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Current Trends in Trichosporon-Related Mycoses in Traslacional Era

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Abstract

White stone is a superficial mycosis caused by fungi of the genus *Trichosporon* spp., and is characterized by the formation of whitish or yellowish nodules firmly attached to the hair shaft. The infection primarily affects the scalp, although it may also appear in the beard, mustache, eyebrows, axillary region, and genital area. The condition is usually asymptomatic; however, mild pruritus or irritation may occur in some cases. White piedra is more prevalent in tropical and temperate regions with high humidity, with Brazil reporting the highest number of documented cases. In Mexico, reported cases remain limited and are mainly concentrated in the states of Tabasco and Chiapas.

The main risk factors associated with this infection include long and persistently moist hair, inadequate hygiene, warm climates, the use of head coverings or veils, hyperhidrosis, immunosuppression, and tying the hair when it is still wet. *Trichosporon* species are widely distributed in nature and may transiently colonize the human microbiota. The species most frequently implicated in white piedra are *T. inkin*, *T. cutaneum*, *T. ovoides*, and *T. loubieri*. These microorganisms exhibit several pathogenic mechanisms, including the production of lytic enzymes such as proteases, lipases, and hemolysins, and the ability to alter their morphology depending on environmental conditions.

Diagnosis is typically established through direct microscopy, which reveals whitish or cream-colored colonies. However, precise species identification requires molecular techniques, particularly sequencing of the IGS1 region, which provides greater discriminatory power than the ITS region.

Keywords: White Stone, Nodules, *Trichosporon*, Arthroconidia

Introduction

White piedra is an uncommon superficial mycosis that may present as asymptomatic and chronic. It typically affects the hair shaft (external portion), appearing as whitish to yellowish adherent nodules or concretions that occur most frequently on the scalp and less commonly on the beard, mustache, eyelashes, axillae, and pubic region. The etiological agent is *Trichosporon* spp., among which *Trichosporon inkin*, *Trichosporon ovoides*, and *Trichosporon cutaneum* are the most notable. Predisposing risk factors include young age, female sex, long hair, and exposure to humidity [1-3].

The genus *Trichosporon* was first described in 1865 by Beigel, who observed this microorganism causing a benign hair infection characterized by irregular nodules on body and scalp hair, later known as white piedra. At that time, the etiological agent was classified as the alga *Pleurococcus beigelii*. It was not until 1890 that Behrend provided a detailed description of this causal agent, naming it *Trichosporon ovoides*. Since then, additional species of *Trichosporon* have been described [1].

The superficial mycosis caused by fungi of the genus *Trichosporon* is known as white piedra. These fungi have a very particular geographic distribution, occurring most frequently in tropical and temperate regions where rainfall is high and constant throughout the year. The majority of reported cases occur in the Brazilian population. Because this mycosis is common and not life-threatening, epidemiological studies tend to be limited, leading to underestimation of cases. In Mexico, there is a case report study documenting 12 patients with white piedra identified between 1996 and 2010 [4].

Trichosporon is an anamorphic organism belonging to the Basidiomycota (Basidiomycota, Hymenomycetes, Tremelloidae, Trichosporonales). With a yeast-like appearance, these organisms are widely distributed in nature. They can be found in substrates such as soil, decaying wood, air, rivers, lakes, seawater, cheese, beetles, bird droppings, bats, pigeons, and livestock [4].

In Mexico, the states with the highest number of described cases are Tabasco and Chiapas. The infection occurs more frequently in young women, and the most commonly affected anatomical site is the occipital region [2, 3]. The incidence of white piedra varies globally and has been associated with long and humid hair. It has been observed with greater frequency in women of Muslim ancestry, likely due to cultural practices where women wear head-covering veils, which increase temperature and humidity, creating conditions favorable for this mycosis. Additionally, white piedra is more common in adults than in pediatric patients. Recently, an 11% colonization rate was identified in a cross-sectional study of 1,004 healthy male volunteers colonized by *Trichosporon* spp. [2, 3].

In humans, *Trichosporon* species may occasionally form part of the gastrointestinal and oral microbiota and can transiently colonize the respiratory tract and the skin [4].

From a clinical standpoint, these mycoses can affect individuals of all ages and genders, although they are more commonly seen in young adult men, with the genital area being the most frequently affected anatomical region. They have also been reported more often in individuals of Black race. Scalp involvement is most frequent in adult women and in individuals under 15 years of age [5]. Predisposing or risk factors in this group include poor hygiene, warm and humid climates, hyperhidrosis, HIV infection, immunosuppression, tying up wet hair and covering it to avoid sun exposure, long hair, and the use of creams and oils [5].

Additionally, white piedra has been reported in a wide variety of hair-bearing areas, including the scalp, beard, mustache, eyebrows, axillae, and particularly the genital hair. White piedra appears to be mainly caused by *Trichosporon inkin*, *Trichosporon cutaneum*, *Trichosporon ovoides*, and *Trichosporon loubieri*, which are considered emerging species primarily associated with superficial infections in humans [6].

Other superficial infections that may also be caused by species of *Trichosporon* spp. include onychomycosis, in which *Trichosporon cutaneum* is the most frequently isolated species. In other isolates from patients with tinea pedis and onychomycosis, its presence ranges from 2.81% to 42.8% of cases [7].

In white piedra of the scalp, the main clinical manifestations are small concretions measuring 1 to 3 mm in diameter, whitish-yellow in color and hard in consistency, which surround the hair shafts without invading them. One or multiple nodules may appear on the same hair shaft. The condition is generally asymptomatic, although it may occasionally be accompanied by mild pruritus, erythema, and scaling in the inguinocrural area [8, 9].

Although *Trichosporon* spp. does not invade the hair shaft, prolonged presence of the organism may weaken and fracture the hair. Likewise, it may affect any hair-bearing site of the body, becoming chronic and remaining clinically unnoticed if its presentation is not recognized [8, 9].

The pathogenic mechanisms caused by the fungus in the skin and its appendages are poorly studied. In *Trichosporon* spp., it has been described that hemolysins, proteases, and lipases enable the degradation of proteins and the destabilization of host cell membranes, thereby increasing fungal pathogenicity. It is important to note that there are reports on the production of lytic enzymes in *Trichosporon asahii*, but not in *Trichosporon asahi*. Phenotypic switching, which involves rapid and reversible changes in colonial morphology and/or microscopic characteristics, may occur in response to different environmental stimuli—such as oxidative stress or nutrient limitation—or to intrinsic factors such as genetic variations in DNA repair systems [10]. When phenotypic switching occurs *in vivo*, it involves modifications in the expression of virulence factors or alterations in the interactions between the microorganism and the host cell, leading to increased pathogenicity and immune evasion [10].

Regarding colonial development in culture media, phenotypic switching has been clearly documented *in vitro* for *T. beigelii*. Macroscopically, one morphotype appears as a rough, cerebriform, moist colony with irregular borders; microscopically, it displays filamentous hyphae. A second morphotype appears powdery, with smoother topography and more regular edges, showing microscopically a higher proportion of arthroconidia or blastoconidia. Thus, a rough colony is accompanied by a greater proportion of hyphae, whereas a powdery colony presents a higher quantity of conidia [10].

The infection mechanism of *Trichosporon* spp. in hair can be described in four stages within its natural history. In the first stage, contact occurs between *Trichosporon* structures and the hair shaft [12]. The second stage is characterized by the adhesion of the yeast's infectious propagules—arthroconidia, blastoconidia, and mycelium—to the hair shaft. In the third stage, invasion of the yeast structures into the external hair sheath is observed, associated with the production of an adhesive polysaccharide that enables the spores to adhere to the hair shaft near the follicular ostium. This produces an ectothrix pattern that forms nodular structures around the hair. Finally, in the fourth stage, the formation of a mature nodule occurs, consisting of a compact structure and the secretion of a cement-like substance. It has been emphasized that as the hair grows, whitish, soft concretions or nodules form around the hair shaft without invading it [13].

Recently, the isolation of bacteria from affected hairs has also been reported, and a possible synergistic interaction has been proposed in which fungal metabolites may provide the nutrients necessary for the growth of certain *Corynebacterium* species, while their proteolytic activity may facilitate damage to the hair shaft [14].

The diagnosis of *Trichosporon* spp. is carried out through conventional microscopy, based on the morphological observation of arthroconidia. Cultures are performed on solid media such as Sabouraud dextrose agar, where colonies of the *Trichosporon* genus grow with a cream or white coloration, typically displaying a cerebriform and radial appearance, and sometimes even a membranous texture—features previously described. Since morphological and biochemical characteristics alone do not allow for species-level identification, molecular studies are necessary [14].

Considering these aspects, the main objective of the present study was to describe four cases of *Trichosporon* spp. mycosis (white piedra) in individuals of Afro-Mexican ancestry from the state of Oaxaca.

Biochemical Identification

The biochemical profile of *Trichosporon* spp. can be obtained through auxanography, which evaluates the ability of the organism to assimilate different carbon sources.

However, the complete biochemical characterization of *Trichosporon* requires testing the assimilation of approximately 50 carbon compounds and takes 5 to 15 days; therefore, this method is not practical for routine use when precise species identification is needed.

Commercial methods have been developed to systematize assimilation tests and reduce identification time. The API 20C AUX system (bioMérieux) is a commercial micromethod that has become the most widely used routine identification tool. This system evaluates the assimilation of 19 carbohydrates and allows identification within 24 to 72 hours of incubation. However, a limitation of this and other commercially available methods is that they allow identification of only three species within the genus: *T. asahii*, *T. inkin*, and *T. mucoides*.

Molecular Identification

Various molecular methods have been developed as rapid and effective alternatives for accurate species-level identification of many pathogens (Table 1). Among these, ribosomal DNA sequencing is widely used in the systematic identification of microorganisms. Molecular identification of fungi is typically performed by sequencing the internal transcribed spacer (ITS). One limitation of this region is its high degree of homology among different *Trichosporon* species, making it necessary to analyze other genes or regions with greater variability for precise species differentiation.

Sugita and colleagues analyzed 84 strains corresponding to 25 *Trichosporon* species to compare the efficiency of sequencing the intergenic spacer 1 (IGS1) versus the ITS region for accurate species-level identification. They found greater heterogeneity in the IGS1 sequences compared with ITS. This study established that IGS1 analysis is superior to ITS for differentiating species within this genus. Additionally, this method simultaneously enables the genotyping of *T. asahii* [15].

Table 1: Type strains of *Trichosporon* sp. used for the alignment and identification of clinical isolates

Specie	*GenBank acces number*
T. asahii Genotipo I	AB066386
T. asahii Genotipo II	AB072606
T. asahii Genotipo III	AB066397
T. asahii Genotipo IV	AB066399
T. asahii Genotipo V	AB066401
T. asahii Genotipo VI	AB180192
T. asahii Genotipo VII	AB180193
T. asahii Genotipo VIII	AB439002
T. asahii Genotipo IX	AB439003
T. asahii Genotipo X	EU441158
T. asahii Genotipo XI	EU441160
T. asahii Genotipo XII	JF412789

Thus, species of the genus Trichosporon are anamorphic basidiomycete fungi, similar to yeasts, that inhabit tropical and temperate regions and are widely distributed in the environment. Although most strains isolated in clinical laboratories are typically associated with colonization or superficial infections, this fungus has been identified as an opportunistic pathogen responsible for emerging and invasive infections in high-complexity hospitals across different countries. Invasive Trichosporon infections occur mainly in patients with cancer and critically ill individuals undergoing multiple medical procedures. The ability of these strains to adhere to and form biofilms on implanted medical devices may explain the progression of invasive trichosporonosis, as this facilitates antifungal resistance and immune system evasion. Likewise, the presence of glucuronoxylomannan (GXM) in its cell wall and the production of enzymes such as proteases and lipases appear to contribute to its virulence.

The former taxon T. beigelii was replaced by several independently defined species, and the classification of the genus has been updated through molecular techniques capable of distinguishing closely related species. Currently, approximately 50 Trichosporon species have been described, of which 16 can cause disease in humans. Among them, T. asahii is the species most frequently associated with invasive infections, and nine genotypes have been identified based on the IGS1 region, whose distribution varies significantly by geographic area.

Phenotypic methods for identifying Trichosporon species rely on the study of their microscopic characteristics and biochemical profiles. Tools such as microculture for detecting arthroconidia and the urease test are useful for initial screening; however, both morphology and biochemical tests are insufficient for accurate species-level identification. Therefore, it is necessary to use molecular techniques, such as sequencing of the **IGS region**, for reliable identification.

The diagnosis of invasive trichosporonosis is complex, and over the past twenty years various molecular tools have been developed, including **PCR-based methods**, **Luminex xMAP technology**—an advanced flow-cytometry technique with potential for detecting clinically relevant fungi—and proteomics.

Despite the growing importance of Trichosporon in medical practice, treatment remains challenging due to the limited information available regarding the *in vitro* and *in vivo* efficacy of antifungal agents against the species with the greatest clinical impact.

In summary, **disseminated trichosporonosis** has been increasingly reported worldwide and presents significant challenges for its diagnosis and for the identification of the species involved. Prognosis is generally poor, and **triazoles currently represent the most effective therapeutic option**. Additionally, removing central venous catheters and adequately managing the patient's underlying conditions are recommended to improve clinical outcomes.

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