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TRATAMIENTO EXITOSO DE UNA INFECCION ZIGOMICOTICA CUTANEA PRIMARIA DEBIDA A ABSIDIA CORYMBIFERA EN UN NEONATO PREMATURO REPORTE DE CASO Y REVISION DE LA LITERATURA

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Successful Treatment of a Primary Cutaneous Zygomycosis Infection due to *Absidia corymbifera* in a Premature Newborn.

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Abstract

Mucormycosis (Zygomycosis) in most cases presents itself among individuals with predisposing factors such as prematurity, use of broad-spectrum antibiotics, metabolic acidosis, or advanced stages of immunosupression. There have been reports of sporadic cases of cutaneous mucormycosis related to predisposing skin lesions and contact with contaminated material such as adhesive bandages and tongue depressors placed close to intravenous catheter insertion sites. We report successful treatment of a case of *Absidia corymbifera* infection with the combination of amphotericin B and surgical debridement of the affected area.

Key words: Zygomycosis, *Absidia corymbifera*, newborns

Abbreviated tittle: Cutaneous *Absidia* Zygomycosis

Introduction

Mucormycosis (Zygomycosis) is a relatively uncommon infection caused by fungi of the Order Mucorales and the Family Mucoraceae, wich in most cases presents itself among individuals with predisposing factors such as prematurity, use of broad-spectrum antibiotics, metabolic acidosis, or advanced stages of immunosupression[1]. There have been reports of sporadic cases of cutaneous mucormycosis related to predisposing skin lesions and contact with contaminated material such as adhesive bandages and tongue depressors placed close to intravenous catheter insertion sites[2]

There have only been 19 reported cases of Zygomycosis in newborn since 1959, two of wich died from *Absidia corymbifera* infection[3]. We report a case of a premature newborn presenting with primary cutaneous infection due to *Absidia corymbifera* wich successfully responded to combined therapy with amphotericin B and surgical debridement

Herein we report a case of primary cutaneous Zygomycosis in a 36-week old newborn with various risk factors for this infection. The newborn had favorable results to the combination treatment with amphotericin B and surgical debridement. We also reviewed the cases of cutaneous Zygomycosis reported in the literature.

Case report

A 1600 g infant female was born in the 36th week of gestation at a second-level hospital with an abdominal wall defect. Apgar score at the time of birth is unknown. She was transferred to our institution 24-hours after her birth. While on route, the defect was covered with a sterile intravenous fluid-bag, wich allowed the child be moved without significant drops in temperature. She was given ampicillin and amikacina for possible sepsis. Upon admission, she was placed on assisted ventilation and insulin infusion drip was administered (0.02 unit/kg/h) due the presence of hyperglycemia. In addition, a diagnosis of persistent ductus arteriosus was stablished. On day 3 closure of the adminal wall defect and a gastrostomy tube placement was performed. On the same day parenteral nutrition was begun and the antibiotic regimen was switched to cefotaxime and amikacina.

On day 11 ceftazidime and gentamicina were administered due to the presence of a hypo-ventilated area in the left lower lung associated with increased oxygen requirements on the ventilator, thrombocytopenia and leucocytosis with bands on the CBC. On day 5 an abdominal mesh was placed in order to close the abdominal wall defect without any complications. On day 18 violaceous scabs were identified on the borders of the surgical wound but neither secretions nor necrotic areas were noted. By day 19 a serosanguineous secretion was found on the borders, but it was until day 21 that hemodynamic instability, generalized edema, and profound changes in ventilation that required increased pressure support and increased oxygen requirements appeared, signaing the presence of septic picture. At this point in time, cefepime and vancomycin were started along with gentamicina for suspected catheter associated sepsis. However, blood cultures remained negative and by day 27 abundant purulent secretions on the surgical wound were identified as the possible culprit. Fungi compatible with Zygomycetes were identified from theses secretions. In addition, a skin biopsy and a microscopic analysis of the mesh disclosed the presence of a 90º angle, non-septated hyphae. Two days later, cultures showed the presence of hiphae with collumellae and rudimentary hyaline rhizoids. At 45º C, cultures of *Absidia corymbifera* were isolated. The abdominal mesh was surgically removed upon the identification of the fungi with debridement of the necrotic areas. Amphotericin B was started at dose of 0.5 mg/kg/d that was scaled up to 1.5 mg/kg/d 48 hours after starting therapy, with significant improvement in hemodynamic and ventilatory parameters. The patient completed 4 weeks of treatment with amphotericin B with full recovery.

Discussion

We reviewed published cases of primary cutaneous Zygomycosis (table). Of the 20 cases reported among neonates (including the present case), 12 (63%) died.

The etiologic agents causing these deaths were: *Absidia corymbifera* in 2 cases, *Rhizopus microsporum* in 2 cases, *Rhizopus orizae* in 1 case, *Rhizopus arrhizus* in 2 cases, *Rhizopus sp* in 2 cases, and identification only went as far as *Mucorales* in 3 cases. Among those who died, 4/12 (33%) did not receive medical treatment because the diagnosis was made postmortem. In another 4 (33%), treatment was initiated promptly, and in 3 (25%) cases, treatment was delayed 4-7 days. There is no information regarding the time between diagnosis and treatment for one of the cases. All reported cases received broad spectrum antibiotics before onset of disease. We also found that 11/12 (92%) cases had an existing cutaneous condition that possibly facilitated the invasion of the fungi.

With respect to the cases that survived this infection, only 8 (including ours) have been described in the literature and are attributed to *Rhizopus microsporum, Rhizopus oryzae* and *Rhizopus sp* in two cases each and *Absidia corymbifera* in two cases.

We analized several risk factors among the 20 cases that might be associated with a higher mortality. There was no mention of gestational age at birth for one of the cases. Of the remaining 19 cases, 17 (89%) were born before the 37th week of gestation , and 2 (11%) were born on or after the 37th week (OR:4; 95% CI 0.79, 27.23; p= 0.11). there was no statistically significant difference for gender. Of the 12 cases who died, 8 (67%) were male and 6 (75%) of the 8 who survived were male. In terms of weight, 8 (67%) of the 12 who died weighed less than 1500 grams (OR: 2.33; 95% CI 0.55, 11.35; p=0.34). With respect to local cutaneous factors such as umbilical catheters and tongue depressors used as splint of IV devices we observed that 17 (85%) of the 20 cases had previously received broad spectrum antibiotics even though the risk of death was no able to be determined since those that died also received antibiotics before doing so.

Of the 12 patients who died, 5 (41%) were treated with debridement and amphotericin B compared with the 75% (6 of 8 patients) who survived. We believe that there was a favorable clinical outcome in patients who received the combined treatment at an early stage of the disease as exemplified by the case present in this report.

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Table. Cases of Cutaneous Zygomycosis Reported in the literature.

Reference	*Gender*	*Age (w)*	*BW (g)*	*Age Dx (d)*	*LF*	*Ab*	*Treatment*	*Outcome*	*Isolation*
Robertson et al[4]	M	24	430	5	AB	+	No	Death	*Rhizopus sp*
Amin et al[2]	M	>37	-	-	-	+	No	Death	*A. corymbifera*
Amin et al[2]	F	31	1500	11	UC	+	Deb, Ampho B	Death	A. corymbifera
Hughes et al[5]	F	26	670	17	AB; UC	-	Deb, ampho B	Survival	*Rhizopus sp*
Arisoy et al[6]	F	23	560	33	IVC	+	Deb, Ampho B	Death	*Rhizopus sp*
Linder et al[7]	M	26	915	21	AB	-	Ampho B	Survival*	R. oryzae
NG and Dear[8]	M	26	1100	21	AB, IVC	+	Deb, Ig, Ampho B	Survival	*Rhizopus sp*
Mitchell et al[9]	M	25	850	22	AB, TD	+	Ampho B, Itra	Death	*R. microsporum*
Mitchell et al[9]	F	25	525	6	CVC, TD	+	Ampho B., Itra	Survival	*R. microsporum*
Mitchell et al[9]	F	25	750	20	CVC, TD, AB	+	Ampho B, Itra, amputation	Survival	*R. microsporum*
Mitchell et al[9]	F	24	680	4	TD	+	Ampho B, Itra	Survival**	*R. microsporum*
White et al[10]	M	26	800	33	AB	+	Sulf Ag	Death	*R. oryzae*
Lewis et al[11]	M	-	430	24	NGT	+	Deb, Ampho B	Death	*Mucormycosis*
Hadley[12]	M	<37	1600	4	-	+	Deb	Death	*Mucormycosis*
Craig et al[13]	M	28	1245	16	ETT, AB	+	Deb, Ampho B	Death	*R .arrhizus*
du Plessis et al[14]	M	35	1100	8	AB	+	-	Death	*Mucormycosis*
Daniel Oh et al[15]	F	37	3650	7	AB	+	Deb, Ampho B	Death	*R .arrhizus*
Daniel Oh et al[15]	F	25	625	14	IVC	+	Deb, Ampho B	Survival	*R .arrhizus*
Buchta V et al[16]	F	24	740	17	-	+	Ampho B	Survival	*A. corymbifera*
Morales et al	F	36	1600	27	Sx	+	Deb, Ampho B	Survival	A. corymbifera

Modified from Daniel Oh et al[15]

M: male; **F:** female; **BW:** birth weight; **Age Dx:** age at diagnosis; **LF:** local factors; **Ab:** antibiotics; **AB:** adhesive bandages; **UC:** umbilical catheter; **Deb:** surgical debridement; **Ampho B:** amphotericin B; **Itra:** Itraconazole; **IVC:** intravenous catheters; **CVC:** central venous catheter; **Ig:** immunoglobulins; **TD:** tongue depressors; **Sulf Ag:** 1% sulfadiazine cream; **NGT:** nasogastric tube; **ETT:** endotracheal tube; **Sx:** containment mesh associated surgical wound.

* Death at 10 months of age due to respiratory failure

** Death at age 42 days due to cystic periventricular leukomalacia