

Tuberculous Uveitis, Erythema Induratum, and Persistent Genital Warts in a Female Patient: A Rare Case Report

Abstract

Uveitis and erythema induratum are two uncommon extrapulmonary manifestations of tuberculosis (TB). In most circumstances, we cannot isolate mycobacterium from those sites, so diagnosis is difficult. In the presented case, panuveitis, erythema induratum, and persistent anogenital warts were found concurrently in a 19-year-old girl who had a history of pulmonary TB 10 years ago. Assessment of her immune condition ruled out any immunodeficiency state. Extrapulmonary TB and persistent warts responded dramatically to anti-TB drugs and interferon-gamma, respectively. Our case reveals that a constellation of these clinical manifestations may also occur in immunocompetent individuals.

Keywords: *Condyloma acuminata, cutaneous tuberculosis, ocular tuberculosis, uveitis*

Introduction

An uncommon clinical manifestation of extrapulmonary tuberculosis (TB) is ophthalmic involvement. TB may affect any component of the eye including cornea, uvea, choroid, and sclera.^[1] Uveitis is usually classified into anterior, intermediate, posterior, and panuveitis, among which posterior uveitis is the most common form.^[2]

Ophthalmic TB is more common in the developing world.^[3] It has been stated that TB, Vogt–Koyanagi–Harada syndrome, sympathetic ophthalmia, Behcet's disease, and sarcoidosis are common causes of panuveitis.^[4]

Another extrapulmonary manifestation of TB is erythema induratum which may present as tender, erythematous to violaceous nodules typically seen on the flexural surface of the lower extremities. There is a controversy over the etiology of erythema induratum and its association with TB.^[5]

Genital warts appear as flat, papular, or pedunculated lesions on the genital area^[6] and are usually caused by human papillomavirus type 6 (HPV6) or less commonly HPV11. Less than half of genital warts are resolved over a period of 6 months. Warts in individuals with

impaired cell-mediated immunity resolve more slowly and have a higher likelihood of recurrence.^[7]

Herein, we present a case with bilateral uveitis, erythema induratum, and persistent genital warts.

Case Report

The patient was a 19-year-old girl, inhabitant of urban area of Hamadan Province, West Iran. She presented to Sina Hospital at the end of 2017, with complaints of pain, redness, and blurred vision of both the eyes since 2 months ago. Examination of her eyes by an ophthalmologist revealed panuveitis. The patient denied other complaints such as cough, weight loss, fever, and chills or perspiration.

Physical examination revealed some nodular erythematous lesions with an approximate size of 2 cm × 2 cm on the anterior and posterior aspects of both the lower legs, which was treated as eczema for 1 year [Figure 1]. Furthermore, some condyloma acuminata were seen on her genitalia and perianal area, persistent over the past 2 years despite numerous medical and electrosurgical therapies.

She had a history of smear-positive pulmonary TB 10 years ago with good

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Access this article online

Website: www.advbiores.net

DOI: 10.4103/abr.abr_154_19

Quick Response Code:



How to cite this article: Majzoobi MM, Akbarzadeh S, Ebrahimi G, Ghasemibasir HR, Alirezaei P. Tuberculous uveitis, erythema induratum, and persistent genital warts in a female patient: A rare case report. *Adv Biomed Res* 2019;8:70.

Received: 13 July 2019; **Revised:** 06 October 2019; **Accepted:** 03 November 2019; **Published:** 27 November 2019.

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response to standard treatment. Her brother had a history of disseminated TB as well, with simultaneous involvement of the brain, omentum, and gastrointestinal tract. The patient's brother had been successfully treated with anti-TB treatment and interferon-gamma (IFN- γ).

Results of laboratory tests and imaging studies were as follows: white blood cell = 7000, hemoglobin = 10.4 g/dl, erythrocyte sedimentation rate = 29 mm/h, C-reactive protein = +1, angiotensin-converting enzyme = 34, tuberculin skin test (TST) = 25 mm, HIV test (fourth-generation enzyme-linked immunosorbent assay): negative, venereal disease research laboratory: negative, and chest X-ray: normal. Histopathologic examination of skin biopsies obtained from lower leg and perianal lesions confirmed the diagnosis of erythema induratum and condyloma acuminatum, respectively. With respect to familial history of disseminated TB, personal history of pulmonary TB, existence of erythema induratum, and persistent genital warts, we decided to evaluate the patient's immune system by laboratory tests including C3, C4, CH50, immunoglobulin G (IgG), IgM, IgA, CD3, CD4, CD8, CD16, and CD56. However, these tests were all normal.

Based on the result of TST, past TB history, presence of erythema induratum, and exclusion of other causes of panuveitis, anti-TB drugs as well as short course of oral prednisolone were started. Uveitis responded dramatically to this medical treatment, but the improvement of erythema induratum was slow and took a few months to appear.

After 3 weeks, the patient was admitted again to the infectious ward with drug hepatotoxicity. Chief complaints of the patient were nausea, vomiting, and abdominal discomfort concomitant with abnormal laboratory tests (aspartate aminotransferase = 134 U/L, alanine aminotransferase = 157 U/L, alkaline phosphatase = 418 U/L, total bilirubin = 1.99 mg/dL, direct bilirubin = 1.66 mg/dl, and international normalized ratio = 1.1). After normalization of liver function tests, anti-TB treatment was restarted and continued without any problem. Taking into consideration, the role of stimulation of immune system on improvement of her genital warts, along with an unfavorable response of her condyloma to previous electrosurgical treatments, we started intralesional and systemic IFN- γ twice a week for 2 months. This treatment resulted in disappearance of all her genital lesions.

Discussion

Distinction between infectious and noninfectious causes of uveitis is of utmost significance, since different causes require different treatment strategies. Immune-mediated disorders respond favorably to corticosteroids or immunosuppressive treatments,^[4] whereas infectious uveitis should be treated with specific antimicrobials for an appropriate period of time.^[2]



Figure 1: Erythematous lesions in both the lower extremities

In Iran (like developed countries), noninfectious uveitis is more common than infectious uveitis,^[8] and the most common causes of panuveitis are Behcet's disease, idiopathic uveitis, and Vogt-Koyanagi-Harada syndrome, followed by herpetic uveitis, TB, toxoplasmosis, and sarcoidosis.^[9]

TB has recently attracted an increasing interest as a cause of uveitis. This is probably because its incidence has increased even in developed countries.^[10] In a study conducted on patients with presumed tuberculous uveitis, more than 48% had chronic panuveitis.^[11] It is worth mentioning that the clinical presentation of TB uveitis is not specific, and the diagnosis may be difficult. Clinical suspicion generally rests on resistance to anti-inflammatory drugs, presence of latent TB, and no evidence of other causes of uveitis.^[10]

Cutaneous TB is quite uncommon. It has been estimated that only 1%–2% of TB patients have skin manifestations.^[1] Erythema induratum of Bazin is one of these rare manifestations of TB, which is usually categorized as a form of tuberculid.^[12] The lesions of erythema induratum of Bazin usually involve posterior and anterolateral aspects of the legs. In these lesions, like other tuberculids, it is too difficult to find acid-fast bacilli.^[12] Histopathology of erythema induratum often reveals lobular panniculitis with granuloma formation, vasculitis, and necrosis.^[13] Although it is generally believed that a delayed-type hypersensitivity reaction to TB is the most common underlying cause of erythema induratum, other etiologies may also exist.^[5]

In addition to uveitis and erythema induratum, our patient also suffered from persistent anogenital warts. It is well documented that defective cellular immunity predisposes the patient to persistence of HPV infection.^[14] Moreover, certain studies have shown that the persistence of HPV infection might be related to modulation of host immune responses by the virus itself.^[15] Hence, persistent genital warts might have several underlying causes, and not every patient with persistent condyloma acuminata has defective

immune system (like the present patient). The refractory genital warts of our patient showed a favorable response to treatment with IFN- γ . There are also several studies that have shown the usefulness of interferons (especially IFN- α) in the treatment of genital warts.^[16] Moreover, IFN- γ has shown beneficial effects in the treatment of pulmonary TB.^[17] This case report highlights the importance of detailed history taking and thorough physical examination when approaching a patient with an organ-specific chief complaint.

Conclusion

Although the present patient had recurrence of TB at two extrapulmonary sites, persistent genital warts, and history of disseminated TB in her brother, her immunologic tests proved to be normal. Our case reveals that a constellation of these clinical manifestations may also occur in immunocompetent individuals.

Declaration of patient consent

To publish this case report, written informed consent was obtained from the patient. The patient has given her consent for her image and other clinical data to be reported in the journal. The patient realizes that her name will not be published and the authors try to conceal her identity.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

- Bravo FG, Gotuzzo E. Cutaneous tuberculosis. *Clin Dermatol* 2007;25:173-80.
- Dalvin LA, Smith WM. Intraocular manifestations of *Mycobacterium tuberculosis*: A review of the literature. *J Clin Tuberc Mycobact Dis* 2017;7:13-21.
- Bansal R, Gupta V, Gupta A. Current approach in the diagnosis and management of panuveitis. *Indian J Ophthalmol* 2010;58:45-54.
- Tabbara KF. Infectious uveitis: A review. *Arch Soc Esp Ophthalmol* 2000;75:215-59.
- Mascaró JM Jr., Baselga E. Erythema induratum of bazin. *Dermatol Clin* 2008;26:439-45, v.
- Chen X, Li L, Lai Y, Liu Q, Yan J, Tang Y. Characteristics of human papillomavirus infection in men with genital warts in Shanghai. *Oncotarget* 2016;7:53903-10.
- Jardine D, Lu J, Pang J, Palmer C, Tu Q, Chuah J, *et al.* A randomized trial of immunotherapy for persistent genital warts. *Hum Vaccin Immunother* 2012;8:623-9.
- Hosseini SM, Shoeibi N, Ebrahimi R, Ghasemi M. Patterns of uveitis at a tertiary referral center in Northeastern Iran. *J Ophthalmic Vis Res* 2018;13:138-43.
- Soheilian M, Heidari K, Yazdani S, Shahsavari M, Ahmadi H, Dehghan M. Patterns of uveitis in a tertiary eye care center in Iran. *Ocul Immunol Inflamm* 2004;12:297-310.
- Vos AG, Wassenberg MW, de Hoog J, Oosterheert JJ. Diagnosis and treatment of tuberculous uveitis in a low endemic setting. *Int J Infect Dis* 2013;17:e993-9.
- Sanghvi C, Bell C, Woodhead M, Hardy C, Jones N. Presumed tuberculous uveitis: Diagnosis, management, and outcome. *Eye (Lond)* 2011;25:475-80.
- von Huth S, Øvrehus AL, Lindahl KH, Johansen IS. Two cases of erythema induratum of Bazin – a rare cutaneous manifestation of tuberculosis. *Int J Infect Dis* 2015;38:121-4.
- Babu AK, Krishnan P, Dharmaratnam AD. Erythema induratum of Bazin – Tuberculosis in disguise. *J Dermatol Dermatol Surg* 2015;19:66-8.
- Scott M, Nakagawa M, Moscicki AB. Cell-mediated immune response to human papillomavirus infection. *Clin Diagn Lab Immunol* 2001;8:209-20.
- Nunes RA, Morale MG, Silva GÁ, Villa LL, Termini L. Innate immunity and HPV: Friends or foes. *Clinics (Sao Paulo)* 2018;73:e549s.
- Yang J, Pu YG, Zeng ZM, Yu ZJ, Huang N, Deng QW. Interferon for the treatment of genital warts: A systematic review. *BMC Infect Dis* 2009;9:156.
- Gao XF, Yang ZW, Li J. Adjunctive therapy with interferon-gamma for the treatment of pulmonary tuberculosis: A systematic review. *Int J Infect Dis* 2011;15:e594-600.