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Brief report

## Ringworm by *Nannizzia nana*: Clinical case and literature review

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### ABSTRACT

**Introduction:** Human dermatophytoses are the most widespread infections caused by fungi. These are capable of invading the keratin-containing tissues of animals. *Nannizzia nana* (*N. nana*) can cause ringworm in pigs and rarely cause infections in humans.

**Methods:** We conducted a search using PUBMED for articles published from January 1, 1990 to March 31, 2022 to identify additional cases. The search terms used were “*Microsporium nanum*” and “*Nannizzia nana*”.

**Results:** After reviewing the literature, we identified a total of 16 cases of dermatophytosis due to *N. nana* since 1990. In most of the patients, the clinical diagnosis was tinea corporis and the most widely used antifungals were: terbinafine and griseofulvin.

**Conclusion:** *N. nana* is a dermatophyte species isolated infrequently in humans, but it represents a potential source of dermatophytosis in people who come into direct or indirect contact with animals and soil.

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### Tiña por *Nannizzia nana*: caso clínico y revisión bibliográfica

#### RESUMEN

**Introducción:** Las dermatofitosis humanas son el grupo más extendido de infecciones causadas por hongos. Estos son capaces de invadir los tejidos que contienen queratina de los animales. *Nannizzia nana* (*N. nana*) puede causar tiña en cerdos y que de manera excepcional puede producir infecciones en humanos.

**Métodos:** Realizamos una búsqueda en PubMed de artículos publicados desde el 1 de enero de 1990 hasta el 31 de marzo de 2022 para identificar casos adicionales. Los términos de búsqueda empleados fueron «*Microsporium nanum*» y «*Nannizzia nana*».

**Resultados:** Tras la revisión bibliográfica identificamos un total 16 casos de dermatofitosis por *N. nana* desde 1990. En la mayoría de los pacientes, el diagnóstico clínico fue tinea corporis y los antifúngicos más utilizados fueron: terbinafina y griseofulvina.

**Conclusión:** *N. nana* es una especie de dermatofito aislada infrecuentemente en humanos, pero que representa una fuente potencial de dermatofitosis en personas que entran en contacto directo o indirecto con animales y con el suelo.

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#### Palabras clave:

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### Introduction

Dermatophytes are keratinophilic fungi capable of invading keratin-containing tissues (skin, nails and hair) in animals and humans and causing infection.<sup>1</sup> *Nannizzia nana* (formerly *Microsporium nanum*) is a geophilic and zoophilic fungus that can cause ringworm in pigs and occasionally causes infections in humans.

Just over 40 cases have been described in humans worldwide, with *tinea corporis* being the most common form of presentation.<sup>1–3</sup> In Spain, the first case in humans was published in 2007.<sup>4</sup> In this article we present a case report and review all the cases published in humans in the last 30 years.

## Case report

This was a 48-year-old Spanish woman with no relevant medical history who attended the Dermatology clinic with a three-month history of a pruritic skin lesion on the flexure of the right arm, which had been treated topically with corticosteroids, antibiotics and ciclopirox, with no clinical improvement. She reported no trips abroad in the previous 12 months. Four years earlier, she had onychomycosis which was treated with oral itraconazole with clinical improvement. She did not live in a rural environment and nor did she have any direct contact with animals. However, she worked in a textile company handling virgin wool from sheep, wearing gloves as personal protective equipment.

The patient had a ring-like lesion of approximately 7 cm in diameter on physical examination cm in diameter with a scaly, erythematous border. Based on the above data, a clinical diagnosis was made of probable *tinea corporis*. Mycology culture was carried out by scraping scales from the active edge of the lesion which were then inoculated on Sabouraud glucose agar plates (bioMérieux SA 376, Chemin de l'Orme, 69,280 Marcy-l'Etoile, France) and Dermatophyte selective medium (Thermo Fisher Diagnostics S.L.U. via de los Poblados, No 17, Nave 3–13, 20833 Madrid, Spain) and incubated at 30°C. After one week of incubation, colonies with a velvety texture, beige-coloured on the surface, and red/brown on the reverse, grew in the culture media (Fig. 1). Microscopic examination of the colony with lactophenol cotton blue revealed short, thick-walled, pyriform macroconidia of one to three cells (mostly two), identified as *N. nana*. The identification was confirmed by culture and microscopy at the Mycology Unit of the Instituto de Salud Carlos III National Microbiology Centre in Majadahonda, Spain.

The patient was treated with topical terbinafine 10 mg/g every 12 h and topical methylprednisolone 1 mg/g every 24 h for one month. At the patient's follow-up one month after starting the treatment, there was complete remission of the lesion.

## Methods

We have reported a case and performed a PubMed search for articles published from 1 January 1990 to 31 March 2022 to identify additional cases. The search terms used were "*Microsporium nanum*" and "*Nannizzia nana*". Secondary sources cited in the articles found were also reviewed. We only considered publications in English, French, Portuguese and Spanish. In all the cases found, the following information was reviewed: country of origin, age; gender; type of infection; site of the infection; contact with animals; treatment; and cure.

## Results

After reviewing the literature, we identified 16 cases of dermatophytosis due to *N. nana* since 1990 (Table 1). These cases are distributed across nine countries: Guatemala, Mexico, Brazil, Poland, Spain, Morocco, Malawi, India and Thailand.<sup>1–10</sup> The median age of the patients was 35 (range: 0.9–75 years) with an equivalent proportion of males and females. Half of the cases had had contact with animals, pigs being the most common.

In most of the patients, the clinical diagnosis was *tinea corporis* (50%), followed by *tinea unguium* (18.7%) and *tinea pedis* (18.7%), and less often *tinea capitis* (12.5%).

The treatment used was specified in all but one of the patients. The most used antifungals were: terbinafine (8 cases) and griseofulvin (4 cases). Topical ketoconazole was added in four patients and topical prednisone in two. A different antifungal, such as itraconazole, was used in two patients. The mean duration of therapy was 34.5 days (range: 14–90 days). All the patients were cured.

## Discussion

We have reported on a new case of *tinea corporis* due to *N. nana* and reviewed the cases published over the last 30 years. This is a zoophilic and geophilic fungus which causes ringworm in pigs and other animals and, very occasionally, can cause infection in humans.<sup>1,3</sup> Since 1990, 15 infections related to this dermatophyte have been published in South America, Europe, Asia and Africa, indicating its wide geographic distribution and low incidence.<sup>1–10</sup>

In Spain, two cases have been reported in humans. The first, published in 2007, was in a pig farmer, and the second was an imported case after a trip to Thailand.<sup>2,4</sup> In Spain, a ringworm outbreak was reported on a pig farm that only affected animals.<sup>11</sup>

Infections by *N. nana* are associated with animals and mostly with exposure to pigs, so people in contact with pigs have a higher risk of contracting the infection.<sup>1,4,5</sup> Despite the country's large pig population, its low incidence in Spain is surprising. It may be because the cases are treated empirically, and the samples do not reach the microbiology laboratories due to their low virulence or diagnostic errors.<sup>3</sup>

Infections in humans by zoophilic dermatophytes occur directly through contact with colonised or infected animals or indirectly through materials contaminated with the fungus which have been in contact with the animals.<sup>6</sup> About half of the infections in this review affected people who had no contact with animals, highlighting the importance of the geophilic nature of this dermatophyte. *N. nana* has been isolated from the soil, where it can multiply as a saprophyte. Therefore, in patients who have had no contact with animals, a possible telluric or environmental origin should be investigated as the source of infection.<sup>3,5</sup>

Our patient had no contact with animals and lived in an urban area. Her only contact with animals was indirect, as she worked with wool in a textile factory, which may have been the source of her infection. Sheep are important in the transmission and persistence of some dermatophytes. In one study, *N. nana* was the third most common dermatophyte species isolated from sheep hair after *Trichophyton verrucosum* and *T. mentagrophytes*.<sup>12</sup> We, therefore, think that the most likely route of infection was through the wool that she handled as part of her job. However, it was impossible to analyse wool samples, so this source could not be proven microbiologically. We would also need to rule out a possible route of infection through the soil or the environment, but that could be clearer in our case too.

There is not a well-established treatment for infections by *N. nana*, and therapy is based on that used in other dermatomycoses caused by other species of the genus *Microsporium*.<sup>1,3</sup> There are few data on the sensitivity of *N. nana* to antifungals, but it has been documented to be sensitive *in vitro* to miconazole, clotrimazole, ketoconazole, itraconazole, voriconazole, terbinafine and griseofulvin.<sup>1,3,5,13,14</sup> In the studies analysed, the most used antifungals were terbinafine and griseofulvin. All the patients treated with these antifungals made good progress with a resolution of the lesions. Steroids are also often added to the treatment to reduce the inflammatory reaction that can appear in some cases.<sup>1</sup>

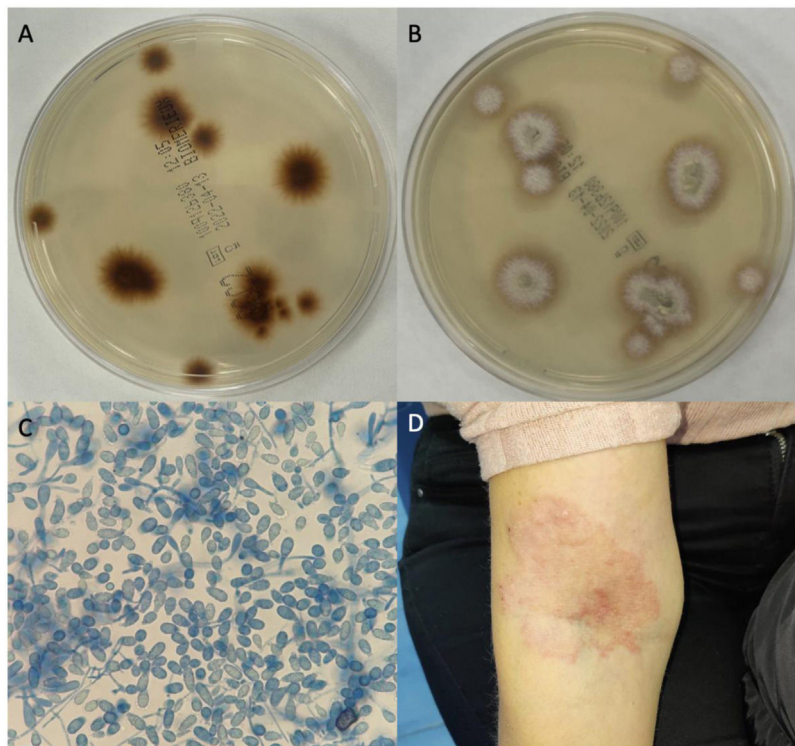
It is important to characterise the fungus at the species level to avoid inappropriate treatment and to determine its epidemiology.<sup>5</sup> In the articles we reviewed, the fungus was correctly identified by microscopic examination of the culture. In some studies, this

**Table 1**  
Sociodemographic and clinical characteristics, treatment and outcomes of infections by *N. nana*.

	Year	Country	Age	Gender	Contact with animals	Site	Treatment	Duration	Clinical course	Infection	Reference	Molecular identification
1	1997	India	16	M	Pigs	Back, leg and chest	Griseofulvin 750 mg PO	1 month	Cured	Ringworm	Ranganathan et al.	No
2	1995	Malawi	17	M	Pigs	Popliteal fossa	Benzoic acid and salicylic acid 5% <sup>a</sup>	ND	Cured	Ringworm	Ponnighaus et al.	No
3	1992	Brazil	9 months	ND	Pigs	Back	ND	ND	Cured	Ringworm	De Camargo et al.	No
4	2007	Spain	35	M	Pigs	Forearm	Terbinafine 250 mg PO	1 month	Cured	<i>Tinea corporis</i>	Lamilla Yerga et al.	No
5	2007	Morocco	50	F	No	Scalp	Griseofulvin 500 mg PO	6 weeks	Cured	<i>Tinea capitis</i>	Moutaj et al.	No
6	2020	Poland	28	M	No	Neck	Terbinafine 250 mg PO and ketoconazole 2%	20 days	Cured	<i>Tinea corporis</i>	Gnat et al.	Yes
7	2020	Poland	41	F	Cows and dogs	Feet	Terbinafine 250 mg PO and ketoconazole 2%	40 days	Cured	<i>Tinea pedis</i>	Gnat et al.	Yes
8	2020	Poland	75	F	Cats	Nail	Terbinafine 250 mg PO and ketoconazole 2%	6 weeks and resection	Cured	<i>Tinea unguium</i>	Gnat et al.	Yes
9	2021	Guatemala	32	M	No	Groin	Terbinafine 250 mg PO	2 weeks	Cured	<i>Tinea cruris</i>	Porrás-López et al.	Yes
10	2021	Guatemala	48	F	No	Feet	Terbinafine 250 mg PO	2 weeks	Cured	<i>Tinea pedis</i>	Porrás-López et al.	Yes
11	2021	Guatemala	35	F	No	Nail	Terbinafine 250 mg PO	3 months	Cured	<i>Tinea unguium</i>	Porrás-López et al.	Yes
12	2014	Brazil	35	F	ND	Nail	Itraconazole <sup>a</sup>	ND	Cured	<i>Tinea unguium</i>	Martínez Herrera et al.	No
13	2020	Thailand	59	M	No	Ankle	Itraconazole 100 mg PO and ciclopirox 1%	1 month	Cured	<i>Tinea pedis</i>	Ramon-Torrell et al.	No
14	2019	Mexico	8	M	Yes	Scalp	Griseofulvin 15 mg/kg/day PO and prednisone 0.5 mg/kg/day PO	40 days	Cured	<i>Tinea capitis</i>	Bonifaz et al.	No
15	2019	Mexico	6	F	Yes	Face, chest and arms	Griseofulvin 15 mg/kg/day PO and ketoconazole 2%	20 days	Cured	<i>Tinea corporis</i>	Bonifaz et al.	No
16	2022	Spain	48	F	No	Arm	Terbinafine 10 mg/g and methylprednisolone	1 month	Cured	<i>Tinea corporis</i>	This article	No

ND: not determined; M: male; F: female; PO: per oral.

<sup>a</sup> Dose not specified.



**Figure 1.** Figure 1 A-B) Reverse-front aspect of the colony on Sabouraud agar. C) Two-cell macroconidia with lactophenol cotton blue (40x) at 14 days (potato agar). D) Skin lesion on the arm and ulnar fold.

identification is complemented with molecular methods by amplifying and sequencing the ITS1-5.8S-ITS2 fragment.<sup>1,5</sup> Microscopy enables a fast and reliable diagnosis thanks to this dermatophyte has distinctive morphological characteristics.<sup>15,16</sup> Other fungi that produce similar fungal elements have to be considered, such as *Trichothecium* spp.,<sup>7</sup> which produces bicellular conidia similar to those of *N. nana*, although the mode of fruiting is different, as the macroconidia of *N. nana* are isolated while those of *Trichothecium* spp. are arranged in clusters.<sup>8,15,16</sup>

This study has limitations inherent to a literature review based on case reports in which publication bias cannot be ruled out. However, the information from the literature review updates the knowledge on this dermatophyte, its epidemiology and associated infections.

In conclusion, *N. nana* is a dermatophyte species isolated only occasionally in humans. Still, it represents a potential dermatophytosis source in people with direct or indirect contact with animals and the soil. Clinically it mainly presents as *tinea corporis*, although there are other clinical forms. The prognosis is good if adequate antifungal treatment is provided.

**Conflicts of interest**

None.

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