Myiasis in a bancroftian filariasis endemic area

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Abstract

Background: Human myiasis in bancroftian filariasis endemic areas, although rarely reported in the literature, might pose an important aggravating factor for patients with swollen limbs with wounds, such as varicose ulcers and mossy lesions (lymphangiomatosis). Aims: To study the occurrence, clinical and parasitological characteristics of wound myiasis in individuals living in a filariasis endemic area in Brazil. Methods: The study was conducted at the Center for Teaching, Research and Tertiary Referral for Bancroftian Filariasis (NEPAF) in Recife, Brazil. Data were extracted retrospectively from the patients' charts, which included information on the type of treatment used as well as the psychosocial aspects of the disease. Results: Myiasis caused by *Cochliomyia hominivorax* was identified in 21 of 832 (2.5%) patients with swollen limbs. *Conclusions*: The authors hypothesise that in a filariasis endemic area in Brazil, patients with lymphangiomatosis and myiasis are at increased risk of secondary bacterial skin infections. Oral ivermectin was very effective against the larvae. The psychosocial burden for people with myiasis can be devastating, having consequences that go beyond the medical aspects of the infection. *Declaration of interest*: The authors have no conflicts of interest concerning the work reported in this paper.

Key words

Myiasis Cochliomyia hominivorax Ivermectin Lymphatic filariasis

yiasis is a condition seen in both animals and humans caused by parasitic fly larvae feeding on the host's tissues. Cutaneous myiasis is the most frequently encountered clinical form. It is further subclassified according to the nature of its clinical manifestation, such as furunculoid (subcutaneous infestation with tunnel formation), wound infestation, and subcutaneous with migratory swellings (White, 2003).

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Opportunistic invasion of wounds by fly larvae is seen sporadically in nursing homes (Chan et al, 2005) and hospitals (Lukin, 1989). A proportion of patients may have underlying problems, such as diabetes or peripheral vascular disease, debilitation or old age. Although Wuchereria bancrofti — the parasite that causes lymphatic filariasis (LF) does not directly or indirectly provoke any kind of skin wounds (Dreyer, personal communication), oedema/lymphoedema patients living in endemic areas may have wounds due to other causes such as varicose ulcers and mossy lesions (lymphangiomatosis). These wounds are ideal sites for parasitic larvae to lay their eggs, leaving these patients at risk of wound myiasis

In filariasis endemic countries, patients with lymphoedema/LF belong, for the most part, to socially neglected groups (Dreyer and Mattos, 2007). Some have inadequate health behaviours and they usually live in places with poor public health assistance. As pointed out by Sherman, cases of nosocomially-acquired myiasis are not necessarily associated with patient neglect (Sherman, 2000). While infestations are usually self-limited, in patients in endemic areas there is a risk of their being self-perpetuated for longer periods, as wounds infested by larvae of the screworm fly become extensive and attractive to gravid females. Although the fly larvae do not carry infectious agents themselves, there is, however, an increased risk for complications due to secondary bacterial infection.

Cochliomyia hominivorax (Figure 1) is the most prevalent species in tropical Latin America and comprises almost 60% of the 42 cases reported in a study by Donoso-Barros in Chile (Donoso-Barros, 1947), and almost half of the cases studied by Fraiha and Leão (Fraiha and Leão, 1986; Fraiha Neto and Leão, 1997). Maturer larvae are often more invasive, readily leaving necrotic tissue for viable tissue, which leads to significant local destruction. There are few reports of myiasis in oedema/lymphoedema patients living in areas endemic with bancroftian filariasis (Srinivasan and Pani, 1992; Radhakrishnan et al, 1994). This retrospective study was conducted to

learn about the occurrence and clinical characteristics of myiasis in patients with oedema/lymphoedema living in a filariasis endemic area and seen in a public hospital of Recife, Brazil.

Material and methods

The patients' data were retrospectively retrieved from the databases at NEPAF, a Center for Teaching, Research and Tertiary Referral for Bancroftian Filariasis (located at the Hospital das Clinicas at the Federal University of Pernambuco in Brazil). Patients were selected from 832 patients who presented with swollen legs if they:

- 1. Presented with wound myiasis at first consultation
- 2. Provided written informed consent to allow staff to use their medical information for scientific purposes, keeping their identity confidential.

Information extracted from their charts included:

- ▶ age
- ▶ gender
- treatment for myiasis
- underlying disease(s)
- past history of an acute bacterial episode of the skin, called dermatolymphangioadenitis (ADLA) in endemic areas (Dreyer et al, 1999b)
- past history of myiasis and treatment used
- >> past use of diethylcarbamazine
- >> per capita income
- notes of psychological and social repercussions of myiasis in the patient's life.

Larvae were sent alive immediately after collection from the patient's wound to the laboratory of the Department of Parasitology at the Rural Federal University of Pernambuco, Recife, Brazil. They were dropped into boiling water for one to two minutes to kill them, and then placed in a small bottle with 70% alcohol as a preservative. They were identified by their morphological characteristics. The larval species was confirmed later on by a medical entomologist (Professor Fraiha), using still pictures and videos of the live larvae. Descriptive statistics were used in the analysis of the data (Excel 2002).

Results

Twenty-one patients with lymphangiomatosis or venous ulcer and wound myiasis in the ipsilateral lower limbs (nine on the right and 12 on the left) were included in the study. Their average age was 54 years; the male: female ratio was 2:19 (Table 1). No infestations were nosocomially acquired and all patients resided in urban areas of the Greater Recife, Brazil. From personal communication, four patients were bedridden for one to two days. Two of them due to an earlier acute bacterial episode of the skin (Dreyer et al, 1999b) in the swollen contralateral limb and the remaining ones because of dengue fever. None of them had heard about the Hope Club. Hope Clubs are the result of an innovative approach launched in Recife, Brazil in 1993 (Dreyer and Addiss, 2000). Their aim is to equip lymphoedema patients with the skills, motivation and enthusiasm to sustain effective. lowcost, convenient self-care for their lymphoedema. Their mean monthly income per capita was US\$ 20.7, ranging from 7.2 to 44.9 (SD=8) with a range of 4.7 people per family (ranging from 2 to 12). For patients' information see Table 1.

Among the patients with a previous history of wound myiasis, five of them had been treated by extraction of larvae by forceps after the topical application of ether or ethanol. All reported excruciating pain immediately on application of ether or ethanol while extracting the larvae. Two other patients in rural areas had been treated by applying topical lvomec[®] (Merial) (an anti-parasite ivermectin preparation designed for livestock) in the wound. These patients reported that the choice of topical lvomec[®] was based on the experience of local farmers who had been successful when treating animals with the same disease. Contrary to the other patients, they did not report any increase in pain with the use of topical ivermectin. They also emphasised the rapid decrease/cessation of pain within a few hours, and that only 'dead larvae' were removed after the application of ivermectin.

Among those with a history of antifilarial treatment, only one man had had a positive thick smear for microfilaria approximately 10 years earlier, and had undergone hydrocele repair some years before having received antifilarial treatment. The other 18 patients (all women) received at least one full course of antifilarial treatment through the public health service because of the diagnosis of filarial lymphoedema made earlier and elsewhere (Dreyer and Mattos, 2007). Three patients presented with diabetes: one had type I and two had type II (one had progressed to require the use of insulin). Table 2 shows the range of comorbidities found among patients. All parasitic larvae were classified as Cochliomyia hominivorax (Figure 2). At consultation, all patients complained about severe pain in the affected limb but did not complain about bad odour. On physical examination, however, the odour was offensive in about half of the cases. All patients presented at least one interdigital lesion in the toes in the ipsilateral affected limb (Dreyer et al, 2006a) and were treated according to NEPAF'S protocol (Centers for Disease Control and Prevention et al, 2000; Dreyer et al, 2002). The diameter of the varicose ulcers varied from small (up to 2cm) to very large (affecting the entire leg circumference and extending 20cm or more).

Five patients (four females with mossy foot and one male with a varicose ulcer and alcoholism) presented with an acute ipsilateral episode, clinically defined as acute dermatolymphangioadenitis (ADLA) (Dreyer et al, 1999b). Among these five patients, three deserve further



Figure 1. Cochliomyia hominivorax, the New World screw-worm fly (from the private collection of Professor Fraiha).



Figure 2. A 57-year-old woman presenting with lymphoedema, mossy foot and myiasis in the right lower limb (A). The odour was offensive and she complained of paroxysmal local pain. She did not present any systemic signs, such as fever, but complained about malaise. A higher magnification (B) of the wound from (A) (circle) shows the tunnels opened by the larvae. (C) Live larvae, classified as Cochliomyia hominivorax, spontaneously came to the surface during physical examination.

comment. A 49-year-old woman, who sought medical care only nine days after having felt the larvae for the first time presented with diabetes type I and was hospitalised because of complicated ADLA. Her wound contained larvae of different stages. Another patient, a 45-year-old woman, was not aware about the presence of larvae on her foot and became distressed when she saw the worms. She became nauseated and vomited. One female patient with a varicose ulcer presented with mild bleeding, which started 12 hours earlier (three days after the patient had first seen the larvae). The varicose ulcer had not healed for three years but this was the first time she had noticed any bleeding. The patients with ADLA episodes had not received prompt medical care, waiting on average five days to be seen by a doctor or healthcare worker (ranging from three to nine days).

At NEPAF these patients were treated with parenteral antibiotics, according to NEPAF's protocol for complicated or potentially complicated ADLA episodes in oedema/ lymphoedema patients (Dreyer, personal communication). However, patients who did not present with ADLA were managed with oral antibiotics, irrespective of signs of wound bacterial infection (Table 1); manual removal of the larvae and irrigation of the site of the infestation with saline solution began around two hours after the start of antibiotic therapy in patients with varicous ulcers. In most patients, the larvae continued to be extracted for up to three days. The number of larvae removed on the first day ranged from dozens to hundreds. Tissue destruction was present in all patients to varying degrees; it was much more severe in patients with mossy lesions (Figure 2). In those patients it was difficult to manually extract most larvae; deeper manual manipulation in such lesions is contraindicated due to the increased risk of bacteraemia and sepsis (G. Dreyer, personal communication). Oral ivermectin 400µg/kg in a single dose was then administered to all patients with mossy lesions. There were no adverse reactions recorded. Four to five hours after the ivermectin intake, paroxysmal pain disappeared in two

patients who did not have ADLA. The role of ivermectin in decreasing pain in the remaining patients was difficult to assess, since other measures (e.g. cold compresses/analgesics) were also used. Twenty-four hours after treatment with ivermectin, dozens to hundreds of immobile/dead larvae were easily removed from the patients. Three dead larvae were recovered 48 hours after ivermectin in one patient. Daily skin care (Centers for Disease Control and Prevention et al, 2000) of the limbs (both affected and non-affected) was done up to the fifth day by NEPAF's staff and later by the patient themselves, or by a family member under the supervision of staff from NEPAF

— every two days for eight visits. The patients had a mean duration of follow up of 5.2 years (ranging from 3 to 7). None of them had recurrent myiasis during this period.

Detailed information about daily skin care through a video (which offers training for healthcare professionals and programme managers in bancroftian filariasis endemic areas where morbidity control is implemented) (Centers for Disease Control and Prevention et al, 2000) and the patient's manual (Dreyer et al, 1999a) were given to the patients. Information about myiasis and tips to avoid contact with flies were also provided. The proper use of bandages on the open wounds during the day was encouraged. All patients then became active participants in the Hope Club (Dreyer and Addiss, 2000; Dreyer et al, 2006b). Tetanus immunoprophylaxis was updated as necessary in 15 of the patients.

Information about psychosocial suffering was recorded in all patients' charts during the routine social interview at NEPAF. Strong shame was the main feeling expressed by the patients, followed by sadness. 'The feeling of being eaten alive, it is something that cannot be expressed in words. It is so very awful' said one of the patients with mossy foot. Among the patients included in this study, all recognised the need to seek help; however, 15 patients did not tell anybody in their family about the presence of maggots. They all kept the

Table I

Information of the 21 patients with oedema/lymphoedema and myiasis in Recife-Brazil

		Associated lesion	
	Total	Mossy foot (%)	Varicose ulcer (%)
Number of patients	21 (100)	06 (28.6)	15 (71,4)
Mean age in years (range)	53.9 (38–73)	50.0 (44–63)	55.4 (38–73)
Number (%) with prior history of myiasis	07/21 (33.3)	03 (14.3)	04 (19)
Number (%) with history of previous DEC treatment*	19/21 (90.5)	04 (19)	15 (71.4)
Mean number of days to seek help (range)**	4.8 (3–9)	4.6 (3–8)	5.0 (4–9)
Number (%) with current ADLA#	05/21 (23.8)	04 (19)	01 (4.8)
Number (%) with infected wound	10/21 (47.6)	04 (19)	06 (28.6)
Number (%) with other diseases##	17/21 (80.9)	06 (28.6)	(52.4)
Number treated with ivermectin	06/21 (28.6)	06	-

*Diethylcarbamazine full course at least one treatment

**After noticing the first larva (one patient with an acute episode was unaware of maggots)

#acute dermatolymphangioadenitis

##See Table 2

wound covered until they were seen by a doctor or healthcare professional and demonstrated a profound sense of shame when the wounds were uncovered in the washing room, many humbly asking for forgiveness with tears in their eyes before uncovering the wound. One male cried saying, 'I was raised under rule that crying was prohibited and I feel doubly ashamed for having shown this feminine characteristic for the first time in my life and for having worms in my body. I simply do not know what to say. I am so sorry'.

Discussion

To our knowledge, this study represents the largest case series of wound myiasis in patients with ipsilateral oedema/ lymphoedema living in an urban bancroftian filariasis endemic area, and the first report of myiasis in association

with ADLA episodes. A previous report from Sri Lanka, also an endemic area for bancroftian filariasis (World Health Organization [WHO], 2005), described 16 patients with cutaneous myiasis caused by Chrysomya bezziana (in 14 of them), but these patients either suffered from morbidities other than oedema/ lymphoedema of the lower limbs or their myiasis was not at the site of the swelling (Kumarasinghe et al, 2000).

The clinical picture of wound myiasis varies with the body part(s) affected, the number of larvae, and the fly species. Even a very small wound can lead to myiasis. All patients in the study were infected in the lower limbs by the same Diptera species — C. hominivorax — which can be invasive and very destructive. Patients with myiasis infection and varicose ulcers are seen

at a vascular surgery clinic located at a different department of the hospital from where the patients for this study were selected (G. Dreyer, personal communication). Unfortunately, information about the larvae species could not be found in 81 patients' medical records that were retrieved, nor was any report on human wound myiasis from Recife, Brazil found by an internet search. Thus, it was not possible to discover whether or not other species of Diptera cause myiasis in this part of Brazil. On the other hand, several species have been described in human cases in other states in Brazil, including C. hominivorax (Fraiha and Leão, 1986; Fraiha Neto and Leão, 1997; Ribeiro et al, 2001; Shinohara et al, 2004; Saraiva et al, 2006). The C. hominivorax larval forms invade human skin and subcutaneous tissues justifying their scientific Latin name which means 'human eater', coined in 1858 by the French entomologist Charles Coquerel after he received clinical specimens from physicians who associated this maggot with the death of hundreds of Devil's Island prisoners (Scruggs, 1975). The larvae are voracious and destroy integral tissues and may cause serious haemorrhage and be life threatening (Shinohara et al, 2004). Of interest, one patient in the current study presented with bleeding likely to be related to myiasis.

On the other hand, the larvae damaging the healthy tissues can increase the risk for secondary infection which, in turn, can make lymphatic dysfunction worsen in patients living in bancroftian filariasis endemic areas (Dreyer et al, 2000). Mossy lesions pose a challenge for the patients themselves and for healthcare professionals in lymphatic filariasis endemic areas because most of the time the lesion is moist as a result of leakage of lymph-sanguinolent fluid (Dreyer et al, 2002). This condition constitutes a true 'culture medium' not only for bacteria but for *C. hominivorax* as well. Female flies are attracted to human secretions, including blood or pus. Wound myiasis has also been implicated in Bahia (north-eastern Brazil) as a portal entry for Clostridium

Table 2

Comorbidities in patients presenting with swollen legs and ipsilateral myiasis

	Total	Mossy foot (%)	Varicose ulcer (%)		
Total of patients	21 (100)	6	15		
No comorbidity	04/21 (19)	0	4		
Hypothyroid	I.	I	0		
Gastric ulcer	I.	0	I		
Obesity*	2	I	I		
HBP	4	3	I		
HBP + obesity	2	0	2		
PTS	I	0	I		
PTS + alcoholism	I	0	I		
PTS + obesity	I	0	I		
PTS + HBP	I	0	I		
Diabetes + HBP	I	I	0		
Diabetes + HBP + obesity*	2	0	2		
*defined as body index >30; High blood pressure (HBP); post-thrombotic syndrome (PTS)					

tetani (Greco et al, 2001), and a recent publication pointed out myiasis as a risk factor for prion diseases in humans (Lupi, 2006).

The treatment of wound myiasis still rests on simple manual extraction of the larvae. However, there is growing evidence that topical and oral use of ivermectin is an indication for the treatment of human myiasis caused by *C. hominivorax* and other Diptera species (Jelinek et al, 1995; Cabrera et al, 1998; MacDonald et al, 1999; Victoria et al, 1999; Ribeiro et al, 2001; Shinohara et al, 2004; Osorio et al, 2006; Clyti et al, 2007). The current study corroborates these previous reports and gives additional evidence that ivermectin is a safe and efficient oral drug for myiasis in patients with mossy lesions. Ivermectin has been used (150µg/kg) in large-scale mass treatment of human onchocerciasis worldwide since 1987, and in the Global Program to Eliminate Lymphatic Filariasis (LF) since 1998 in African countries and in Yemen where onchocerciasis and LF are co-endemic (Alleman et al, 2006).

The use of single oral dose of ivermectin at 400µg/kg and higher doses such as 400µg/kg every 15 days for six months are safe, as demonstrated by Dreyer et al in 1995 and 1996 respectively, when evaluation of the efficacy of the drug on adult worms of *W. bancrofti* was studied (Dreyer et al, 1995, 1996). In Brazil, ivermectin is currently supplied by several pharmaceutical companies in a 6mg tablet and, besides LF and onchocerciasis, is also used worldwide for strongyloidiasis (Speare and Durrheim, 2004) and scabies (Santoro et al, 2003). Cutaneous larva migrans (Del Mar Saez-De-Ocariz et al, 2002) and pediculosis (Foucault et al, 2006) are also indications. In veterinary medicine, parenteral ivermectin is prescribed and it is produced commercially in Brazil by several pharmaceutical companies varying from 1-3.15% suspension in propylene glycol. The results of five trials conducted in Paraguay, Brazil and Colombia showed that ivermectin administered subcutaneously at a dose level of 200µg/kg body weight was highly effective against the three larval stages of Dermatobia hominis in cattle (Roncalli et al, 1998).

In the current study, the relief of pain a few hours after ivermectin intake in two patients was remarkable. The use of topical solution of 1% ivermectin (lvomec®) in cutaneous myiasis caused by *D. hominis* has been successfully reported in an HIV-infected subject and also the paroxysmal pains ceased within four to five hours (Clyti et al, 2007). A dramatic response in four patients with wound myiasis by C. hominivorax using topical 1% ivermectin in propylene glycol (400µg/kg as the total amount of medication) covered by a dressing for two hours was described by Victoria et al (1999). Over the next 15 minutes the patients reported a decrease in pain at the affected area. One hour after the initiation of the therapy, the majority of larvae had died and the remaining ones showed slow and erratic movements. No additional larvae were recovered and there were no adverse reactions.

The ideal dose of oral ivermectin for human myiasis still has to be determined. A single dose of 200µg/kg has been used successively in two patients (a 76- and a 79-year-old male from Colombia) with orbital myiasis caused by C. hominivorax (Osorio et al, 2006). However, reports do not always give the dose prescribed by weight. Shinohara et al describe a successful treatment of oral myiasis caused by C. hominivorax in a 20-yearold Brazilian woman using 6mg orally repeated 24 hours after (Shinohara et al, 2004). On the first day, an 80% decrease in the number of larvae was observed and the remaining larvae were immobile. After three days there were no larvae in the patient's mouth (Shinohara et al, 2004). Macdonald et al used 9, 12 and 18mg single doses successfully in three patients aged 16, 16 and 17 years respectively, all of whom had nasal myiasis in New Zealand caused by Oestrus ovis (MacDonald et al, 1999). Ribeiro et al treated six patients with cavitary myiasis (unclassified species) with a 12mg single dose. Three patients still had moribund larvae 24 hours after drug intake, two of them received an additional 6mg, and the third one was considered cured three days later without any additional treatment (Ribeiro et al, 2001).

The epidemiologic characteristics of human myiasis remain underreported. The literature consists predominantly of case reports and a few prospective studies have been published. One was from the Australian city of Brisbane (Lukin, 1989) during a 17month period where all infections occurred within preexisting wounds. Larvae from 12 out of 14 cases were identified and 10 (83%) of those were blowflies (Calliphoridae: P. cuprina). Six infections (43%) were nosocomial, occurring in hospital rooms. Diabetes and/or peripheral vascular disease predominated among the patients.

A comprehensive study was done by Sherman in 2000 (Sherman, 2000). He reported the occurrence of 42 cases in the USA of acquired urban myiasis (40 of them wound myiasis) from 20 participating centers with a host average of 60 years and a male: female ratio of 5.5:1. Frequent cofactors were homelessness, alcoholism, and peripheral vascular disease. The most common species (71%) was Phanicia sericata (family Calliphoridae). The most recent study reported the occurrence of human myiasis in urban areas of four municipalities in the State of Rio de Janeiro, Brazil. Seventy-one patients were seen and the disease was more prevalent among adults. From all the cases studied, wound myiasis accounted for 94.4%, male:female ratio was 3:2, 62% were of low socioeconomic level and 33.8% were unemployed. The species identified were Cochliomyia hominivorax (61% of the cases), Dermatobia hominis and Cochliomyia macellaria (Marquez et al, 2007).

In the present study, seven patients presented with morbid obesity. Although rarely described (Koss et al, 2004), the authors considered morbid obesity as a risk factor for myiasis.

The psychological and social burden for myiasis carriers can be devastating, with consequences that go beyond the medical aspects of the infection for the patients and their families. Actions must be directed initially to improving the well-being of the patients, including psychological support, minimising the social isolation and addressing the medical complications as a priority. The authors can testify that wound myiasis in patients with swollen legs in Recife, Brazil is associated with physical disability and significant mental anguish. For these patients, extreme shame and embarrassment were the major feelings, in addition to the unhappiness and sadness in the context of poverty and a deformed swollen leg, already reported in patients with elephantiasis in Recife, Brazil (Dreyer and Mattos, 2007).

Awareness among healthcare professionals of the importance of preserving and identifying the larvae can help determine the likely timing and circumstances that led to the infection, and also the virulence of the organism. Although myiasis is not a reportable disease, making it reportable may be cost-effective in LF endemic areas in which prevention and morbidity control (Seim et al, 1999) have been implemented. This will help to know whether or not myiasis is a rare condition in endemic areas, especially in patients with oedema/lymphoedema. For several reasons (e.g. low income per capita and the type of house) it is likely that patients cannot afford to have window screens to protect the indoors against insects in their homes, or other preventive measures such as fans or air conditioning that would help to keep flies away from their wounds

It was beyond the scope of this study to investigate the presence of animal myiasis in the areas from where the patients came. Unless the myiasis is threatening the important livestock of a given country/region, control of screwworm fly is likely to be a low priority for the government (Lindquist et al, 1992; Reichard et al, 1992).

Acknowledgements

We are grateful to NEPAF's healthcare personnel, including the medical students who went beyond their functions and played an important role in giving emotional support to the patients to help them cope with the infestation by larvae; to NGO Amaury Coutinho for the financial support and providing the infrastructure to assist the patients

Key points

- Fly larvae can damage healthy tissues and can increase the risk of secondary infection, which, in turn, can make lymphatic dysfunction worsen in patients living in bancroftian filariasis endemic areas.
- There is a growing body of evidence that topical and oral use of ivermectin could be used to treat people with myiasis caused by *C. hominivorax* and other Diptera species.
- Patients with myiasis expressed feelings of extreme shame and embarrassment.
- The psychological and social burden for people with myiasis can be devastating and have consequences that go beyond the medical aspects of the infection.
- Awareness among healthcare personnel of the importance of preserving and identifying the parasitic larvae can help determine the likely timing and circumstances that led to the infection, and also the virulence of the organism.

at NEPAF; to Wendilynn W McAfee for invaluable help with the literature retrieval; and to David Addiss and Anne Dreyer for the useful suggestions on the original manuscript.

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