

Primary Cutaneous Coccidioidomycosis: Incidental Finding

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Introduction

The Coccidioidomycosis is a deep mycosis caused by two dimorphic fungi, *Coccidioides immitis* and *Coccidioides posadasii* characterized by diverse clinical manifestations. This fungus is found in the southern of the United States and Northern Mexico. It causes an infectious disease but that is not contagious. Skin involvement in coccidioidomycosis is usually secondary to disseminated infection.

Primary cutaneous coccidioidomycosis is rare clinical condition and may be misdiagnosed as tuberculosis, leprosy, and presented as ulcers, erythematous lesion, verrucous granuloma, intact nodules, and subcutaneous abscess. The prevalence of primary extrapulmonary disease is 0.5%, therefore, a high degree of suspicion is needed to diagnose the cutaneous form of the disease [1-3]. We present five cases of primary cutaneous coccidioidomycosis (Table 1).

Case 1

The first patient is a 35-year-old man without any relevant previous history except that he is a teacher in an endemic area (Cadereyta, Nuevo Leon, Mexico). He presents a two month history of an asymptomatic, 2-cm in diameter elevated nodule that is located in the left preauricular region (Figure 1A). He noticed a single cystic fluctuating abscess-type lesion within increase in local temperature with no associated symptoms. He mentioned trauma to his finger nails two weeks before the lesion appeared. In addition, an external lymph node was palpated during physical examination.

The lesion was surgically removed, suspecting an epidermoid cyst. The histological diagnosis was cutaneous coccidioidomycosis (Figure 2A). A coccidioidin test (<15 mm) was positive two weeks after surgery. Itraconazole 400 mg/day for 4 months was prescribed. The patient was cured by week 20.

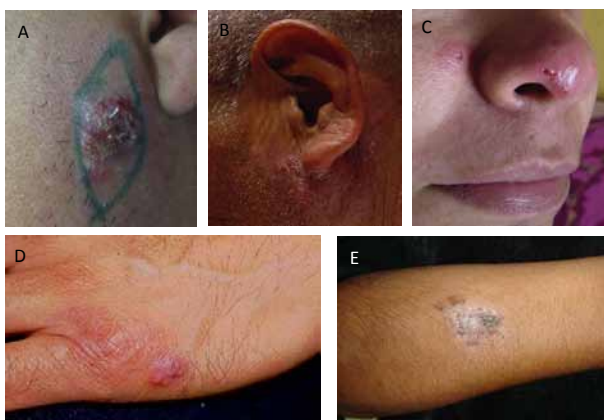


Figure 1: Cutaneous coccidioidomycosis A: elevated nodule, localized in the left preauricular region B: A fluctuating abscess with palpable adenopathies in neck C: Face redness with papules on the nose and cheek D: fluctuating redness on the left hand, with multiple papules E: Rough exophytic growth with purulent swelling.

Case 2

A 65-year-old healthy male farmer who herds goats in a rural desert area in Dr. Coss, Nuevo Leon, Mexico, was seen because of a fluctuating abscess in the left pre-auricular region of 4 months of evolution that was accompanied by palpable adenopathies in the neck and intense pruritus two weeks before the appearance of the lesion. Partial surgical removal of the lesion was performed and cutaneous coccidioidomycosis was reported (Figure 2B). A chest x-ray was taken, which was normal. A coccidioidin test was positive (20 mm) at 48 hours. Treatment was started with itraconazol 400 mg/day for 6 months with a cure being achieved (Figure 1B).

Case 3

A 32-year-old healthy women who lives in Monterrey, Mexico frequently vacations in the rural city of Sabinas Hidalgo in Nuevo Leon

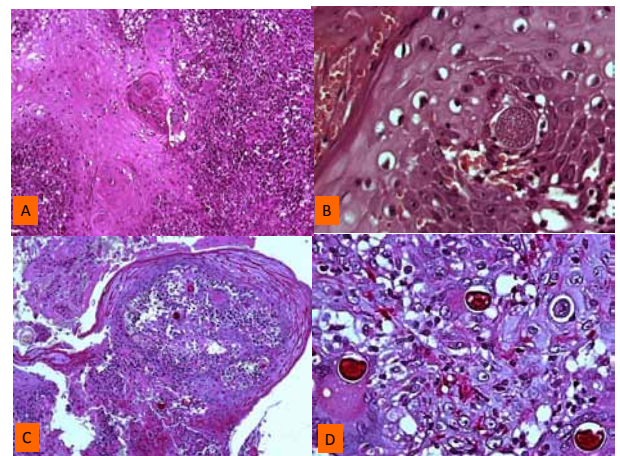


Figure 2: A) Pseudoepitheliomatous hyperplasia of the epidermis and a dense infiltrate in papillary dermis (X10, haematoxylin-eosin stain); (B) Intraepidermal spherule with endospores (X40 haematoxylin and eosin stain); (C) granulomatous infiltrate in the dermis with spherules (X5 PAS stain) D) inflammatory granulation tissue with spherules inside of the multinucleate giant cells (X40 PAS stain).

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Case No.	Patient	Site	Clinical features	Laboratory studies/CST*	Treatment	Outcome
1	35 yo man, teacher in rural area Cadereyta, Nuevo Leon state.	Left preauricular region. Trauma of his fingernails.	Epidermal cyst-like lesion. Regional LAD+	Incidental finding at skin biopsy. Chest X-ray normal. CST+	Excision and oral itraconazole 400 mg/day for 4 months	Resolution in 20 weeks.
2	65 yo man, goat-farmer from Dr. Coss, Nuevo Leon state	Left preauricular region. Trauma of his fingernails.	Epydermal cyst-like lesion. Regional LAD+	Incidental finding at skin biopsy. Chest X-ray normal. CST+	Excision and Itraconazole 400 mg/day for 6 months	Resolution in 36 weeks
3	32 yo woman who visited a rural area in northern Nuevo Leon state.	Nose and cheeks affected. Treated as Rosacea with minocycline 200 mg/day for 3 months. No history of trauma	Rosacea-like lesions. LAD-	Incidental finding at skin biopsy. Chest X-ray normal. CST+	Oral Itraconazole 400 mg/day for 4 months	Resolution in 14 weeks
4	68 yo man, cattle herder in Torreon, Coahuila state.	Dorsum of left hand. Trauma with barbed wire.	Verrucose tuberculosis, Sporotrichosis, vs. Orf. LAD+	Incidental finding at skin biopsy. Chest X-ray normal. CST+ CF 1:128 Culture +	Oral itraconazole 300 mg/day for 8 months	Resolution in 10 months, CF 1:8.
5	38 yo male farmer from Tijuana.	Trauma of left forearm with cactus thorn in Anaheim, CA.	Sporotrichosis, verrucose tuberculosis LAD+	Incidental finding at skin biopsy. Chest X-ray normal. CST+ CF 1:128 Culture +	Oral itraconazole 300 mg/day for 10 months	Resolution in 12 months CF1:8

Table 1: Summary of the 5 cases with Primary Cutaneous Coccidioidomycosis. YO, Years old; LAD, lymphadenopathy; CST, coccidioidin skin test; CF, coccidioidin-fixation test.

state. She presents erythematous papules and small ulcers on the nose and cheeks of 6 months evolution. In the last three weeks she refers itching and a burning sensation. She was treated with minocycline 100 mg for three months because of a suspicion of acne rosacea with no success. A biopsy was performed and coccidioidomycosis spherules and granulomas were found in the specimen studied (Figure 2C). A chest x-ray was normal and the coccidioidin test was positive (18 mm) at 36 hours. Oral itraconazole was given and the lesion cured 14 weeks after starting treatment (Figure 1C).

Case 4

A 68-year-old male farmer from Torreon, state presents an erythematous area with multiple papules on his left hand after an injury with barbed wire (Figure 1-D). His symptoms started 6 months before and after the injury with barbed wire when herding cattle. He presented small suppurative micronodular lesions on the dorsum and side of the hand with discrete itching.

The presumptive diagnosis was verrucose tuberculosis, sporotrichosis vs. Orf. A biopsy was performed that reported a granuloma and some spherules of *Coccidioides* spp within of the multinucleate giant cells (Figure 2D). A coccidioidin skin test was positive with 8 x 10 cm of induration and erythema (hyperergic). *Coccidioides* spp was isolated from Sabouraud culture and complement fixation reported a value of 1:128. The patient was treated with itraconazole 400 mg/day for eight months with a clinical cure and a complement fixation test result of 1:8.

Case 5

This patient is a 38-year-old man, farmer by profession, who is from Tijuana, Mexico. He suffered a thorn prick from a cactus in Anaheim, California (Figure 1E) and a month and a half later presented a verrucose lesion and an increase of axillary lymph nodes. He presents with a verrucose plaque 2x2 cm in diameter of nine months evolution accompanied by itching and pain. The presumptive diagnosis was cutaneous tuberculosis. A skin biopsy was reported as a granuloma with coccidioidomycosis spherules. The coccidioidin skin test was

positive with an induration of 10x10 cm and a complement fixation test of 1:128. *Coccidioides* spp was isolated in culture.

Discussion

These patients are from northern Mexico and in four a history of trauma was confirmed. They also had no relevant medical history and pulmonary, cardiac, neurologic, and other examinations were normal.

The diagnosis of primary cutaneous coccidioidomycosis was an incidental finding evidenced by the skin biopsy results associated with a normal chest x-ray and a coccidioidin test > 5 mm in diameter. In two patients, the first clinical diagnosis was epidermal cyst, which was treated with surgical removal with a surprising dermatopathology diagnosis. The third case was considered acne rosacea and after therapy failed, a skin biopsy was decided. Finally in cases 4 and 5, cutaneous tuberculosis was the initial diagnosis.

A recent search for publications of primary cutaneous coccidioidomycosis in PubMed (June 1, 2012) resulted in approximately 25 cases of this disease. The last case was published in 2010 as an incidental finding as in ours [4].

Due to the clinical variety of skin coccidioidomycosis (ulcers, nodule, abscesses, even leprosy-skin lesions, verrucose lesions, lupus perniosis-like), a high degree of suspicion is necessary to make the correct diagnosis, especially after a history of trauma. Fever and regional lymphadenopathy may occur [2,5,6]. The diagnostic criteria are no history of lung disease, a history of trauma, a 1-3 week incubation period, a primary cutaneous "chancre" as an initial injury, a painless nodule, or a plaque with central ulceration, a quickly positive coccidioidin reaction, a negative complement fixation for several weeks with subsequently low titers, lymphadenopathy, or regional lymphadenitis with sporotrichoid nodules, spontaneous resolution of the skin lesion with the exception of patients with problems of immunity. Imaging studies do not preclude the diagnosis of disseminated coccidioidomycosis. The intradermal coccidioidin skin test should be read in 48-72 hrs and it is positive if the induration is greater than or equal to 5 mm. Disseminated infections can course with anergy with a poor skin reaction [7].

The “gold standard” for diagnosing coccidioidomycosis is either a positive culture for *C immitis* or evidence of the spherules on histopathologic examination. Oral azole antifungal agents during 3 to 13 months are generally recommended for uncomplicated cutaneous manifestations with good clinical response [8].

In conclusion, primary cutaneous coccidioidomycosis, can be easily misdiagnosed. It is important to have a high clinical suspicion in the presence of lesions such as nodules, abscesses, redness of the skin, exophytic growths that do not heal, or warts in patients who have lived, worked or travelled in an endemic area and have a history of trauma at the site of the lesion.

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