An Over View of Dermatophytosis in Rabbits

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Author’s contribution
The sole author designed, analysed, interpreted and prepared the manuscript.

ABSTRACT
Dermatophytosis is a fungal infection of the skin caused by dermatophytes-filamentous fungi which have ability to invade the epidermis and keratinized structure derived from it such as hair or nails. Rabbits are one of dermatophytes host; young rabbit below 12 months of age were more frequently affected with the disease. *T. mentagrophytes* is the most common dermatophytes isolated species. The disease can be diagnosed by direct examination, fungal culture, skin biopsy sero and molecular diagnosis methods. This overview forecast more light of the different aspects of this disease.

Keywords: Dermatophytosis; rabbit; clinical feature; diagnosis; treatment.

1. INTRODUCTION
Rabbits are calm by nature. They are prone to many bacterial, fungal or parasitic skin diseases if proper care is not taken. Among them dermatophytosis is one of the most common diseases [1]. Dermatophytosis is a superficial cutaneous infection with one or more of the fungal species in the keratinophilic genera *Microsporum*, *Trichophyton*, or *Epidermophyton* [2,3]. Young or immune compromised rabbits are most susceptible to the disease [4]. Dermatophytosis is a zoonotic disease so it has important implications in public health [5]. Infection with dermatophytosis can occurred in receptive hosts via arthrospores present on the
1.1 Epidemiology

The possibility of infection of dermatophytosis depends on fungal species, host age, immunocompetence, condition of exposed skin surfaces, host grooming behavior, and nutritional status [6,7].

Young below 12 months of age or immune compromised rabbits are thought to be most susceptible. The susceptibility of young rabbit to dermatophytes could be as a result of immunity not fully developed [8]. However, differences in skin secretions, especially lower levels of fungistatic fatty acids in sebum and lower levels of fungal inhibitory sphingosine, and the fast growth and replacement of hair may also play a role in facilitating infection [9]. The presence of ectoparasites, especially fleas and Cheyletiella mites, can also lead to spread of dermatophytosis [9].

1.2 Risk Factors

1- Young animal
2- Overcrowding
3- high humidity
4- poor sanitation
5- malnutrition
6- Immunosuppression (including immunosuppressive treatment)
7- Injury by ectoparasites or scratches due to pruritus

Reported by Cafarchia et al. [10]

1.3 Transmission

Dermatophytosis can be transmitted by direct or indirect contact with infected hair, scales or materials. Infectious microconidia in the environment or on fomites can persist for many months. The pathogenesis of dermatophytosis includes several stages; adhesion, germination, invasion, penetration. Natural defences against dermatophytes depend on both immunological and non-immunological mechanisms so infectious microconidia must first overcome a couple of local defenses to be able to adhere the keratinized tissue, the stratum corneum [11,12].

2. CLINICAL FEATURES

Clinically, dermatophytes infect the epidermis and adhering structures, including hair follicles and shafts [13,14]. In rabbits dermatophytic infections may cause alopecia, redness scaly and scurf localized mainly on the face, head, auricles, and dorsal area of the neck (Figs. 1-3 [15-17]. This disease can also result in rabbit malnutrition, growth retardation, feed remuneration reduction and even death.

Fig. 1. Alopecia in rabbit mouth [17]

Fig. 2. Localized skin lesion of dermatophytes on rabbit leg [25]

2.1 Etiology

T. mentagrophyte's is the most common dermatophytes isolated from rabbits and some researchers consider rabbits as asymptomatic carriers of this organism [18-22]. M. gypseum was also isolated from rabbits [23]. M. canis was reported by [24]. T. verrucosum Arthroderma benhamiae were also recorded [25]. Rabbits are reported to be carrier for dermatophytes [26] so isolated T. mentagrophytes, M. gypseum, M. nanum and M. canis from healthy rabbits [27].
Fig. 3. Numerous canary crusts and large scales were present on the head of rabbits with hair loss [21]

2.2 Diagnosis

Hair and scrapings samples from rabbit suspected of dermatophytes infection are collected on the basis of gross lesions. Samples can be kept in polyethylene bags. [28]

2.3 Direct Examination

Hairs and scraping samples can be mounted in potassium hydroxide (KOH) of varying concentrations [29-31]. Infected hairs appear pale, wide and filamentous compared with normal hairs when microscopically examined at x4 or x10 magnification. Arthrospores can be visible on high magnification (x40) (Fig. 4). Positive result of KOH direct test can lead to positive cultures, which are considered as the gold standard. Calcofluor white (a textile brightener) can be used as an alternative to KOH because it binds specifically to the fungal cell wall and fluoresces strongly when viewed under a fluorescence microscope [27] as shown in Figs. 5 and 6.

Fig. 4. Ectothrix arthrospores infection in hair

In addition to technique steps mentioned above, pigment production on corn meal agar, urease activity on urea agar base (Fig. 15), growth at 37°C on SDA.

Fig. 5. Fluorescent microscopy (calcofluor white stain) of Trichophyton mentagrophytes complex hyphae and conidia isolated from healthy rabbits [27]

2.4 Fungal Culture

Fungal culture is considered the ‘gold standard’ for diagnosis [32]. Sabouraud’s dextrose agar (SDA) containing cycloheximide, penicillin and streptomycin were used in most diagnostic laboratories. Plates should be incubated at 25°C for 5 weeks. Dermatophytes test media (DTM) is recommended as the best media for isolation of dermatophytes because the presence of the red color indicated positive result, this can help in early identification of highly suspected cultures [33]. The isolates should be examined macroscopically and microscopically after staining with lactophenol cotton blue using wet mount technique [34] (Figs. 7 - 14).

In addition to technique steps mentioned above, pigments production on corn meal agar, urease activity on urea agar base (Fig. 15), growth at 37°C on SDA.

Fig. 6. Macroscopic aspect of dermatophytes test media (DTM) containing red color colonies at 5 weeks of incubation

2.5 Molecular Diagnosis

Diagnosis with conventional methods is time-consuming because it might take up to 4 weeks or longer to give the final results [35]. Furthermore, morphological identification may be confusing due to polymorphism of dermatophytes [36]. During the last decade, a wide variety of molecular techniques has become available as possible alternatives for routine identification of fungi in clinical microbiology laboratories [37,38].
T. mentagrophytes isolated from nine rabbits and three farm staff were identified by using amplification of CHS-1 gene and ITS+ sequence. The results of sequences of CHS-1 and ITS from different DNA samples revealed that they were identical [21].

Fig. 6. Fluorescent microscopy (calcofluor white stain) of Microsporum gypseum hyphae and macroconidia isolated from healthy rabbits [27]

Fig. 7. Culture of T. mentagrophytes: Surface of colony show powder-like shape, white, loose irregular mycelium on the edge [21]

2.6 Serodiagnosis

Indirect ELISA tests developed to detect specific IgG in rabbits infected with T. mentagrophytes, found that (ELISA-rabbits test) is highly sensitive (96.0 %) and highly specific (94.1 %) [39].

2.7 Skin Biopsy

Skin biopsy from rabbit infected with T. mentagrophytes showed pathological changes with adherence of fungus to keratinocytes, through the stratum granulosum of the epidermis. In this period of infection there was a hyperkeratosis, thickening of epidermis with hair follicle plugging in addition to keratinized squamous epithelial lining with underlying moderate periappendageal tissue and perivascular chronic inflammatory cells infiltration (lymphocytes) 

Fig. 8. Microsporum canis culture [50]

Fig. 9. Microsporum gypseum culture, [50]

In 8-10 days of induced infection there is keratinized squamous epithelial lining with focal area of surface erosion and underlying moderate periappendageal tissue chronic inflammatory cells infiltration (lymphocytes) haematoxylin and eosin staining (H&E) may or may not identify dermatophytes and special stains such as periodic acid Schiff (PAS) and Grocott methenamine silver (GMS) are needed. The epidermis infiltrated with variable fungal septate hyphae in size in the surface of the squamous epithelium [40] Figs. 16-18.
Fig. 10. Small conidia (size: 2-3×2-4 μm) and mycelium of *T. mentagrophytes* [21]

Fig. 11. Spiral hyphae of *T. mentogrophytes var mentogrophytes* slide stained with LPCB stain [42]

2.8 Treatment

Optimal therapy of dermatophytosis requires a combination of topical antifungal therapy, concurrent systemic antifungal therapy and environmental decontamination. The treatment should be continued until two consecutive negative cultures (at weekly or bi-weekly
intervals) are obtained [41]. Topical treatments speed resolution of clinical lesions and may help prevent zoonotic contagion. Systemic therapies that have prolonged residual activity in the skin and hair provide the most effective treatments.

2.9 Topical Therapy

1. Nystatin ointment for treatment of rabbit experimentally infected with *T. mentagrophytes* for 3 weeks [42].
2. Clotrimazole is well-documented antifungal agent for treatment of rabbits [43].
3. 0.12 g of terbinaphine 1% cream, for 28 days [44].

2.10 Systemic Therapy

1. Griseofulvin 25–30 mg / kg during 5–6 weeks. Avoid its use in pregnant animals [45,46].
2. Itraconazole 5-10 mg/kg daily, for 1 month [47].

Fig. 12. *Microsporum canis* microscopic observation in lactophenol cotton blue [50]

Fig. 13. *Microsporum gypseum* microscopic observation in lactophenol cotton blue [50]
Fig. 14. Lactophenol cotton blue mount shows chains of chlamydospore of *Trichophyton verrucosum* culture incubated at 37°C [25]

2.10.1 Environmental decontamination

Eniliconazole emulsifiable concentrate will be sprayed onto the walls and ceiling of rabbit house (50 mg per m²) twice weekly for 23 weeks. Treated farm showed reduction of number of clinically infected rabbits [48].

2.10.2 Vaccination

It is a dried culture of an attenuated strain of *T. mentagrophytes*. It has a high immunogenic activity for dermatophytosis in rabbits. The vaccine is non-reactogenic and is injected intramuscularly. The vaccine has been recommended for practical use in USSR [49].

Fig. 15. Growth of *T. mentagrophytes* on urea agar after 4 days showing hydrolysis of the urea. [42]

Fig. 16. The bland looking (A) Hyperkeratosis, thickening of epidermis with (B) hair follicle plugging in 4-5 days (stained with H&E, 10X)[40]

Fig. 17. The bland looking with A- surface erosion and B- lymphocytes infiltration in 8-10 days (stained with H&E, 10X)[40]
Fig. 18. Proliferation of septate hyphae of *T. mentagrophytes* in epidermis in 8-10 days (stained with PAS, 40X) [40]

3. CONCLUSION

Dermatophytoses are the most common fungal infections in rabbits. Many studies were done considering different aspects of the disease (e.g., epidemiology, clinical presentation and diagnosis, treatment, prevention, and control). As many rabbits share the environment with owners as companion animal so they become a source of infection to human this can lead to public health problem.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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