CASE REPORTS

Diagnosis of fusariosis in urine cytology

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Fusarium is a filamentous fungus widely distributed in plants and in the soil. Most species are more common at tropical and subtropical areas. Besides being a common contaminant and a well-known plant pathogen, *Fusarium* sp may cause various infections in humans. However, it has not yet been reported as being the pathogen of urinary tract infection. A 67-year-old woman had extracorporeal shock wave lithotripsy and percutaneous nephrolithotomy for renal stones 7 and 6 years ago, respectively. She had had fever, chillness, urinary urgency and frequency for 6 days. Routine testing of urine showed numerous leucocytes. She was admitted under the impression of urinary tract infection. On admission, many spindle-shaped structures were found in the urine smears. This shows that *Fusarium* was identified. *Fusarium* may be the pathogen of the urinary tract infection, particularly when urolithiasis is present.

Over the past decade, there has been a marked increase in opportunist infection by fungal pathogens involving the urinary tract. This increasing incidence in fungal urinary tract infection is associated with extensive and prolonged use of broad-spectrum antimicrobial agents, corticosteroids, immunosuppressive and cytotoxic drugs.[1] Other important risk factors include higher age, diabetes mellitus, chronic renal failure, haemodialysis, renal transplantation, malignancy, nephrolithiasis, and structural or functional abnormalities of the urinary tract, with indwelling urinary catheter or nephrostomy.[1–3] Fungal urinary tract infections are most commonly caused by *Candida* species.[2–4] Fungal infections of the urinary tract may also be caused by *Cryptococcus*,[3] *Coccidioides*,[5] *Aspergillus*,[6] *Histoplasma*[7] and *Curvularia* species.[8] However, *Fusarium* species have not been previously reported as pathogenic fungi in the urinary tract in the English literature.

CASE REPORT

A 67-year-old woman had received extracorporeal shock wave lithotripsy and percutaneous nephrolithotomy for renal stones 7 and 6 years ago, respectively. She had had fever, chills, urinary urgency and frequency, poor appetite and general weakness for 6 days. Urine routine analysis showed numerous leucocytes. Considering the possibility of urinary tract infection, she was admitted to the hospital. On admission, cytological examination of urine specimen showed many sickled to fusiform macroconidia (3−8×11−70 μm) with 3–5 septa (fig 1). Fusariosis of the urinary tract was suspected. The urine specimen was then cultured with Sabouraud dextrose agar at 30℃ for 7 days. The colony surface at first looked like white wool, later turning cream-coloured and leather-like in appearance. The back view of the colony had a leather-like centre and a tan margin (fig 2A). Hyaline septate hyphae, conidiophores, phialides, macroconidia and microconidia were found microscopically (fig 2B). Fusariosis of the urinary tract due to *Fusarium* species was confirmed. The patient was treated with percutaneous nephrostomy, double J and hydration. She was discharged with improved condition.

DISCUSSION

Fusarium is a filamentous fungus widely distributed in plants and in the soil. Most species are common in tropical and subtropical areas.[9] They grow rapidly on Sabouraud dextrose agar at 30℃ and produce woolly to cottony, flat, spreading colonies. From the front, the colour of the colony may be white, cream, tan, salmon, cinnamon, yellow, red, violet, pink or purple. From the back, it may be colourless, tan, red, dark purple or brown.[10]

Hyaline septate hyphae, conidiophores, phialides, macroconidia and microconidia are observed microscopically.[10] Macroconidia (3−8×11−70 μm) are produced from phialides on unbranched or branched conidiophores. They are two or more celled, thick-walled, smooth, and cylindrical or sickle-(canoe-)shaped. Macroconidia have a distinct basal foot cell and pointed distal ends. They tend to accumulate in balls or rafts. Microconidia (2−4×4−8 μm), on the other hand, are formed on long or short simple conidiophores. They are one-celled (occasionally two-celled or three-celled), smooth, hyaline, ovoid to cylindrical and arranged in balls (occasionally occurring in chains).[10] *Fusarium* differs from *Acremonium, Lecythophora* and *Phialemonium* in having macroconidia.[11]

Besides being a common plant pathogen, *Fusarium* is also one of the emerging causes of opportunist by mycoses.[10 12] It may exist in the soil of potted plants in hospitals. These plants constitute a hazardous mycotic reservoir for nosocomial fusariosis.[13] *Fusarium* species are causative agents of superficial and systemic infections in humans. Infections due to *Fusarium* species are collectively referred to as fusariosis. Trauma is the major predisposing factor for development of cutaneous infections due to *Fusarium* strains. Disseminated opportunist infections, on the other hand, develop in immunosuppressed hosts, particularly in neutropenic patients and those undergoing transplants.[14 15] *Fusarium* infections from solid organ

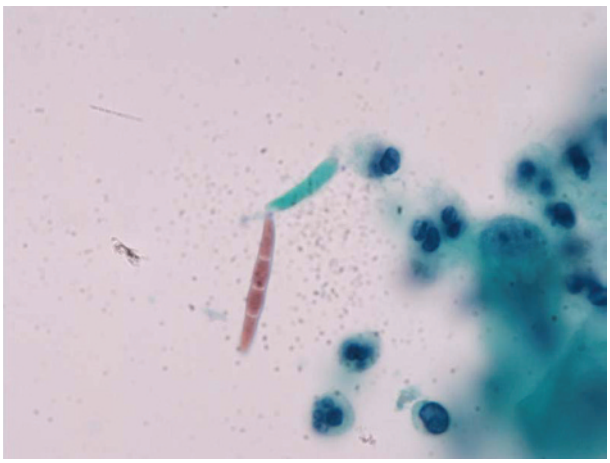

Figure 1 Cytological examinaion of urine with Papanicolaou staining showed many sickled to fusiform macroconidia (3−8×11−70 μm) with 3–5 septa (Papanicolaou stain, original magnification, ×1000).

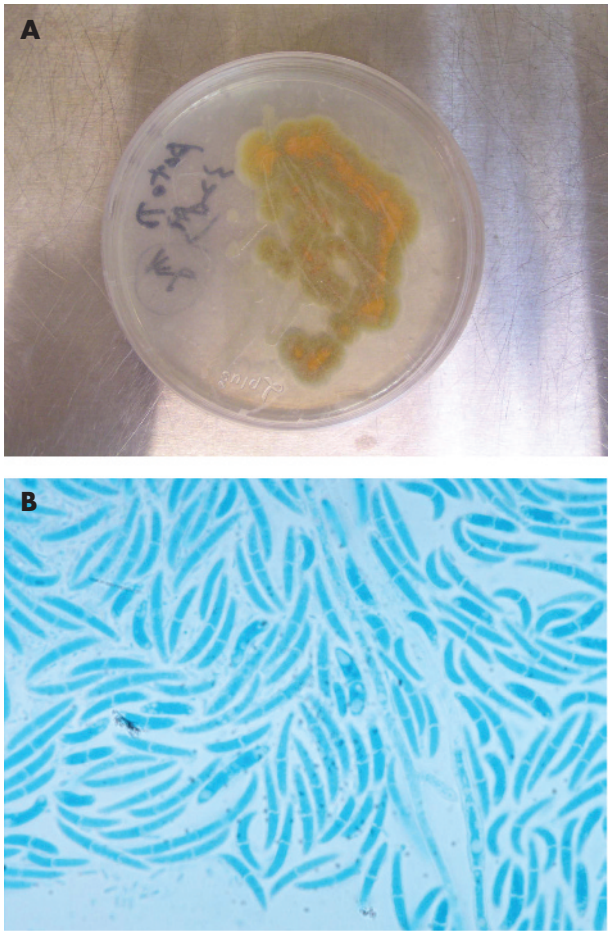

Figure 2 (A) After being cultured with Sabouraud dextrose agar at 30°C for 7 days, the back view of the colony had a leather-like centre and a tan margin. (B) In this field, the hyaline septate hyphae, a phialide, abundant, large, sickle-(canoe)-shaped macroconidia with 1–4 septa, and some small, oval to cylindric, one-celled or two-celled microconidia were found microscopically (lactophenol cotton blue stain, original magnification, ×1000).

transplantation tend to remain local and have a better outcome compared with those that develop in patients with haematological malignancies and patients undergoing bone marrow transplantation.[16]

Keratitis,[17] endophthalmitis,[18] otitis media,[19] onychomycosis,[20] cutaneous infections (particularly of burn wounds, mycetoma),[21] sinusitis,[22] pulmonary infections,[23] endocarditis, peritonitis, central venous catheter infections, septic arthritis, disseminated infections[10 12] and fungaemia[24] due to *Fusarium* species have been reported.

Fusarium is one of the most drug-resistant fungi. The only antifungal drugs that yield relatively low minimal inhibitory concentrations for *Fusarium* are amphotericin B, voriconazole[25] and natamycin.[21] *Fusarium* infections are difficult to treat, and the invasive forms are often fatal. Amphotericin B alone or in combination with flucytosine or rifampin is the most commonly used antifungal drug for treatment of systemic fusariosis.[16]

Being a pathogen of the urinary tract infection, *Fusarium* has not been discussed in the English literature yet. Fusariosis of the urinary tract in this patient might have resulted from ascending infection due to urostasis produced by nephrolithiasis. The best therapeutic method for these patients is to resolve the underlying urolithiasis. In conclusion, *Fusarium* may be a pathogen of the urinary tract infection, particularly when urolithiasis is present.

Take-home messages

- *Fusarium* may be the pathogen of the urinary tract infection, particularly when urostasis is present.
- Thus, resolving the urostasis is the best therapeutic method for these patients.

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Mast-cell sarcoma of the tibia

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The mast-cell sarcoma of a bone is described here for the first time. The tumour presented in a 4-year-old boy, with pain, oedema and deformation of his right lower leg. Radiological findings revealed a destructive tumourous mass. Histopathological examination showed the tumour to be composed of large, atypical cells, with hyperchromatic oval and polygonal nuclei. The cytoplasm around them was eosinophilic with many basophilic and toluidine-blue-positive granules. These atypical mast cells were positive for chloroacetate esterase, c-kit, tryptase and negative for myeloperoxidase. The primary disease quickly progressed to mast-cell leukaemia, and despite intensive chemotherapy the patient died 18 months after first symptoms.

Mast-cell sarcoma is a rare disease characterised by local proliferation of atypical mast cells, destructive growth and poor prognosis. Here we present a case of mast-cell sarcoma arising in bone.

A 4-year-old boy was admitted to the Clinical Hospital Osijek, Osijek, Croatia with 8-month history of painful oedema and deformation of right lower leg. *x* Rays and CT-scan revealed a tumourous mass on the right tibia (fig 1). There was no hepatosplenomegaly, and blood counts were normal. After biopsy and pathohystological diagnosis at the Institute of Pathology, Medical School, University of Zagreb, Zagreb, Croatia, the patient was moved to the Children's Hospital, Zagreb, Croatia. Soon after admission, a skin rash developed, with high serum tryptase level, but still blood counts were normal. Sternal fine-needle aspiration biopsy was performed and an aleukaemic variant of mast-cell leukaemia was diagnosed. The patient was subjected to acute myeloid leukaemia-Berlin–Frankfurt–Munster (AML-BFM) 2004 therapy protocol. A follow-up CT-scan showed oval masses in both tibias, without the involvement of soft tissue. Follow-up biopsy of the right tibia was performed. A few weeks before death the patient's blood count revealed low leucocytes. Liver and spleen were enlarged. Despite intensive therapy the patient died 18 months after initial symptoms occurred.

Histologically, bone and soft tissue samples were partially destroyed or permeated by sarcomatous tumour tissue. The tumour was almost exclusively composed of large, atypical cells, with hyperchromatic oval to polygonal and few larger bilobulated and multilobulated nuclei. Cytoplasm was eosinophilic, filled with basophilic granules on haematoxylin-eosin (fig 2A,B), and periodic acid Schiff staining, displaying metachromatic-like granules on toluidine-blue (fig 2C) and Giemsa-stained slides. Among the tumour cells, many eosinophils and some histiocyte-like cells were present. Mitotic activity was very low, and blast-like cells with high nucleus-to-cytoplasm ratio were only occasionally observed. No spindle-shaped mast cells were present. Chloroacetate esterase reaction was positive, whereas myeloperoxidase was negative. Immunohistochemically atypical mast cells were positive for tryptase, CD68, vimentin, c-kit (fig 2D), CD45 and CD43. They were negative for CD3, CD15 and CD34 (all antibodies from DAKO, Glostrup, Denmark). Cytopathological analysis showed 90% of atypical cells being toluidine-blue, c-kit and tryptase positive. A follow-up smear revealed hypercellular bone marrow infiltrated with atypical mast cells positive for toluidine-blue, CD45, CD68, occasionally for CD2, and negative for myeloperoxidase, with suppressed erythropoietic, granulopoietic and thrombopoietic cells.

Mast-cell sarcoma has been to the best of our knowledge, described in only three cases, presenting as subglottic tumour, as a tumour of the ascending colon and as an intracranial tumour.[1–3] Our patient did not meet the criteria for systemic mastocitosis.[4] Based on our histological, histochemical and immunohistochemical data we were able to exclude myeloid

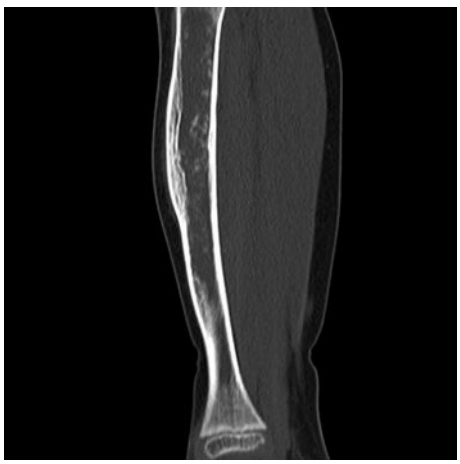

Figure 1 CT scan showing tumourous mass in the right tibia.