

# Clinical Characteristics of Community-Acquired Pneumonia due to Infection with *Trichosporon asahii*

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## ABSTRACT

**Objectives:** The aim of this study was to evaluate the clinical characteristics of Community-Acquired Pneumonia (CAP) patients with infected *Trichosporon asahii* in urinary tract.

**Methods:** Patients diagnosed with *Trichosporon asahii* isolated from the patients with urinary tract infection between January 2015 and November 2019, were retrospectively reviewed in this study. Clinical data were collected for each patient, including age, gender, co-morbid diseases, relevant tests, antimicrobial susceptibility test and impact on patient's antifungal drugs, etc.

**Results:** Ten patients (9 males and 1 female; range of age: 63-91, and average age of 80.1) were enrolled into this study. Of the ten patients, ten patients had old cerebral infarction, ten patient had coronary heart disease, five patient had hypertension, three patient had diabetes, three patient had gastrointestinal bleeding, one patient had lung cancer. Of the ten enrolled patients, all patients were suffering from cough and sputum, and five patients were presented with fever. However, there were no urinary tract symptoms such as frequent urination, urgency and pain. No complications occurred. Furthermore, all patients had increased

C-reactive Protein (CRP), only three patients had increased White Blood Cell (WBC). At the same time, nine had decreased albumin (ALB), seven had percentage of Eosinophils (EO%), and five had helper T lymphocytes (CD4). All patients were treated with anti-infection, and expectorant. Among antifungal drugs, amphotericin and voriconazole have higher sensitive rate. Finally, five patients were discharged with a better health condition, two patients were automatically discharged, and three patients were died. The average follow-up for patients was 3 months, three patients were died.

**Conclusion:** The results suggested that the mortality rate of *Trichosporon asahii* pneumonia is very high; therefore, patients with infected *Trichosporon asahii* should be more actively treated by antifungal drug such as voriconazole.

**Keywords:** Community-Acquired Pneumonia, Urinary tract infection, *Trichosporon asahii*, Clinical characteristics

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## INTRODUCTION

Community Acquired Pneumonia (CAP) refers to infectious inflammation of pulmonary parenchyma outside the hospital, including pneumonia with a clear incubation period of pathogen infection during the incubation period after admission (Cao B, *et al.*, 2018). The CAP is a common in respiratory disease, and the incidence is very high in the world. The patients with CAP whose pathogens were detected by the regular sputum culture and blood culture, while the urine culture was ignored. In particular, some patients with urinary tract infection were easy to be clinically ignored, though they had obvious clinical symptoms. Finally, the diseases resulted into the aggravation. Therefore, clinician must pay more attention to urine culture (Sugita T, *et al.*, 2000).

*Trichosporon asahii* is pertain to Trichospores in yeast-like fungi. At present, there are 51 species of Trichomonas, and studies have found that 16 can cause human diseases (Mariné M, *et al.*, 2015). The world's first Trichospores was reported in 1970; In 2001, China was reported the first case of disseminated trichosporidiosis caused by *Trichosporon asahii*, and then it was reported that this bacterium was isolated from blood, sputum, urine and other specimens successively (Chen J, *et al.*, 2014). The area of infection and clinical types found in skin infection, blood, etc., urinary tract infection restricted to case reports. There are very few reports about *Trichosporon asahii*. Year by year increase in the number of immunocompromised hosts, nearly 40 years of *Trichosporon asahii* in global incidence increased gradually, but patients with poor prognosis, high mortality (Liao Y, *et al.*, 2015).

This paper retrospectively analyzed the clinical data of ten cases of community acquired pneumonia complicated with *Trichosporon asahii* infection admitted to Nankai Hospital of Tianjin from

January 2015 to November 2019, aiming to improve clinicians' understanding and diagnosis level of community acquired pneumonia complicated with Trichoderma ashoderma infection, and draw attention to early diagnosis and antifungal treatment to reduce mortality.

## METHODS

### Patients

Hospitalized pneumonia patients were retrospectively analyzed from January 2015 to November 2019 in Tianjin Nankai Hospital. The ages of the patients ranged from 63 to 91 years old. This study was approved by the ethic committee of our hospital.

According to the guidelines on diagnosis and treatment of Community-Acquired Pneumonia (2006 edition), Chinese association of respiratory diseases (Cao B, *et al.*, 2018). The diagnostic criteria were as follow:

- The disease was acquired in the community.
- Patients with pneumonia-related clinical manifestations: fever, increased symptoms of cough, sputum or original respiratory diseases, accompanied or not accompanied by purulent sputum, chest pain, dyspnea and hemoptysis, pulmonary consolidation signs and/or audible and moist rales, peripheral blood leukocyte  $>10 \times 10^9 /L$  or  $<4 \times 10^9 /L$ , with or without left shift of nucleus.
- Pulmonary imaging examination showed the appearance of new patchy invasive shadow, leaf or segment consolidation shadow, ground glass shadow or interstitial change, with or without pleural effusion.

In accordance with item 1 and one of the item 2 or item 3, and excluded pulmonary tuberculosis, non-infectious pulmonary interstitial disease, pulmonary tumor, pulmonary edema, atelectasis, pulmonary embolism, pulmonary vasculitis, pulmonary eosinophil infiltration and pulmonary vasculitis. Urinary tract infection in 2014 edition of the China urology disease diagnosis and treatment guidelines in the diagnostic criteria; *Trichosporon asahii* was isolated from urine culture and the colony count was  $\geq 105$  CFU/m L. The bacterium can be confirmed as the pathogen of urinary tract infection.

Ten pneumonia patients infected by *Trichosporon asahii* were retrospectively analysed.

**Data collection**

Patients diagnosed with *Trichosporon asahii* isolated from the patients with urinary tract infection between January 2015 and November 2019, were retrospectively reviewed in this study. Clinical data were collected for each patient, including age, gender, co-morbid diseases, relevant tests, antimicrobial test and impact on patient’s antifungal drugs, duration of follow-up, and the final outcomes.

**RESULTS**

**Basic information of the patients**

All of the 10 patients in this study had Community-Acquired Pneumonia, including 9 males and 1 female. The mean age was  $(80.1 \pm 9.1)$  years, and the mean hospital stay was  $(24.2 \pm 12.5)$  days. The shortest length of stay was 11 days, and the longest length of stay was 44 days. To some degree, the Clinical Characteristics of patients had related to the severity of the disease (Table 1).

**Table 1: Basic clinical information of patients**

Variable	Number (n=10)	Proportion %
<b>Gender</b>		
Male	9	90%
Female	1	10%
<b>Age</b>		
<80	6	60%
80-90	2	20%
>90	2	20%
<b>Inpatient days</b>		
<24	6	60%
24-35	1	10%
>35	3	30%

Among them, there were 10 patients with old cerebral infarction, 10 with coronary heart disease, 5 with hypertension, 3 with diabetes and 3 with gastrointestinal bleeding. There were 1 cases of lung cancer. Ten of them were positive for *Trichosporon asahii* form urine culture, mainly from duct-related infections. The characteristics of the patients were listed in Table 2.

**Table 2: Clinical characteristics of patients**

Variable	Number(n=10)	Proportion %
<b>Clinical symptom</b>		
Fever	5	50%
Cough	10	100%
Wheezing	6	60%
<b>Underlying disease</b>		
Cerebral infarction	10	100%
Diabetes	3	30%
Heart disease	10	100%
Gastrointestinal bleeding	3	30%
Hypertension	5	50%

<b>Outcome</b>		
Better	5	50%
Automatic discharge	2	20%
Die	3	30%

The main clinical manifestations of 10 patients were cough and sputum. There were 6 cases with wheezing and 5 cases with different degrees fever. However, there were no urinary tract symptoms in all patients, such as frequent urination, urgency and pain.

**The laboratory results**

The characteristics of the patients were shown in Table 3. All patients had increased C - reactive protein (CRP), only three patients had increased White Blood Cell (WBC). At the same time, patients had decreased albumin (ALB), percentage of Eosinophils (EO%), and helper T lymphocytes (CD4). There were no in differences in all patients related to immune function.

**Table 3: Laboratory test results of the patients**

Variable	Number (n=10)	Proportion/%
<b>Laboratory test</b>		
WBC>10 × 10 <sup>9</sup> /L	3	30%
CRP>8.2 mg/L	10	100%
ALB<35 g/L	9	90%
EO%<0.5%	7	70%
CD4<60%	5	50%

According the cultivation of drug sensitive points, 8 patients were sensitive to amphotericin B and 2 were resistant to amphotericin B. Fluconazole was sensitive in 8 cases and resistant in 1 case. There were 9 patients with voriconazole sensitivity and 1 patient with drug resistance. Seven cases were sensitive to fluorocytosine. Itraconazole was sensitive in 5 cases and resistant in 1 case. Through culture, a. asahii was highly sensitive to voriconazole and least sensitive to itraconazole. The characteristics of the patients were listed in Table 4.

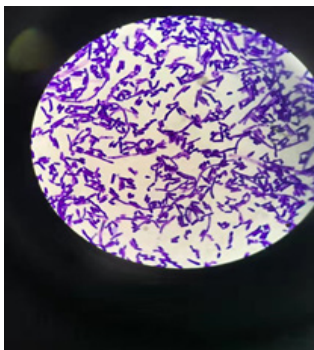
**Table 4: Sensitivity analysis of 10 *Trichosporon asahii* strains to commonly used antibacterial agents (%)**

Sensitive bacteria	S	I	R
Itraconazole	50	40	40
Flucytosine	70	30	0
Amhotericin B	80	0	20
Fluconazole	80	10	10
Voriconazole	90	0	10

The bacterial colony growth characteristics, staining and microscopic morphological characteristics of *Trichosporidium Asashi* are shown in Figures 1 and 2.



**Figure 1: Petri dishes of *Trichosporidium asahii***



**Figure 2: *Trichosporidium asahii* under the microscope**

All 10 patients were treated with anti-infection, expectorant and other drugs after admission. Among them, 3 cases died, 2 cases were discharged automatically, and 5 cases were discharged after improvement, with the fatality rate of 30%. The characteristics of the patients were listed in *Table 2*.

Indwelling catheter was used in 10 cases. 3 cases were treated with antifungal agents (3 cases were treated with fluconazole); two cases were treated with fluconazole for 2 weeks, and the urine fungus culture in the middle section was negative. The other 2 patients died, the main cause of death was not related to the effect of antifungal therapy.

#### Follow-up results

The average follow-up for patients was 3 months. During the follow-up, which discharged from hospital after follow-up, six of them to come on, one person was killed.

#### DISCUSSION

As the most common pathogenic bacteria of *trichosporidium asahii*, *trichosporidium asahii* is the main pathogen of disseminated trichosporidiosis (Fernández-Ruiz M, *et al.*, 2017; Chagas-Neto TC, *et al.*, 2009). It is an opportunistic pathogenic fungus, accounting for 74% of the species of trichosporium (Ruan SY, *et al.*, 2009). Currently, it is been considered that ascaris is a opportunistic pathogen that can affect the skin, lymph nodes, blood flow, craniocerebral, respiratory, liver and other systems (Zhang LH, *et al.*, 2018; Basiri K, *et al.*, 2012). May have lung, skin, haematogenous and disseminated infections, such as pneumonia and endocarditis; In general, pathogenesis often occurs in patients with low immune function, tumors, combined with blood or organ transplantation, through hematogenous infection or systemic invasion, such as human immunodeficiency virus infection, duct-related infection, burns, artificial heart valve disease and peritoneal dialysis (Ebright JR, *et al.*, 2001). Thus, current studies indicate that risk factors for infection include neutropenia, organ transplantation, diabetes, end-stage kidney disease, HIV infection, immunosuppressive agents, and the use of invasive medical devices. Catheter infection is a major source (Colombo AL, *et al.*, 2011; Almeida JN, *et al.*, 2017). In this group, 10 patients were cultured from the urine culture and underwent invasive surgery to preserve the catheter. The presence of catheter-related infection was the main source of *Trichoderma asahi*. In particular, immunocompromised patients, such as cancer, blood diseases and AIDS, have a mortality rate of up to 80%. In this group, there were 1 patients with lung cancer, with a mortality rate of 30%. The major risk factors for the pathogenesis of *trichosporidium asahi* include malignant tumors, cirrhosis, chronic renal insufficiency, granulocytosis, long-term use of ultra-broad-spectrum antibiotics and immunosuppressants, and damage to the skin and mucosal barrier (Chen J, *et al.*, 2014). However, we found that there were 10 patients with old cerebral infar-

tion in this group. Albumin was decreased in 9 cases, among which 4 cases were diagnosed with hypoproteinemia. So advanced age, cerebral infarction, hypoproteinemia may also be one of the risk factors.

Patients with neutropenia are more likely to cause infection, which is often fatal, with a fatality rate of 42% to 80% (Chen J, *et al.*, 2014). Higher mortality may be associated with prolonged neutropenia, a high disease burden, delayed diagnosis, and inappropriate antifungal therapy (Sugita T, *et al.*, 1999; Chan-Tack KM, 2005). However, in this group, the percentage of neutrophils increased in 7 cases, which was inconsistent with the report. It may be due to the high inflammatory index caused by acute infection and pneumonia. However, the percentage of eosinophil decreased in 7 patients in this group, possibly because eosinophil is closely related to the immune system by affecting the maturation of T cells and B cells and secreting a variety of cytokines to regulate the secondary immune reaction. Therefore, whether the decrease in the percentage of eosinophil can be used as an independent risk factor for the discovery of *mucosporium asahi* infection is open to question.

The determination of T cell subsets is an accurate method to determine cellular immune function (Yang X, 2000). CD3+ cells reflect the maturation level of T cells in peripheral blood (Kemeny DM, *et al.*, 1999). CD4+ helper T cells, is a kind of has a proinflammatory role of cells, the main function is to produce antibodies and promote B cells differentiation, prompt T cells and other immune cells proliferation and differentiation, the coordination of the interaction between the immune cells, can also produce interleukin-2, and so on the immune response to start the final expression form and play a key role on the strength, is a T cell subgroup with auxiliary and induced, it said the proliferation of B cells to produce the immune globulin increased and cell immune enhancement. CD8+ molecule is the early anti-infection cells, the main function is to kill the target antigen, can eliminate the pathogen, but the excessive number of cells can cause the body damage, it is one of the important causes of various immune dysfunction. CD8+ cells undergo apoptosis soon after killing target cells, showing unstable levels in peripheral blood (Liu E, *et al.*, 2010). CD4+ and CD8+ subsets maintain a certain proportion when normal, interact with and antagonize each other functionally, and jointly maintain the functional balance of the body's immune system (Zhao W, *et al.*, 1994). The CD4+/CD8+ cell ratio is one of the important indicators to reflect the stability of immune system function, and its decline indicates the decline of human immune function (Xu Y, *et al.*, 2012). This indicates that the immune function of the patients is decreased in different degrees, which is also one of the causes of the infection of *trichosporidium asahi*, consistent with the report.

Studies showed that voriconazole was the first choice for drug treatment of a. asasicum, followed by itraconazole and fluconazole (Kalkan- ci A, *et al.*, 2010; Yang MF, *et al.*, 2014; Gonul S, *et al.*, 2015; Toriumi Y, *et al.*, 2002), and drug resistance to carprofennet and amphotericin B (Chagas-Neto TC, *et al.*, 2009; Hazirolan G, *et al.*, 2013; Kalkan- ci A, *et al.*, 2003). Some reports suggest that there are regional differences in sensitivity to amphotericin B, with most drug resistance in foreign countries, but still sensitivity in mainland China (Chagas-Neto TC, *et al.*, 2009; Kalkan- ci A, *et al.*, 2003). Published in 2014, the European Society of Clinical Microbiology and Infectious Diseases Of Medic- al Mycology and Europe union (ESCMID and ECMM) launched the guidelines also recommend three azole antifungal drug therapy for invasive piedra, recommends voriconazole can be used as the preferred treatment (Arendrup MC, *et al.*, 2014), studies have shown that voriconazole can significantly inhibit the sassy MAO spore fungus infection (Fournier S, *et al.*, 2002). Liao Y, *et al.* found that triazole antifungal drugs, especially voriconazole, can significantly improve

the prognosis of patients, and it can be used as the first choice for the treatment of invasive trichosporidiosis, but its response to amphotericin B treatment is not good. In addition, studies have found that amphotericin B combined with fluconazole can also achieve a good therapeutic effect (Liao Y, *et al.*, 2015; Arendrup MC, *et al.*, 2014). Falk R, *et al.* reported the multi-drug resistance of antifungal drugs such as fluconazole and itraconazole, which is sensitive to voriconazole (Falk R, *et al.*, 2003). And after culture, the drug sensitive break point, found that the *asahii* trichosporium is highly sensitive to voriconazole, itraconazole sensitivity is the lowest. In addition, in this case, 1 patient had lung cancer complicated with the infection of trichosporidium *asahii*, which worsened with the progression of the disease and sustained fever. The application of a variety of antibiotics had no significant effect, but the antifungal treatment of voriconazole was effectively relieved, which was considered to be related to the infection of trichosporidium *asahii*.

### The literature support

Based on the statistical analysis of data from PubMed, CnKI and Wanfang, the infection of *Trichoderma asahi* is more and more serious, and the mortality rate is also increasing gradually. Through analysis, lots of cases occur in Africa, Europe, North and South America, but the most in Asia. Also, male patients are more than female. Among the cases, the top three are hematopathy, diabetes, and lung infection. There are also patients with other diseases, such as cancer, organ transplants, AIDS. Blood infection is the most common, followed by urinary system, respiratory system and skin system. It's found that neutropenia is the main feature of the disease. It is suggested that voriconazole, fluconazole and itraconazole are effective in treatment. Voriconazole was preferred, followed by fluconazole, amphotericin B and itraconazole.

*Trichoderma asahi* infection between China and other countries, it is found that among fungal infections, lung infection in Chinese patients is higher than that in other countries, while the number of patients with urinary tract infection in other countries is higher than that in China. For the mortality rate, China is lower than other countries.

Therefore, review of the literature found; although the number of cases in this paper is small, the analyzed clinical characteristics are roughly the same as those in domestic and foreign. The male patients were more than female patients. Among the cases of *Trichoderma asahi* infection, lung infection was the most common. In this case, It was also found that diseases such as advanced age, old cerebral infarction and hypoproteinemia were the main disease types of infection with *Hirsutia asahi*, and were mainly characterized by decreased percentage of eosinophils, low albumin and decreased CD4. The treatment was consistent with the literature review, which showed the highest sensitivity to Voriconazole in The treatment of *Trichoderma asaxidium* with good efficacy.

### CONCLUSION

In conclusion, the infection of community acquired pneumonia complicated with *Trichoderma asahi* showed an increasing trend year by year. In particular, after catheter implantation, vigilance should be enhanced. Clinical microbiology laboratory should also strengthen the awareness of identification of this fungus, actively retain and culture, find sensitive drugs, and provide clinical reasonable drug advice.

### DECLARATIONS

#### Authors' contributions

All authors have made substantial contributions to the conception and design of the study, data acquisition, analysis and interpretation of data. All authors read and approved the final manuscript.

### Ethics approval and consent to participate

The study was approved by the Tianjin Hospital of Integrated Traditional Chinese and Western Medicine committee (General consent was obtained according to the institutional guidelines).

### Availability of data and materials

The datasets generated and analyzed in the current study have not yet been published.

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