

## Skin Manifestation of *Stenotrophomonas maltophilia* Infection – A Case Report and Review Article

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### Abstract

**Introduction:** *Stenotrophomonas maltophilia* is an aerobic gram-negative bacillus that is a frequent coloniser of fluids used in the hospital setting. It causes infection in immunosuppressed hosts, especially those who are neutropaenic, on chemotherapy and broad spectrum antibiotics. Skin and soft tissue manifestations of *Stenotrophomonas maltophilia* infection are becoming an increasingly recognised entity; the clinical spectrum ranges from mucocutaneous, skin to soft tissue infections. **Materials and Methods:** We present a case of an 8-year-old girl with acute myeloid leukaemia who developed metastatic skin lesions secondary to *Stenotrophomonas maltophilia* bacteraemia. The authors reviewed a total of 24 reported cases of mucocutaneous, skin and soft tissue infections by *Stenotrophomonas maltophilia*. The presentations include metastatic cellulitis, primary cellulitis and infected mucocutaneous ulcers. **Results:** This is the first locally reported case of metastatic nodular skin lesions caused by *Stenotrophomonas maltophilia* bacteraemia. This is also the first reported paediatric case of embolic skin lesions caused by *Stenotrophomonas maltophilia*. Of the 6 cases of *Stenotrophomonas maltophilia* bacteraemia seen in the paediatric oncology patients from year 2000 to 2004 at our hospital, only 1 case developed metastatic skin lesions. **Conclusion:** *Stenotrophomonas maltophilia* skin infection should be included into the list of differential diagnoses for metastatic skin lesions in neutropaenic patients, especially with an underlying haematologic malignancy who has received recent chemotherapy and broad spectrum antibiotics. Haematologic malignancy, transplantation, neutropaenic, immunosuppressive therapy and a high severity of illness score were important prognostic factors.

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**Key words:** Acute myeloid leukaemia, Mucocutaneous, Skin, Soft tissue, *Stenotrophomonas maltophilia*

### Introduction

*Stenotrophomonas maltophilia* is an aerobic gram-negative bacillus that is found in aquatic environments. It is a frequent coloniser of fluids used in the hospital setting, such as nebulisers, water baths, dialysis machines and intravenous fluids. It is an organism of low virulence and is an opportunistic organism. Infections by *Stenotrophomonas maltophilia* can result from any combination of the following events: prolonged hospitalisation especially in intensive care units, medical devices, foreign body implants, intravenous drug abuse, administration of broad spectrum antibiotics and malignancy. *Stenotrophomonas maltophilia* causes infection in immunosuppressed hosts, especially those who are neutropaenic, on chemotherapy and broad spectrum antibiotics. Skin and soft tissue

manifestations of *Stenotrophomonas maltophilia* infection are becoming an increasingly recognised entity. We present the first locally reported case of metastatic nodular skin lesions caused by *Stenotrophomonas maltophilia* bacteraemia in an 8-year-old girl with acute myeloid leukaemia. This is also the first reported paediatric case of embolic skin lesions caused by *Stenotrophomonas maltophilia*.

### Case Report

JM, an 8-year-old Chinese girl, was diagnosed with acute myeloid leukaemia (AML M5a) in April 2004 when she presented with diplopia, proptosis of the right eye, convergent squint and right sixth nerve palsy. Investigations showed soft tissue masses at right orbit and temporal dural

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Fig. 1a. Lesion over leg on Day 1: Painful, erythematous, poorly demarcated.



Fig. 1b. Lesion over leg on Day 5: Painful, poorly demarcated, with exfoliative and pigmentary changes.

based lesion. Biopsy of the temporal dural based lesion showed granulocytic sarcoma, and bone marrow aspirate confirmed the presence of AML. She was treated on the Medical Research Council (MRC) AML 10 protocol.

She developed pulmonary aspergillosis after one course of chemotherapy, which was successfully treated with 6 weeks of intravenous amphotericin, itraconazole prophylaxis and a right lower lobectomy. She also developed a right eye hypopyon secondary to leukaemic infiltrates which responded to topical steroids and intrathecal chemotherapy. She was scheduled for a sibling matched allogeneic transplant but relapsed in the bone marrow after 4 courses of chemotherapy.

She was re-induced with a course of FLAG-Ida chemotherapy (relapsed protocol). Unfortunately, she developed multiple episodes of neutropaenic septicaemia which included extended spectrum beta-lactamase producing *Klebsiella pneumoniae* and *Enterobacter cloacae*, both in stool cultures with negative blood cultures; *Staphylococcus aureus*, *Streptococcus viridans* and a *Bacillus* species in blood cultures from the Hickman central line. She was initially treated with intravenous ceftazidime and amikacin which was changed to vancomycin and amphotericin. Meropenem and amikacin were added to the antibiotic regimen. Computed tomography (CT) chest showed small areas of infective consolidation and a small right pleural effusion. Intravenous amphotericin was changed to lipid-complex amphotericin in view of the persistent fever. She was severely neutropaenic and was given intravenous granulocyte colony stimulating factor (G-CSF) throughout this illness.

Three weeks post chemotherapy, blood cultures taken from Hickman line grew *Stenotrophomonas maltophilia* which was sensitive to trimethoprim-sulphamethoxazole (TMP-SMX). Over the next few days, she developed

painful skin lesions mainly on the limbs. The lesions were nodular, tender, target-like with surrounding erythema, but no central necrosis was noted (Fig. 1). A skin biopsy of one of the lesions was done. Histology did not reveal evidence of leukaemic infiltrates but tissue culture grew *Stenotrophomonas maltophilia*. A 2D echocardiography showed no evidence of vegetations. She was given intravenous TMP-SMX. After a week of TMP-SMX, the lesions gradually resolved, the fever was settling and subsequent repeat blood cultures were negative. She subsequently refused further treatment and left for a foreign country for alternative therapies. She relapsed again and finally succumbed to her malignancy in December 2004.

## Discussion

*Stenotrophomonas maltophilia* causes a wide spectrum of infections, namely bacteraemia, endocarditis and respiratory tract infections, especially in patients with cystic fibrosis, urinary tract infections usually secondary to urinary tract surgery or instrumentation, meningitis, ophthalmologic infections, skin and soft tissue infections and uncommonly, bone and joint infections. Skin and soft tissue manifestations of *Stenotrophomonas maltophilia* infection are becoming an increasingly recognised entity. Clinical skin presentations include primary cellulitis, metastatic nodular skin lesions or cellulitis, gangrenous cellulitis, soft tissue necrosis, ecthyma gangrenosum<sup>1</sup> and infected mucocutaneous ulcers.<sup>2</sup>

The routes of spread include haematogenous seeding and direct inoculation through mucocutaneous surfaces.<sup>3</sup> The latter group is further subdivided into patients with primary cellulitis and those with mucocutaneous infections.

From the literature review, there were a total of 24 reported cases of mucocutaneous, skin and soft tissue infections by *Stenotrophomonas maltophilia*. The

presentations include metastatic cellulitis, primary cellulitis and infected mucocutaneous ulcers.<sup>1,3-5</sup>

#### *Skin Manifestation: Metastatic Cellulitis*

Metastatic cellulitic lesions are characteristically tender, erythematous, warm subcutaneous infiltrates that can be either well demarcated or poorly demarcated.<sup>4</sup> There can be tender areas of cellulitis surrounding these nodules or distant from these nodules, usually located on the limbs or chest. Two cases with black central necrosis and 2 cases of ulceration were reported.<sup>3</sup> A total of 13 cases of metastatic cellulitis have been reported previously, including 1 case of multiple erythematous macular lesion typical of ecthyma gangrenosum.<sup>1,3,4,6</sup>

The nodular lesions caused by *Stenotrophomonas maltophilia*<sup>3</sup> differ from ecthyma gangrenosum by their striking nodularity, the absence of bulla or vesicle formation, the associated pain and tenderness, and the tender areas of cellulitis distant from the nodules. In addition, necrosis was not universally present. Histologically, the differences were significant for the absence of microbial invasion, necrosis of the vessel walls and vascular thrombosis.

#### *Skin Manifestation: Primary Cellulitis*

Vartivarian<sup>3</sup> reported 5 cases of primary cellulitis associated with catheter use. The lesions were tender cellulitis without clear demarcation of the borders. One patient had the lesion surrounding a neck mass whereas 4 other patients had exudative lesions at catheter insertion site.

#### *Mucocutaneous Manifestation*

Mucocutaneous infection by *Stenotrophomonas maltophilia* consisted of infected ulcers of the gingiva, lips and buccal mucosa. So far 10 cases were reported, including 4 cases which were associated with metastatic lesions.<sup>3-5</sup>

#### *Histology*

In other series, histology of the biopsy tissue from 3 of the 5 patients with nodular lesions<sup>3</sup> showed swelling of the endothelial cells and inflammatory infiltrates of the subcutaneous tissue and dermis. Two out of the 5 patients biopsied had necrotising inflammation of the dermis. Our patient's histology of the skin biopsy revealed swelling of the endothelial cells.

#### *Risk Factors*

The risk factors for *Stenotrophomonas maltophilia* infection include neutropaenic, haematologic malignancy, use of broad spectrum antibiotics, immunosuppression especially from chemotherapy, prolonged hospital stay and intravenous catheter use.<sup>3-8</sup>

In the literature, haematologic malignancy is the most

common malignancy found in *Stenotrophomonas maltophilia* infections.<sup>3,4</sup> These patients are myelo-suppressed and usually receive broad spectrum antibiotics for neutropaenic sepsis.

#### *Differential Diagnoses*

The differential diagnoses for metastatic nodular lesions in a neutropaenic patient with a malignancy especially haematologic malignancy, include disseminated fungal infection, leukaemic infiltrates, and *Stenotrophomonas maltophilia* skin infection. In our patient, disseminated skin aspergillosis and leukaemic infiltrates were our initial working diagnoses. Thus, this case illustrates that *Stenotrophomonas maltophilia* is an important differential diagnosis to consider for patients with metastatic nodular skin lesions.

Our patient is the first locally reported case of metastatic nodular skin lesions caused by *Stenotrophomonas maltophilia* bacteraemia. This is also the first reported paediatric case of embolic skin lesions caused by *Stenotrophomonas maltophilia*. Of the 6 cases of *Stenotrophomonas maltophilia* bacteraemia seen in the paediatric oncology patients from year 2000 to 2004 at our hospital, only 1 case developed metastatic skin lesions. Our patient had several risk factors as described above: neutropaenic, AML with recent chemotherapy, multiple courses of broad-spectrum antibiotics and a tunnelled Hickman central venous line.

#### *Treatment*

TMP-SMX is recommended as the agent of choice for therapy of *Stenotrophomonas maltophilia* infection as it is found to be active against most strains although resistance is increasing.<sup>2</sup> Ticarcillin-clavulanate is noted to have good activity against *Stenotrophomonas maltophilia* and is suggested as the agent of choice in individuals intolerant of TMP-SMX.<sup>2</sup>

Moser et al<sup>4</sup> reported 3 cases of *Stenotrophomonas maltophilia* skin cellulitis which were successfully treated with combination of ceftazidime and TMP-SMX or netilmicin (after sensitivity testing of the organisms), for a duration of 10 to 12 days. All 3 patients survived and the dermal lesions gradually disappeared. Antibiotic resistance develops rapidly and therefore, combination therapy is recommended. This is in agreement with a recent study where mortality was significantly lower in patients with *Stenotrophomonas maltophilia* bacteraemia who were treated with combination therapy.<sup>9</sup> Muder et al<sup>9</sup> suggested that a combination of TMP-SMX and either ticarcillin-clavulanate or an extended spectrum cephalosporin may be superior to TMP-SMX alone.

In another study,<sup>3</sup> 2 out of 6 patients with metastatic

cellulitis responded to TMP-SMX when they recovered from myelosuppression; the remaining 4 died of active *Stenotrophomonas maltophilia* infection and persistent neutropaenic within a median of 10 days after the onset of skin lesions. Of the 6 cases of mucocutaneous lesions described, 3 responded to treatment with TMP-SMX. As for the 5 cases of primary cellulites described, 3 responded to antimicrobials which coincided with the removal of the catheter; for the other 2 patients, removal of the catheter was the only therapeutic manoeuvre to achieve response.

### Prognosis

The recovery from *Stenotrophomonas maltophilia* infection is dependent on treatment with appropriate antibiotics, reversal of myelosuppression and removal of intravenous catheter (if central-catheter associated). *Stenotrophomonas maltophilia* infection associated with metastatic skin nodules and to a certain degree, mucocutaneous infections in neutropaenic patients with cancer seem to be poor prognostic signs because many of these patients died of their infections and of causes that were probably secondary to their severe immunosuppression.<sup>3</sup> Haematologic malignancy, transplantation, neutropaenic, immunosuppressive therapy and a high severity of illness score (based on temperature, presence of hypotension, mental status and need for ventilatory support) were important prognostic factors.<sup>9,10</sup>

### Conclusion

Skin and soft tissue manifestations of *Stenotrophomonas maltophilia* infection are becoming an increasingly recognised entity. *Stenotrophomonas maltophilia* skin infection should be included in the list of differential diagnoses for metastatic skin lesions in neutropaenic patients, especially with an underlying haematologic malignancy, who have received recent chemotherapy and

broad spectrum antibiotics. Haematologic malignancy, transplantation, neutropaenic, immunosuppressive therapy and a high severity of illness score (based on temperature, presence of hypotension, mental status and need for ventilatory support) were important prognostic factors.<sup>9,10</sup>

### REFERENCES

1. Bottone EJ, Reitano M, Janda JM, Troy K, Cuttner J. *Pseudomonas maltophilia* exoenzyme activity as correlate in pathogenesis of ecthyma gangrenosum. *J Clin Microbiol* 1986;24:995-7.
2. Denton M, Kerr KG. Microbiological and clinical aspects of infection associated with *Stenotrophomonas maltophilia*. *Clin Microbiol Rev* 1998;11:57-80.
3. Vartivarian SE, Papadakis KA, Palacios JA, Manning JT Jr, Anaissie EJ. Mucocutaneous and soft tissue infections caused by *Xanthomonas maltophilia*. A new spectrum. *Ann Intern Med* 1994;121:969-73.
4. Moser C, Jonsson V, Thomsen K, Albrechtsen J, Hansen MM, Prag J. Subcutaneous lesions and bacteraemia due to *Stenotrophomonas maltophilia* in three leukaemic patients with neutropenia. *Br J Dermatol* 1997;136:949-52.
5. Sakhnini E, Weissmann A, Oren I. Fulminant *Stenotrophomonas maltophilia* soft tissue infection in immunocompromised patients: an outbreak transmitted via tap water. *Am J Med Sci* 2002;323:269-72.
6. Villarino ME, Stevens LE, Schable B, Mayers G, Miller JM, Burke JP, et al. Risk factors for epidemic *Xanthomonas maltophilia* infection/colonization in intensive care unit patients. *Infect Control Hosp Epidemiol* 1992;13:201-6.
7. VanCouwenberghe CJ, Farver TB, Cohen SH. Risk factors associated with isolation of *Stenotrophomonas (Xanthomonas) maltophilia* in clinical specimens. *Infect Control Hosp Epidemiol* 1997;18:316-21.
8. Elting LS, Bodey GP. Septicemia due to *Xanthomonas* species and non-aeruginosa *Pseudomonas* species: increasing incidence of catheter-related infections. *Medicine (Baltimore)* 1990;69:296-306.
9. Muder RR, Harris AP, Muller S, Edmond M, Chow JW, Papadakis K, et al. Bacteremia due to *Stenotrophomonas (Xanthomonas) maltophilia*: a prospective multicenter study of 91 episodes. *Clin Infect Dis* 1996;22:508-12.
10. Morrison AJ Jr, Hoffmann KK, Wenzel RP. Associated mortality and clinical characteristics of nosocomial *Pseudomonas maltophilia* in a university hospital. *J Clin Microbiol* 1986;24:52-5.