Clinical Features and Survival Outcomes of Invasive Aspergillosis in Pediatric Patients at a Medical School in Thailand

Suvaporn Anugulruengkitt MD*, Panruethai Trinavarat MD**,
Punchavit Chantranuwat MD***, Suchada Sritippayawan MD*,
Chitsanu Pancharoen MD*, Thanyawee Puthanakit MD*

** Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*
*** Department of Radiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*
**** Department of Pathology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*

Background: *Invasive aspergillosis (IA) is a severe infection in immunocompromised patients. Recently, serum galactomannan has been widely used for diagnosis and voriconazole as an antifungal agent. The objective of this study is to describe clinical features and survival outcomes of IA.*

Material and Method: *A retrospective chart review of IA in patients younger than 18 years old at King Chulalongkorn Memorial Hospital, Thailand, was conducted. Clinical definitions were based on criteria of the European Organization for Research and Treatment of Cancer/Mycoses Study Group (EORTC/MSG) 2008.*

Results: *Between January 2006 and December 2012, 40 cases of invasive aspergillosis were identified, classified as proven (8 patients, 20%), probable (28, 70%), and possible IA (4, 10%). Median age of patients was 10 years (range, 42 days-17 years). The most common underlying disease was hematologic malignancy (60%). The major risk factor was neutropenia (65%) with median duration of 21 days (range, 4-58 days). The most common site of infection was in the lungs (80%). The most common computed tomography chest finding was nodules (71%). An air crescent sign was seen only in 11% and a halo sign was found only in 7% of patients. Serum galactomannan was positive in 78% of patients with median value of 1.34 (range 0.5-5.6). Only seven patients (17%) had microbiological confirmation, of which were Aspergillus flavus (4 cases) and Aspergillus fumigates (3 cases). Antifungal therapy included voriconazole (23 patients, 58%), amphotericin B (12, 30%), liposomal amphotericin B (3, 8%), caspofungin (1, 2%) and itraconazole (1, 2%). Two deaths related to angioinvasive complications of aspergillosis (pulmonary hemorrhage and rupture mycotic aneurysm) were reported. The 3-month and 12-month survival rates after diagnosed IA were 73.7% and 56.7%, respectively. The major cause of death was new episode of sepsis found in 11 cases (52%).*

Conclusion: *The 1-year survival rate was poor; however, cause of death is related to complications of the immunocompromised state not from IA.*

Keywords: *Invasive aspergillosis, Antifungal therapy, Treatment outcome*

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Invasive aspergillosis (IA) is a severe and progressive infection that occurs in immunocompromised patients such as patients with neutropenia, bone marrow or solid organ transplants, AIDS or chronic granulomatous disease[1]. The frequency of invasive aspergillosis reflects disease states and treatments that result in prolonged neutropenia and immunosuppression. Invasive aspergillosis is a major cause of morbidity and mortality in immunocompromised patients. The mortality rates are between 23 and 58%[2-4]. Effective management strategies of invasive aspergillosis are optimizing prevention and initiating treatment promptly.

Invasive pulmonary aspergillosis is the most common form of invasive aspergillosis. Clinical manifestations typically present with fever, cough, hemoptysis, dyspnea, or pleuritic chest pain[1,5]. However, absence of symptoms can be found in some patients. Radiological findings are variable with nodules, cavitary lesions, or alveolar infiltration[6,7]. In recent years, there are more sensitive diagnostic tools

Correspondence to:
Puthanakit T, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.
Phone & Fax: +66-2-2564930
E-mail: thanyawee.p@hivnat.org

such as serum galactomannan and computer tomography (CT scan); consequently, they increase the number of patients diagnosed[1,2,8,9]. Common CT scan findings in invasive pulmonary aspergillosis are consolidation, nodules, cavity, air crescents, and halo signs, of which the last two findings are more common in older children[2]. Galactomannan is a polysaccharide cell-wall component that is released into the surrounding environment by growing *Aspergillus* spp[10]. The sensitivity and specificity have been reported in a range of 57 to 100% and 66 to 100%, respectively[2,8,11]. Currently, three antifungal drug classes are effective against invasive aspergillosis. They include amphotericin B, new azole drugs such as voriconazole, and echinocandins such as caspofungin[1,2,12].

There is limited data regarding invasive aspergillosis in pediatric population, especially in an era with new diagnostic tests and more effective antifungal treatments. The objective of this study is to review clinical features, diagnosis, treatment, and survival outcomes of invasive aspergillosis in pediatric patients in a tertiary-care hospital setting in Thailand.

Material and Method

The study was a retrospective chart review at King Chulalongkorn Memorial Hospital, Bangkok, Thailand between April 2012 and October 2013. The study was approved by the Institutional Review Board, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand (IRB No. 069/55).

In King Chulalongkorn Memorial Hospital, due to limitation in cost of treatment in a developing country setting, the conventional amphotericin B deoxycholate was used as a first-line antifungal agent. Voriconazole was first used at the hospital in January 2009.

The inclusion criteria were patients younger than18 years who were diagnosed with IA between January 2006 and December 2012. Cases were identified using the hospital medical database using ICD-10 code B44, Aspergillosis. Information collected included demographic data, underlying diseases, duration of neutropenia, clinical manifestations, diagnostic procedures (radiologic findings, serum galactomannan assay, and pathology), treatment, and outcome.

Clinical definitions

Cases were categorized as proven, probable or possible IA based on the definition of the European Organization for Research and Treatment of Cancer and the Mycoses Study Group (EORTC/MSG)[13]. The criteria included host factor, clinical criteria, and microbiological criteria. Proven IA required histopathologic or microbiologic documentation of *Aspergillus* spp. from a sterile site obtained by biopsy, autopsy or in culture samples. Probable IA was defined as at least one host factor criterion with clinical and microbiological criterion. Cases that met the criteria for a host factor and a clinical criterion but had an absence of microbiological were considered as possible IA. Host factors were patients who had at least one of the following conditions; recent history of neutropenia (absolute neutrophil count <500/mm^3), recipient of an allogeneic stem cell transplant, received corticosteroids or other T-cell suppressants as well as patients with primary immunodeficiencies. Microbiological criteria included direct tests (cytology, direct microscopy, or culture) and indirect tests (detection of antigen or cell-wall constituents).

Treatment outcome evaluation[14]

Treatment outcome evaluation was categorized in five categories. (1) Complete response, defined by resolution of the clinical picture and 90-100% improvement in radiological findings. (2) Partial response, defined by clinical improvement and 50 to 89% improvement in radiological findings. (3) Stable, defined by clinical improvement or stable and <50% improvement in radiological findings. (4) Worsened, progression of fungal infection and no change or worsening in radiological findings. (5) Undetermined. The outcomes were summarized twice. The first time was within 12 weeks after treatment and the second time was at 1-year after diagnosis.

Death attributed to IA was defined by positive results of fungal culture or histopathological examination at autopsy or negative results of other fungi, bacterial culture and virus detection or undefined other causes of death.

Laboratory tests for IA

At King Chulalongkorn Memorial Hospital, a serum galactomannan assay was available in January 2005 using Aspergillus Enzyme Immuno Assay (EIA, the Platellia Aspergillus Ag, Bio-Rad, US). It is an immunoenzymatic sandwich microplate assay for the detection of the *Aspergillus* galactomannan antigen in serum and bronchoalveolar lavage (BAL) samples. Positive results were defined by a cut-off index of $\geq$0.5.

A chest computed tomography was performed in patients with suspected invasive aspergillosis. All scans were reviewed unblinded by a pediatric

radiologist (PT) but were done so in a systematical fashion with a semistructure evaluation form.

Statistical analysis

Continuous variables were shown as mean (standard deviation) or median (range). Categorical data were constructed using frequencies and percentages. The Kaplan-Meier analysis was applied to estimate survival times**.** Statistical analysis was performed by SPSS version 18.0.

Results

Between January 2006 and December 2012, there were 40 cases of IA. Median age of patients was 10 years (range, 42 days to 17 years), 21 patients (53%) were female. Underlying diseases were hematologic malignancy (n = 24, 60%), systemic lupus erythematosus (SLE) (n = 4, 10%), chronic granulomatous disease (n = 3, 7.5%), post bone marrow transplantation (n = 3, 7.5%), and others (n = 6, 15%). Among 24 patients with hematologic malignancy, there were 11 (46%) acute lymphoblastic leukemia (ALL), nine (38%) acute non-lymphoblastic leukemia (ANLL), three (12%) solid tumor, and one (4%) chronic myeloid leukemia (CML). Among 24 children with hematologic malignancy, invasive aspergillosis was diagnosed during induction/reintensification chemotherapy (54%), consolidation phase (29%) and maintenance phase (17%), respectively. Immunosuppressive risk factors were neutropenia in 26 patients (65%), receiving corticosteroid therapy in seven patients (18%), receiving immunosuppressive drugs in four patients (10%), and inherited immunodeficiency in three patients (7%). Of the three patients who underwent bone marrow transplantation, none had graft-versus-host disease (GVHD). Median duration of neutropenia before diagnosis of invasive aspergillosis was 21 days (range, 4 to 58 days) and 18 out of 26 patients who had neutropenia (69%) had prolonged neutropenia for more than 10 days. The median length of stay on admission was 50 days (range, 7-226 days) for those who were diagnosed with IA. Median follow-up time was 135 days (range, 11-456 days).

There were eight patients (20%) with proven IA, 28 patients (70%) with probable IA, and four patients (10%) with possible IA. There were 35 patients with single site of aspergillus infection, five of them with disseminated (two sites in four patients and three sites in one patient). The most common site of infection was the pulmonary system (37 sites, 80.5%), followed by the sinus (three sites, 6.5%), skin (two sites, 4.3%), gastrointestinal tract (two sites, 4.3%), eyes (one site, 2.2%), and brain (one site, 2.2%).

Clinical presentations were non-specific, fever unresponsive to antibiotics, cough, and dyspnea. Out of the 40 patients with IA, 34 patients (85%) had fever at the time of diagnosis. Twenty-five patients (63%) had at least one symptom such as cough, dyspnea that was suggestive of pulmonary disease. Other symptoms observed were pleuritic chest pain (three patients) and hemoptysis (two patients).

Radiologic findings of invasive pulmonary aspergillosis (Table 1 and 2)

Thirty-seven chest x-ray findings were seen in 37 patients with pulmonary disease. The most common finding was non-specific infiltration 41% (n = 15). A computed tomography scan of the chest was performed in 28 patients (76%) with pulmonary disease. The most common finding was nodules 71% (n = 20) whereas findings of specific signs of IA were less common, air crescent sign (11%), and halo sign (7%) (Fig. 1).

Table 1. Radiologic findings of 37 patients with invasive pulmonary aspergillosis

Chest x-ray findings	Number (%)
Nonspecific infiltration	15 (41)
Nodule	6 (16)
Mass like	6 (16)
Consolidation	5 (14)
Air crescent sign	1 (2.7)
Pleural effusion	1 (2.7)
Nodule with pleural effusion	1 (2.7)
Mass like with pleural effusion	1 (2.7)
Consolidation with pleural effusion	1 (2.7)

Table 2. Pulmonary computed tomography chest findings in 28 patients with pulmonary disease, n (%)

Pulmonary CT chest findings	Number (%)
Nodule	20 (71)
Nonspecific infiltration	12 (43)
Cavitation	9 (32)
Mass like	8 (28)
Pleural effusion	4 (14)
Air crescent sign	3 (11)
Halo sign	2 (7)

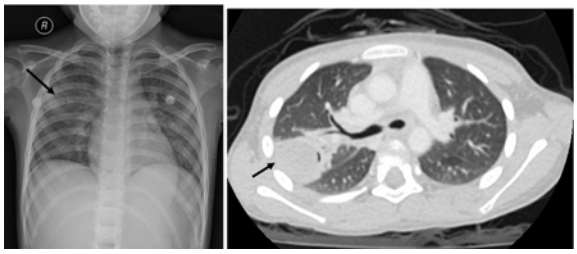

Fig. 1 Radiological findings of a 5-year-old girl with invasive pulmonary aspergillosis. (A) Chest x-ray demonstrated a round-shaped density in right upper lung with an air crescent (arrow), (B) CT chest demonstrated infiltration at posterior segment of right upper lung with fluid and air bubble inside, with an air crescent sign (arrow).

Microbiologic findings of IA (Table 3)

Eight patients met the criteria of definite invasive aspergillosis. In these definite cases, five patients were diagnosed from culture; the other three patients were diagnosed from pathological reports. The culture identified one isolate of *Aspergillus fumigates* and four isolates of *A. flavus.* Cultures were collected from two of three patients who had sinusitis, one of two patients who had skin infection, and two of 37 patients who had invasive pulmonary aspergillosis. The specimens included one pus swab from a wound at the neck, two nasal septum biopsies, and two lung biopsy tissues.

Histopathologic examinations were performed in nine biopsy specimens (1 bronchoalveolar lavage, 2 nasal septum biopsies, 2 skin biopsies, and 4 lung tissue), findings are shown in Table 3. In these nine biopsy specimens, one case had positive culture for *A. fumigates* from the lung tissue biopsy, four cases had positive culture for *A. flavus*, and the other four cases had a negative culture report.

Serum galactomannan assay was tested in 33 from 40 of patients (83%); BAL galactomannan was tested in four patients. Twenty-nine children had a galactomannan index of >0.5 (40% in proven, 96% in probable, 0% in possible). The median galactomannan level was 1.34 (range, 0.5-5.6).

Treatment

Out of 40 patients who initiated antifungal treatment, 23 children (58%) received voriconazole for a median of 88 days (range 14-318 days), 12 children (30%) received Amphotericin B for median duration of 26 days (range 5-106 days). Other treatments were liposomal amphotericin B in three patients, one patient received caspofungin, and one patient received itraconazole. One patient with sinusitis had debridement under endoscopy.

Among 37 invasive pulmonary aspergillosis cases, six patients (16%) could not be evaluated because they lost to follow-up or discharged against advice. Thirty-one children (84%) were evaluated for outcome at 12 weeks. Fourteen children had follow-up chest CT scans available within three months after initiation of antifungal treatment. Thirty-seven children had follow-up by chest x-ray. Primary outcomes within three months after treatment were evaluated; four patients (11%) and 11 patients (31%) had complete and partial response to the treatment, respectively. One patient had stable disease and 15 patients had worsened outcomes. Thus, successful treatment was found in 15 of 31 patients (48%).

Two patients with chronic granulomatous disease had relapse during antifungal prophylaxis at 307 and 407 days after treatment. One patient with AML had relapse after treatment at 176 days, which was 24 days after termination of antifungal prophylaxis (Table 4).

Survival outcome

As of October 2013, 21 patients had died. Only two patients had IA related disease. One patient died with pulmonary hemorrhage at day 13 after diagnosis. The other, had a ruptured mycotic aneurysm and died at 20 days after diagnosis. Major causes of death was sepsis in 11 patients, others were six bacterial pneumonia, one relapse leukemia, and one heart failure. The 3-month and 12-month survival rate was 73.7% and 56.7%, respectively. Median survival from all causes of death was 406 days (95% confidence interval [CI], 216-596). The 3-month survival rate was 67.3% and 78% in the voriconazole and non-voriconazole groups, respectively ($p = 0.007$). The 12-month survival rate was 67.3% and 50.5% in the voriconazole and non-voriconazole groups, respectively ($p = 0.74$).

Discussion

Clinical characteristics and presentations among Thai patients were comparable to those in Western countries[2,4,5,15]. A challenge in diagnosing IA is due to non-specific signs and symptoms. Despite advances in diagnostic tools and treatment, there is still a poor outcome with a one-year survival rate at 56.7%.

In this study, the median age at diagnosis

Table 3. Microbiologic and histopathologic findings in 11 patients with proven and probable invasive aspergillosis

Sex, age	Underlying disease	Site of infection (Specimen)	Culture	Pathological report	Serum GM	Outcome at 12 weeks	Outcome at 1 year
Proven invasive aspergillosis							
F, 7 year	ALL	Pulmonary (lung biopsy)	*A. flavus*	Acute angled dichotomous branching fungal hyphae, no definite tissue invasion seen	Not done	Worsen	Dead
M, 8 year	ALL	Sinus (middle turbinate)	*A. flavus*	Acute angled dichotomous branching fungal hyphae, invasive infection	Not done	Worsen	Alive
F, 7 year	ALL	Skin (skin biopsy)	*A. flavus*	Negative for fungus	0.2	Complete	Alive
M, 16 year	ALL	Sinus (nasal septum)	*A. flavus*	Acute angled dichotomous branching fungal hyphae, invasive infection	0.2	Worsen	Dead
F, 2 month	CGD	Pulmonary (lung biopsy)	*A. fumigatus*	Negative for fungus	3.4	Partial	Alive
M, 1 year	CGD	Pulmonary (lung biopsy)	No growth	Degenerated fungal hyphae, semi-invasive	1.5	Worsen	Alive
M, 8 year	HIV	Pulmonary (lung biopsy)	No growth	Degenerated fungal hyphae, no definite tissue invasion	0.3	Undetermined	Alive
F, 1 year	AML	Skin (skin biopsy)	No growth	Acute angled dichotomous branching fungal hyphae, invasive infection (Fig. 2)	Not done	Complete	Alive
Probable invasive aspergillosis							
M, 13 year	SLE	Pulmonary (tracheal secretion)	*A. fumigatus*	Not done	1.3	Worsen	Dead
F, 3 year	ALL	Pulmonary (sputum)	*A. fumigatus*	Not done	0.52	Partial	Alive
M, 17 year	Lymphoma	Pulmonary (bronchoalveolar lavage)	No growth	Acute angled dichotomous branching fungal hyphae	0.9	Worsen	Dead

ALL = acute lymphoblastic leukemia; AML = acute myeloid leukemia; CGD = chronic granulomatous diseases; F = female; GM = galactomannan; M = male; SLE = systemic lupus erythomatosus

was 10 years compared with that in previous reports of 10 to 10.1 years (17 days to 18 years)[4,5]. Similar to previously published studies[2,5,14,16], the most common site of IA is the respiratory tract. In this study, common clinical presentations were fever and dyspnea. Most underlying diseases included hematologic malignancies corresponding with previous data in Thai adult[16]. In the group of patients with hematological malignancies, most of the patients in the induction phase of chemotherapy (54%) compared to the study of Zdenek et al at 39.8%[15]. The most common risk factor was neutropenia (65%) and corticosteroid therapy (18%), compared with Thai adult[16] was 49% and 20%, respectively. The median duration of neutropenia before diagnosis was 21 days (4 to 58 days), which coincided with the study of Burgos et al that reported a median duration of neutropenia at 18.9 days[5].

In adults, the halo and the crescent signs on CT are suggestive of IA. The incidence of halo signs in IA is high during its early stages and tends to decrease over time[17]. In contrast with adults, the halo and crescent signs on CT scans in pediatric IA are less

Table 4. Clinical characteristics in 3 patients with relapse invasive aspergillosis

Sex, age underlying disease	Site of infection/ diagnosis	Treatment	Outcome at 12 weeks	Date relapse	Condition at relapse time	Final outcome (days after Rx)
M, 1 month CGD	Lung/ probable	Induction with - amphotericin B 33 days - liposomal amphotericin B 7 days - voriconazole 14 days Maintenance with voriconazole	Partial response	307	Voriconazole prophylaxis	Death (407)
M, 1 year CGD	Lung/ proven	Induction with - amphotericin B 105 days Maintenance with itraconazole	Worsen	407	Itraconazole prophylaxis	Death (525)
M, 1 year AML	Lung/ probable	Induction with - amphotericin B 7 days - caspofungin 4 days - voriconazole 21 days Maintenance with voriconazole	Partial response	176	24 days after stop medication	Death (364)

CGD = chronic granulomatous diseases; M = male; Rx = treatment

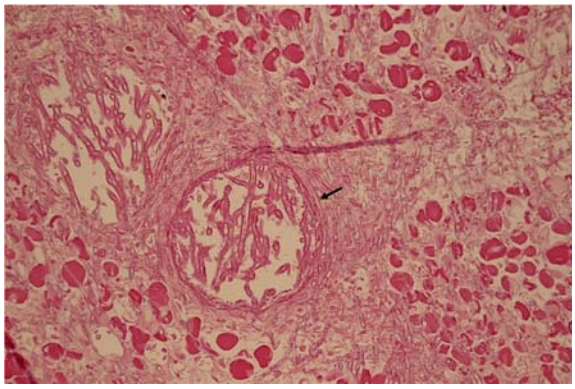

Fig. 2 Pathological finding of a 1-year-old girl with invasive aspergillosis. Skin biopsy from back mass demonstrated fungal hyphae invading blood vessels and adjacent necrotic skeletal muscular tissue. The organisms show dichotomous branching septated hyphae, morphologically characteristic for *Aspergillus* spp. Arrow (H&E x100).

common due to differences in host immune response[5,6,17]. In another study[5], the most common CT findings were nodules and non-specific infiltration. This is the same as our study, which nodules and non-specific infiltrations were found in 71% and 43% of patients, respectively. While halo and crescent signs were found in 11% and 7%, respectively. However, in our study, the air crescent sign was found in 7% of patients, which was higher when compared to other studies at 1.6%[4,10]. Due to the air crescent sign being a late sign of invasive aspergillosis[1,17], this difference may indicate that our patient had been delayed for diagnosis.

Most studies have shown that *A. fumigatus* was the most common strain in IA[2,5]. In Thailand, a study in adults also found that the most common strain was *Aspergillus fumigatus* (67%), followed by *Aspergillus flavus* (24%)[14]. In our study, culture results demonstrated three cases of *Aspergillus fumigatus* and four cases of *Aspergillus flavus*. This difference may be due to the relative distribution of *Aspergillus spp*. In developing countries, *A. flavus* has been isolated comparatively at a higher frequency from sino-orbital aspergillosis or eye infections. Higher environmental contamination due to *A. flavus* may lead to increased frequency of *A. flavus* infections in developing countries[18]. Regarding the galactomannan assay, our study found that it was positive in 40% of proven cases. In a previous study in Thailand, a series of adult neutropenic patients with hematological disorders showed that serum galactomannan antigen testing had a sensitivity of 94.1% with cutoff index of >0.75[11]. The difference of sensitivity may be due to the difference of age group and underlying disease between the two studies.

In our study, mainstay of therapy was voriconazole (58%), followed by amphotericin B (30%), which contrasted with past studies that mainly used amphotericin B in 57.3 to 64.6%, followed by

voriconazole 39.6 to 52.7%[5,14]. The difference shown may be explained by the fact that those studies were performed between 2000 and 2009, in which voriconazole was more difficult to access than at present. Surgical intervention in this study was only one out of 40 patients (2.5%), as the only patient with sinusitis underwent endoscopic debridement. The low rate of surgery in our study was unlike one study in Taiwan where the rate of surgery was 21.9%[19].

At 12 weeks, outcomes in complete or partial response were 40.5% of patients compared to 38% in a previous study in adult IA[20]. This figure is also less than the study done between 2005 and 2009 that reported 53.3% of successfully treated patients[15].

In a published study by Burgos et al[5], the common cause of death was IA-related (69.9%). In contrast, in this study, the major cause of death was sepsis (52%) and only 9.5% died from IA. This finding may be explained by a limitation in data collection and because we did not have autopsies of all deceased patients.

The survival rate at three months in the voriconazole group was less than those who used other medications, 67.3% and 78%, respectively (p-value = 0.007), which is different from past studies which found that treatment with voriconazole yielded a better outcome of 52.8% compared to 31.6% in the amphotericin B group[2,14]. The survival rate at 12 months in the voriconazole group was 67.3% compared to 50.5% in non-voriconazole group but without statistical significance (p-value = 0.739). This study was limited by small number of patients and it was not a randomized controlled trial. To add, the most common cause of death was not caused by invasive aspergillosis, so it cannot directly compare the efficacy of antifungal drugs. Another limitation of this study would be lack of voriconazole level data that affects the outcome of treatments. A study in Thai adults showed that the median of plasma trough voriconazole concentration was 5.35 mg/L (range 0-24)[21].

As shown in a large, multicenter retrospective study in pediatric IA, the overall survival rate was 47.5%[5]. This is similar to the study of Zdenek et al[15] that reported a one-year survival rate of 43%. However, in contrast with our study, the overall survival rate was 56.7%. This better survival outcome may be explained by changes in diagnosis and treatment of aspergillosis during this period in our own treatment settings that included GM antigen detection in 2005 and the availability of voriconazole in 2009.

Two noteworthy strengths of this study are first, this is the first review of childhood IA in Thailand. Second, this study review was conducted in an advanced era with improved diagnostic tools and newer antifungal agents. Some other limitations include missing data and a single-center sampling carried out at a medical school which may not reflect accurate and adequate findings of the overall pediatric IA situation in Thailand.

Conclusion

IA is a significant infection commonly found in immunocompromised hosts. Recent advances in diagnostic tools and newer antifungal drugs improve patient survival outcomes; however, high mortality rates remain. The 1-year survival rate is poor; however, the cause of death is related to complication of an immunocompromised state, not from IA. A high index of suspicion of IA in predisposed patients and prompt administration of effective antifungal agents are needed.

What is already known on this topic?

Invasive aspergillosis causes morbidity and mortality in immunocompromised hosts, requiring prompt diagnosis and proper treatment.

What this study adds?

The present study described the clinical characteristics of invasive aspergillosis in pediatric patients in Thailand, which is mainly compared with other published data from different countries. This study review is carried out in an era of advanced and improved diagnostic tools along with newer antifungal agents for treatment. However, a poor survival outcome remains.

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Potential conflicts of interest

None.

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ลักษณะทางคลินิกและผลการรักษาโรค Invasive aspergillosis ในผู้ป่วยเด็กโรงพยาบาลตติยภูมิในประเทศไทย

สุวพร อนุกูลเรืองกิตติ์, ปานฤทัย ตรีนวรัตน์, ปุญชวิษฐ์ จันทรานุวัฒน์, สุชาดา ศรีทิพยวรรณ, ชิษณุ พันธุ์เจริญ, ธันยวีร์ ภูธนกิจ

วัตถุประสงค์: ศึกษาลักษณะทางคลินิกและการรักษาโรค Invasive aspergillosis (IA) ในผู้ป่วยเด็กที่เข้ารับการรักษาในโรงพยาบาลจุฬาลงกรณ์

วัสดุและวิธีการ: ศึกษาย้อนหลังเชิงพรรณนาในผู้ป่วยอายุน้อยกว่า 18 ปีที่เข้ารับการรักษาในโรงพยาบาลจุฬาลงกรณ์ตั้งแต่เดือนมกราคม พ.ศ. 2549 ถึงธันวาคม พ.ศ. 2554 ที่ได้รับการวินิจฉัยว่าติดเชื้อ aspergillosis ตามเกณฑ์ EORTC/MSG ปี 2551 (Definite, probable และ possible invasive aspergillosis)

ผลการศึกษา: ในระยะเวลาที่ทำการศึกษามีผู้ป่วยเด็กที่ได้รับการวินิจฉัยเป็น invasive aspergillosis จำนวน 40 ราย แบ่งตามระดับการวินิจฉัยออกเป็น proven IA 8 ราย (ร้อยละ 20), probable IA 28 ราย (ร้อยละ 70) และ possible IA 4 ราย (ร้อยละ 10) ค่ามัธยฐานของอายุเมื่อได้รับการวินิจฉัยโรคเท่ากับ 10 ปี (42 วัน-17 ปี) โรคประจำตัวที่พบมากที่สุด คือ มะเร็งระบบโลหิตวิทยาร้อยละ 60 ตำแหน่งที่มีการติดเชื้อมากที่สุด คือ ระบบทางเดินหายใจร้อยละ 80 ปัจจัยเสี่ยงที่พบบ่อยที่สุด คือ ภาวะเม็ดเลือดขาวต่ำร้อยละ 65 ค่ามัธยฐานของระยะเวลาที่เม็ดเลือดขาวต่ำก่อนการวินิจฉัยเท่ากับ 21 วัน (4-58 วัน) ภาพรังสีปอดเอกซเรย์คอมพิวเตอร์ที่พบมากที่สุด ได้แก่ nodule ร้อยละ 71 ในขณะที่พบลักษณะเฉพาะของ air crescent sign และ halo sign ในผู้ป่วยร้อยละ 11 และร้อยละ 7 ตามลำดับ การตรวจระดับซีรัม galactomannan ให้ผลบวกในผู้ป่วยร้อยละ 78 โดยค่ามัธยฐานเท่ากับ 1.34 (0.5-5.6) มีผู้ป่วยเพียง 7 ราย (ร้อยละ 17) ที่วินิจฉัยโดยผลการตรวจทางจุลชีววิทยาโดยพบเป็น Aspergillus flavus 4 ราย และ Aspergillus fumigates 3 ราย ผู้ป่วยที่ได้รับการรักษาด้วยยา voriconazole คิดเป็นร้อยละ 58 สาเหตุหลักของการเสียชีวิต คือ ภาวะติดเชื้อในกระแสเลือดพบจำนวน 11 ราย (ร้อยละ 52) ผู้ป่วยที่เสียชีวิตจากผลแทรกซ้อนของ aspergillosis มีจำนวน 2 ราย (pulmonary hemorrhage และ rupture mycotic aneurysm) อัตราการรอดชีวิตที่ 3 เดือน และ 12 เดือน เท่ากับร้อยละ 73.7 และ ร้อยละ 56.7 ตามลำดับ

สรุป: Invasive aspergillosis มีอัตราการรอดชีวิตที่ 1 ปี ต่ำ โดยสาเหตุการเสียชีวิตส่วนใหญ่ไม่ได้มาจากโรค invasive aspergillosis โดยตรง แต่เสียชีวิตจากภาวะแทรกซ้อนของโรคประจำตัว หรือภาวะที่มีภูมิคุ้มกันต่ำ