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Case Series

Internal Medicine Section

Stenotrophomonas maltophilia: Threat of a Multidrug Resistant Infection in Hosts with Co-morbidities- A Case Series

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ABSTRACT

Stenotrophomonas maltophilia (*S.maltophilia*) was first identified in the year 1943. Since the discovery, the organism has been classified into multiple genus. Finally, *Stenotrophomonas* genus was created in 1993 and has steadily been growing in prevalence since then. *S.maltophilia* is an organism of low virulence but owing to its inherent resistance to commonly used antibiotics and some peculiar resistance mechanism, the organism is poising challenge as a nosocomial infection, hence high index of suspicion is essential in part of physicians for early intervention and better prognosis. Five cases (35 years old male, 18 years old female, 55 years old female,82 years old male and 60 years old male patients) of *S. maltophilia* infection, diagnosed by various diagnostic modalities like chest x-ray and relevant blood investigations, in hosts with co-morbidities (like diabetes, hypertension, sickle cell disease, psychiatric illness etc.) are presented here along with a brief review. The patients were treated by antibiotic therapy according to culture sensitivity report and were discharged at time range of 10-21 days of hospitalisation after improvement of clinical condition and laboratory reports of the patients.

Keywords: Antibiotics, Nosocomial infection, Resistance, Virulence

INTRODUCTION

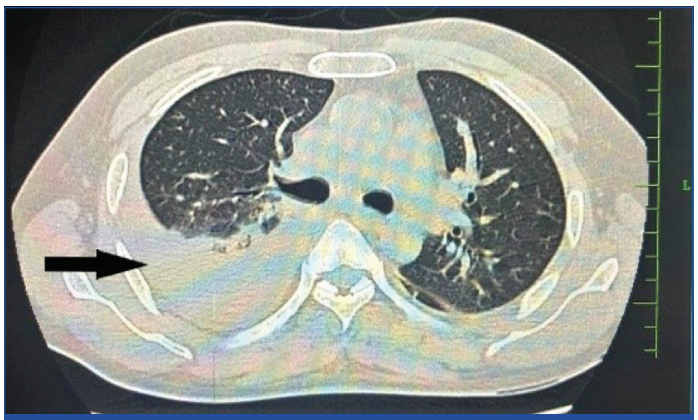
S.maltophilia was first identified from the pleural effusion fluid in the year 1943 and was named Bacterium booker [1]. It was ultimately classified as *Stenotrophomonas* in the year 1993 as proposed by Palleroni and Bradbury [1,2]. The prevalence of the infection due to *Stenotrophomonas* has increased steadily in the general population as well as in critical care set-up as evident by recent studies [2]. The prevalence of infection due to *S.maltophilia* in the general population was 0.8-1.4% from 1997 through 2003, which has increased to 1.3-1.68% during the period 2007-2012 [3]. Similarly, the prevalence of infection in Intensive Care Unit (ICU) setup was 1.6% from 1997-1998 which has increased to 2.6% in 2011 [3]. According to a review on *S.maltophilia* infection in bloodstream, it was found out that the mortality in case of pneumonia ranged from 23-77% while a blood stream infection caused fatality starting at 21% ranging up to 62% [4]. Recently, the World Health Organisation (WHO) has specified *S.maltophilia* as a great public health concern in nosocomial settings from a resistance point of view [5]. Here, five cases of *S.maltophilia* infection in host with co-morbidities and a brief overview of the same is described.

CASE SERIES

Case 1

A 35-year-old, chronic alcoholic male patient, presented with fever, cough with expectoration for three days and chest pain for a day. The patient was admitted to the critical care ward and was put on mechanical ventilation, ionotropic support and was started on empirical antibiotics (piperacillin tazobactam and linezolid).

On first day of investigation, there was neutrophilic leucocytosis (13250/mcl, 85% neutrophils), raised liver enzymes (Serum Glutamic-oxaloacetic Transaminase (SGOT) -227, Serum Glutamic Pyruvic Transaminase (SGPT) -132, Gamma-glutamyl Transferase (GGT) -457, Alkaline Phosphatase (ALP)-153), raised serum procalcitonin (10.8 ng/mL) with the rest of the biochemical parameters (renal function tests, coagulation profile, electrolyte) within normal limits. Right lower lobe consolidation with pleural effusion was evident in Computed Tomography (CT) scan of the thorax [Table/Fig-1] and Endotracheal Tube (ET-tube) aspirate culture showed growth of *S.maltophilia*. Empirical antibiotics were changed to high dose Trimethoprim-Sulfamethoxazole (TMP-SMX) (TMP equivalent dose of 15 mg TMP/kg/day i.v. divided q8hr) according to the culture sensitivity report and was continued for two weeks. He was discharged on tenth day of his hospitalisation as his condition improved [Table/Fig-2].



[Table/Fig-1]: High Resolution Computed Tomography (HRCT)- thorax showing consolidation of right lower lobe with effusion.

Parameters	Day 1	Day 3	Day 7
TLC (Neutrophil)	13250 (85%)	12311 (82%)	7800 (71%)
Serum procalcitonin (ng/dL)	10.8	9.2	2.8
SGOT/SGPT (U/L)	227/132	139/38	70/35
ALP/GGT (U/L)	153/457	115/286	105/257
Serum bilirubin (mg/dL)	5.3	4.1	1.2
Serum direct bilirubin (mg/dL)	4.2	2.9	0.9
Serum Urea/Creatine (mg/dL)	45/0.8	32/0.5	20/0.4

[Table/Fig-2]: Case 1 Laboratory reports.
TLC: Total leucocyte count; SGOT: Serum glutamic-oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase; ALP: Alkaline phosphatase; GGT: Gamma-glutamyl transferase

Case 2

An 18-year-old female patient, who was a known case of sickle cell disease, presented with complaints of fever, cough with

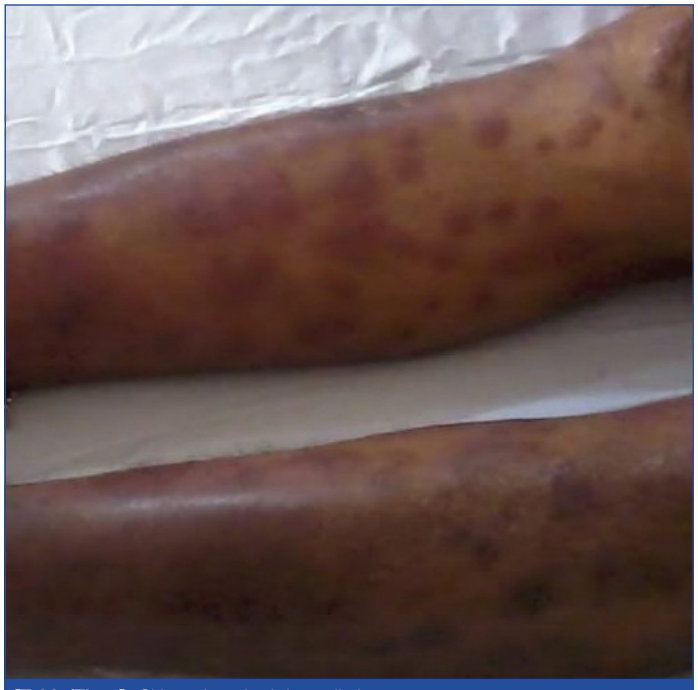
expectoration for five days and seizures for one day. She was diagnosed with posterior reversible encephalopathy syndrome with bilateral pneumonia. She was managed in emergency ward with mechanical ventilation, inotrope support and empirical antibiotics (piperacillin-tazobactam and clarithromycin). Subsequently, investigations revealed neutrophilic leucocytosis (15050/mcl, 89% neutrophils), raised serum procalcitonin level (19.8 ng/mL). Chest x-ray showed a homogenous opacity over right lower zone and ET aspirate culture revealed growth of *S.maltophilia*. Antibiotic was changed to TMP-SMX (TMP equivalent dose of 15 mg TMP/kg/day IV divided q8hr) as per culture sensitivity report. The clinical condition started improving after seven days of starting TMP and after two weeks of treatment she was discharged in a stable clinical condition [Table/Fig-3]. She did well in her last follow-up and thereafter.

Parameters	Day 1	Day 3	Day 7
TLC (Neutrophil) (cumm)	15050 (89%)	12311 (82%)	7509 (66%)
Serum procalcitonin (ng/dL)	19.8	13.2	0.9
Serum bilirubin (mg/dL)	0.8	1.2	0.7
Serum direct bilirubin (mg/dL)	0.2	0.7	0.1
S. Urea/Creatinine (mg/dL)	105/1.01	83/0.9	38/0.6

[Table/Fig-3]: Case 2 Laboratory reports.

Case 3

A 55-year-old female patient, with known psychiatric illness presented with fever, altered sensorium for five days and multiple erythematous skin rashes involving the whole body [Table/Fig-4] as well as oral cavity for three days. There was no history of any new drug intake in the recent past. She was managed conservatively and all samples were sent for investigation. Subsequently, culture of aspirated pus from the skin lesion revealed *S.maltophilia* which was sensitive to TMP-SMX. The patient was treated with TMP-SMX for two weeks and was discharged.



[Table/Fig-4]: Skin rash on both lower limbs.

Case 4

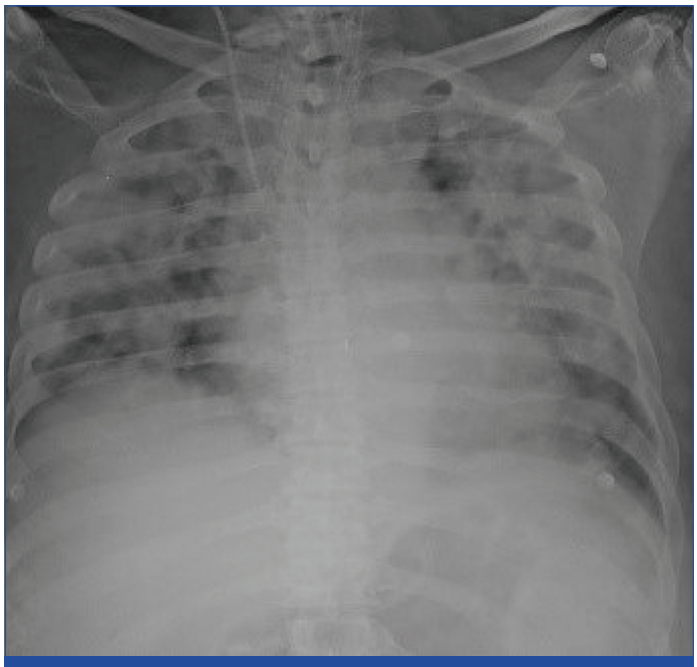
An 82-year-old male patient, with a history of diabetes mellitus, not on regular treatment, attended *emergency ward* with complaints of fever, cough with expectoration for eight days and vomiting for five days. He had a history of hospitalisation 20 days back. The patient was managed in the critical care unit with mechanical ventilation, inotropic support, regular insulin and empirical antibiotics (meropenem and teicoplanin). Investigation revealed, raised HbA1c (Glycated Haemoglobin) (9.1%) and neutrophilic leucocytosis (21,780/mcl, 94% neutrophil) with raised serum procalcitonin (9.7 ng/mL), serum urea (72 mg/dL) and creatinine (1.6 mg/dL). X-ray chest showed a homogenous opacity over right middle zone and the endotracheal tube aspirate revealed growth of *S.maltophilia*. He was managed with high dose TMP-SMX (TMP equivalent dose of 15 mg TMP/kg/day IV divided q8hr) as per the culture sensitivity report along with regular insulin, mechanical ventilation and vasopressors. His clinical condition started improving after two weeks of management in critical care unit and after three weeks of treatment, he was discharged [Table/Fig-5].

Parameters	Day 1	Day 7	Day 14
TLC (Neutrophil) (cumm)	21780 (94%)	13311 (88%)	9250 (79%)
Serum procalcitonin (ng/dL)	9.1	6.7	0.1
Serum bilirubin (mg/dL)	1.4	0.6	0.6
Serum direct bilirubin (mg/dL)	0.9	0.4	0.2
Serum Urea/Creatinine (mg/dL)	72/1.6	47/0.7	34/0.5

[Table/Fig-5]: Case 4 laboratory reports.

Case 5

A 60-year-old diabetic and hypertensive male patient, presented with fever, cough with expectoration for six days, and shortness of breath for three days. He was managed in the emergency ward with mechanical ventilation, vasopressor support and empirical antibiotics (meropenem and teicoplanin). The patient had neutrophilic leucocytosis and high HbA1c (7.8%). Bilateral non homogenous opacities were seen on chest X-ray [Table/Fig-6] and the endotracheal tube aspirate culture showed growth of *S.maltophilia*. As per the sensitivity report, empirical antibiotics were stopped and high dose of TMP-SMX (TMP equivalent dose of 15 mg TMP/kg/day IV divided q8hr) was started. After two weeks of management in critical care unit, his clinical condition started improving and one week later he was discharged with an advice for regular follow-up and is doing well [Table/Fig-7].



[Table/Fig-6]: Chest X-ray showing non homogenous opacities involving both side lung field.

Parameters	Day 1	Day 7	Day 14
TLC (Neutrophil) (cumm)	12340 (91%)	11201 (89%)	7745 (77%)
Serum procalcitonin (ng/dL)	7.1	4.6	0.25
Serum bilirubin (mg/dL)	0.32	0.39	0.74
Serum direct bilirubin (mg/dL)	0.21	0.24	0.16
Serum Urea/Creatinine (mg/dL)	22/0.51	42/0.32	29/0.46

[Table/Fig-7]: Case 5 laboratory reports.

DISCUSSION

S.maltophilia is the only member of the *Stenotrophomonas* genus known to cause infection in humans [2]. The organism is a motile, aerobic, gram-negative, glucose non fermentative bacillus and can be found in extreme of terrains (hospital as well as community) [3,6]. It has been sequestered from a variety of water bodies, soil samples, and plant biospheres [7]. The virulence factors of *S.maltophilia* have been primarily segregated into extracellular and cell-associated factors. The extracellular factors have chiefly been comprised of extracellular enzymes namely proteases, cytotoxins, siderophores. The cell-associated factors mainly are lipopolysaccharide, fimbriae, non pilus adhesin and flagella [8]. The biofilm is a peculiar property of the bacteria, which basically is a cell-associated factor for anti-microbial resistance. Biofilm is formation of a coating on inanimate as well as tissue surfaces, which is an aggregate of bacterial cells that are implanted in an extracellular matrix consisting of polysaccharides and proteins. This mechanism facilitates resistance to different antimicrobial and antiseptic. A newer method to identify the pathogen is Matrix-Assisted Laser Desorption Ionization–Time Of Flight Mass Spectrometry (MALDI-TOF MS), can also segregate biofilm producing organism from others [9,10].

S.maltophilia is generally considered as an organism of low virulence, thus has been identified as an opportunistic pathogen [1,3]. The various predisposing factors for infection are, hosts with haematologic malignancy, cystic fibrosis, prior antibiotic use, diabetes mellitus, immunodeficient patients, individuals admitted to Intensive Care Unit (ICU), patients on mechanical ventilation and presence of indwelling catheters [11].

The most common co-morbidity reported in this case-series was diabetes mellitus which was present in three out of five cases while sickle cell disease, hypertension was present in two cases and one patient was a chronic alcoholic. Four out of five cases were on mechanical ventilation and one patient had prior history of hospital admission (20 days back) in an ICU set-up. These data show a similar pattern as discussed in other case reports and literature [12-23].

Ebara H et al., in their case series of 44 cases, have described the common predisposing factor for the *S.maltophilia* infection was intubation (54.5%), intensive care unit admission (52.3%), haematological malignancy (29.5%), solid organ malignancy (22.7%). The most common site of bacteraemia was central venous line (36.4%). History of Carbapenem and anti-methicillin-resistant *Staphylococcus aureus* (MRSA) drug exposure was present in 63.6% and 47.7and cases, respectively [15].

A previous study found that the most common presentation of *S.maltophilia* infection is pneumonia (55.8%), followed by bloodstream infection (33.8%) [12]. Osteomyelitis, septic arthritis, skin, and soft tissue infections, meningitis, endocarditis are less common manifestation [2,5]. Out of the five cases discussed in this article, four had pneumonia, one had skin and subcutaneous infection and two patients had bilateral lung involvement. As described in literature the most common presentation is pneumonia and a similar picture can be seen in this series also [12-23].

In few cases series endocarditis and pericarditis have also been reported where the patient had either haematological malignancy or were under renal replacement therapy [17,18]. Few cases of rare presentation like spondylodiscitis, cervical osteomyelitis and keratitis were also reported. All the patients had undergone surgical procedures for contaminated wounds [20,21]. Another rare presentation of *S.maltophilia* keratitis (in bandage contact lenses users) has also been reported [22].

The pathogen grows well in commonly used media like blood agar as well as in commercially used systems (Vitek AutoMicrobic, Biolog, etc.,) [2]. *S.maltophilia* is inherently resistant to regularly used antibiotics like β-lactams, carbapenems, macrolides, aminoglycosides, and cephalosporins [11,24]. Most consistent finding in all the cases was neutrophilic leucocytosis along with raised serum procalcitonin levels which is a common finding of infective pathology. Raised hepatic enzymes were seen in only one case. Culture sensitivity report revealed the pathogen which was sensitive to TMP-SMX and quinolones (Levofloxacin) while resistant to the carbapenems and third generation cephalosporines which support the earlier literature description [24,25].

The first-line treatment is primarily comprised of high dose TMP-SMX (TMP equivalent dose of 15mg TMP/kg/day IV divided q6-8hr) [11,25]. The second line treatments are Fluoroquinolones, Ticarcillin with clavulanate, Minocycline, etc., [24,25]. Some of the proposed combination therapies are TMP-SMX with any of the second line agent or Ceftazidime [24].

CONCLUSION(S)

As *S.maltophilia* possesses challenges in the management due to its inherent ability to develop resistance to commonly used antibiotics, there is a need for a high index of suspicion and early initiation of an appropriate antibiotic for a better outcome. However, more studies are needed to ascertain more effective and diverse management options.

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