological system. It is characterized by ineffective haematopoiesis and differing degrees of peripheral cytopenia, with a risk of transformation to acute myeloid leukemia (AML).<sup>6</sup> Infections pose a major threat to all MDS patients alike, regardless of treatment status. This can be

ascribed to functional defects in the myeloid lineage, with or without neutropenia, which is also complicated further by treatments.<sup>7</sup> Immune dysregulation in MDS is complex, accompanied with an increased release of pro-inflammatory cytokines such as tumour-necrosis factor alpha (TNF- $\alpha$ ), interferon gamma (IFN- $\gamma$ ), transforming growth factor-beta (TGF- $\beta$ ), and interleukins (IL-6, IL-10) in the bone marrow microenvironment.<sup>6</sup> Besides immunosuppression, majority of patients diagnosed with MDS are affected by anaemia and anaemia-related symptoms, which can be debilitating and thus result in a poor health-related quality of life (HRQoL).<sup>8</sup> Transfusion dependence, apart from its costs, has also been recognised as a negative prognostic factor leading to reduced overall survival among patients with MDS.<sup>8</sup>

Bacteria is the most common type of pathogen implicated in MDS-related infections.<sup>7</sup> To date, cases of *P.oryzihabitans* infections have been shown to respond well to treatment, with the eradication of the organism whenever suitable antimicrobial therapy is initiated.<sup>3,5</sup> Although the patient in our case responded well to treatment, it is also worth noting that the intravenous piperacillin-tazobactam required was a broad-spectrum antibiotic that is reserved for severe infections involving resistant microorganisms. As opposed to the sensitivity patterns of *P. oryzihabitans* described in earlier studies, the *P. oryzihabitans* isolated in this case exhibited resistance against the cephalosporin groups, further warranting the importance of judicious antibiotics prescription to treat such infections among the at-risk groups. For patients with a baseline neutrophil of less than  $500 \times 10^9/L$ , some studies have suggested the use of antibacterial prophylaxis before commencing therapy with demethylating agents.<sup>7</sup> However, proper risk-benefit analysis of prophylactic antibiotics needs to be done, considering the issue of antibacterial resistance and risk of selecting resistant bacteria.

In this case, a rapid and accurate identification of *P. oryzihabitans* was made possible as a result of the MALDI-TOF MS (refer Figure 1) use in the microbiology laboratory, which allowed the timely prescription of appropriate antibiotics administration to treat the patient. With MALDI-TOF MS, the turnaround time for microorganism identification was dramatically shortened from several hours to less than 20 minutes. The MALDI-TOF MS involves ionizing biological samples and separating the particles based on their mass-to-charge ratio and detection of their time-of-flight in a detector.<sup>9</sup> Subsequently, the resulting spectrum can be compared to an existing spectra database from known organism, which allows prompt identification of organism with high accuracy.<sup>9</sup> Moreover, the superiority of MALDI-TOF MS over traditional detection techniques has also been shown to contribute to the increased reporting of some relatively rare species.<sup>10</sup> In the long run, the MALDI-TOF MS technique represents a cost-effective, straightforward, and robust microbial identification method, allowing proper guidance in managing infectious diseases.<sup>9</sup>

**CONCLUSION**

Although rare, findings from our case and the existing literature suggest the potential of *P. oryzihabitans* as a pathogen in the clinical setting, especially among patients with underlying haematological malignancies and immunosuppression. This emphasizes the need for vigilance and clinical suspicion in this group of patients, prompting the role of appropriate antibiotic in clinical settings. With the increasing use of MALDI-TOF mass spectrometry platform in clinical laboratories, we expect to see significant improvements in accurate identification of microorganisms, thus speeding up diagnoses and reducing the time to appropriate therapy.

**CONFLICT OF INTERESTS**

The authors declare that there is no conflict of interests.

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