·Letter to the editor·

Limbal leproma in lepromatous leprosy

Irimpan Lazar Francis [1], Nadir Ali Mohamed Ali [1], Pemasiri Upali Telisinghe [2], Nayan Joshi [1]

[1]Department of Ophthalmology, RIPAS Hospital, Bandar Seri Begawan, Brunei Darussalam
[2]Department of Pathology, RIPAS Hospital, Bandar Seri Begawan, Brunei Darussalam
Correspondence to: Nadir Ali Mohamed Ali. Department of Ophthalmology, RIPAS Hospital, Bandar Seri Begawan, Brunei Darussalam. nadiramali@hotmail.com
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Dear Sir,

We are writing to you to present an unusual case of leproma growing at the limbus of a lepromatous leprosy patient. This the first report of ocular leprosy in Brunei, where leprosy is extremely rare.

Leprosy, otherwise known as Hansen's disease, is a chronic granulomatous communicable infection caused by Mycobacterium leprae and its genetic variant (Mycobacterium lepromatosis)[1]. A leproma is a superficial, circumscribed, discrete granulomatous nodule rich in lepra bacilli, a characteristic lesion of lepromatous leprosy. Transmission of the infection in humans occurs by prolonged and/or proximate contact with a sufferer of leprosy. The exact portal of entry is unknown but skin and upper respiratory tract are considered as probable portals. Mode of transmission is probably by droplet infection. Lepromatous leprosy is more easily spread. Incubation period in humans ranges between 6 months to 8 years. Leprosy can manifest in different forms, depending on the host response to the organism. World Health Organization (WHO) classifies leprosy depending on the bacterial load into two groups - namely, Paucibacillary and Multibacillary leprosy. Ridley-Jopling's clinical classification comprises: indeterminate type, tuberculoid type, borderline type and lepromatous type. The Neuritic type is an addition in the Indian Classification. There is also a Histoid type, which is considered as an extremely rare variant of lepromatous leprosy by some and a separate entity to others [2]. Histoid leprosy is an uncommon form of multibacillary infection.

The prevalence of leprosy in Brunei Darussalam is very scanty. This case report illustrates a rare case of Histoid lerpomatous leproma of the limbus in the left eye in a Bruneian adult with no history of previous leprosy or contact with any known leprosy patient.

A healthy-looking 30-year-old Malay, male, employed as Airline Service personnel presented to the Eye Clinic with the chief complaint of slowly enlarging swelling in his left eye for 3 weeks, associated with painless blurring of vision. No history of redness, pain, watering, discharge or photophobia. No history of trauma. His past ocular history was unremarkable. Past medical history was otherwise normal. There was no pertinent family, personal or social history. No history of allergy. He had received all basic immunizations.

Examination showed a pleasant, co-operative, moderately built and nourished male not in acute distress. His visual acuity was 6/6 in his right eye and 6/18 in his left eye improving to 6/9 with pin hole. Intraocular pressure was 14 mmHg in both eyes. Ocular adenexae and eyelids were normal in both eyes. The right eye examination was normal. Left eye showed mild perilimbal congestion with a circumscribed nodular, firm, swelling; about 5mm in diameter, not tender and elevated by 2mm above ocular surface. It was located between 9 and 12'o clock position. The conjunctiva over the swelling was oedematous and freely mobile with engorged conjunctival blood vessels coursing over it. There were no abnormal blood vessels. There was an upper nasal sectoral interstitial keratitis extending to the mid-pupillary area with deep and superficial vascularization of the cornea (Figure 1A), with an elevated mass extending on the sclera (Figure 1B). Corneal sensation was normal. Anterior chamber was moderately deep except at the area of corneal swelling due to interstitial keratitis. There was no anterior chamber reaction. Pupils were round, brisk and equal with no afferent pupillary reaction. Iris was free. Gonioscopy of the left eye showed an open and wide angle all round except at the area of interstitial keratitis, where angle was not visible. Both fundi showed no abnormalities.

Systemic examination showed facial macules, thickening of ear lobes and painless freely mobile subcutaneous nodules

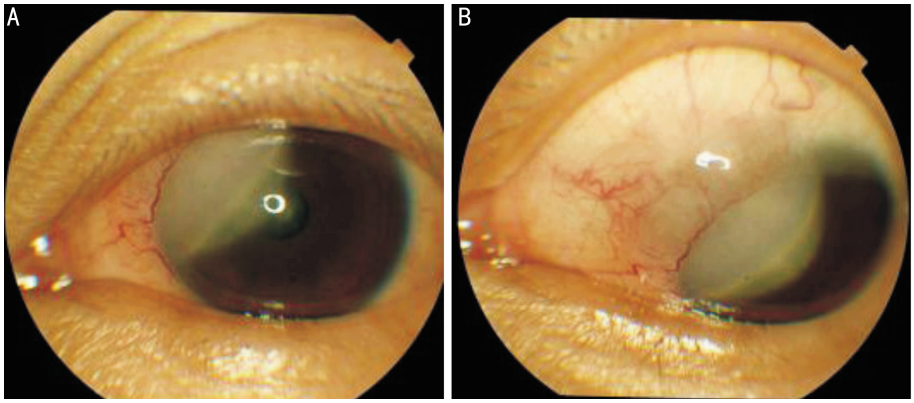

Figure 1 Left eye A: A triangular area of interstitial keratitis with the base extending from 9 to 12' o clock, and the apex reaching the visual axis; B: Extension of the lesion on the sclera

on the outer aspects of his hand and thighs without discolouration, drying, scaling or anaesthesia. A scaly, elevated, plaque was seen on the right elbow (Figure 2).

Routine blood investigation was done and found to be normal, except for a mildly low red blood cell count (4.34× 10^{12}/L) and Hemoglobin (13.1G/DL), and a raised erythrocyte sedimentation rate (ESR) (35mm/Hr). In addition, he turned to be G6PD deficient.

He was referred to the Dermatology department for further assessment. A punch biopsy from the left forearm was taken for histopathological studies, and confirmed the diagnosis of lepromatous leprosy. Microscopy of the tissues revealed the presence of several granular to foamy histiocytes in the oedematous sub-epithelial stroma on HE stain (Figure 3A). The surface squamous epithelium was mildly acanthotic in focal areas. Wade-Fite (Figure 3B) stains showed multiple acid-fast bacilli within the histiocytes as well as in the interstitial tissue. Moreover, several of these bacilli were also present in the upper layer of squamous epithelium, confirming the diagnosis of left histoid leproma of the corneal limbus. An Ear lobe smear also showed abundance of acid fast bacilli, a feature consistent with lepromatous leprosy.

Two incisional biopsies were taken under topical anaesthesia from the limbal nodule of his left eye for histopathological study. The histological findings were similar to those found in the skin biopsy (Figure 4 A, B).

The patient was given a briefing on the diagnosis, treatment, possible after-effects and follow-ups. The case was notified to the Disease Control division in the Ministry of Health, Brunei Darussalam. He was started on Gutt Neomycin/ Dexamethasone qid, 2 hourly; in his left eye for a week, but it was stopped due to steroid-induced rise in intraocular pressure. A milder steroid, Gutt. Fluorometholone, was started instead and administered 4hourly in his left eye. He

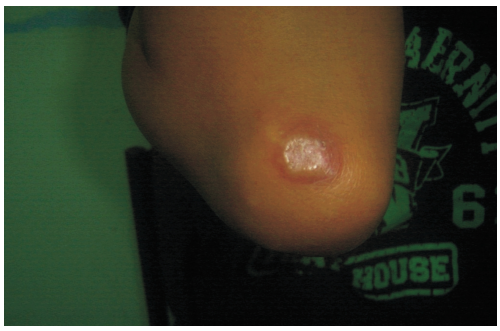

Figure 2 An eroding histoid nodules manifesting as a scaly elevated lesion on the right elbow

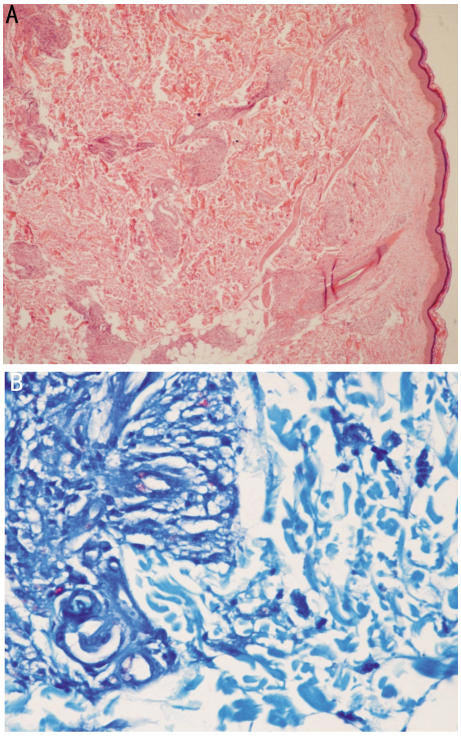

Figure 3 Histopathology of the skin biopsy A: HE section showing circumscribed subcutaneous histiocytic granulomatous lesions (continuous arrow) with ill-defined aggregates of granular, foamy and vacuolated macrophages (dash arrow) including mono- and multi-nucleated histiocytes admixed with fair number of lymphocytes; B: Acid-fast bacilli seen on Wade Fite staining

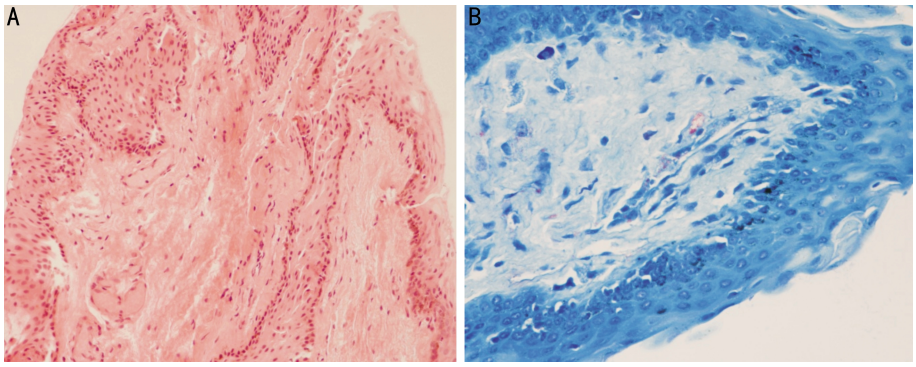

Figure 4 Histopathological features of the limbal biopsy resembled that of the skin biopsy A: H & E staining; B: Wade Fite staining

was reviewed conjointly in both Ophthalmology and Dermatology clinics every two weeks. Intraocular pressure dropped to normal limits afterwards. Simultaneously, he was started on monthly once supervised administration of oral Rifampicin 600mg and Clofazimine 300mg followed by self-administered oral Clofazimin 100mg on alternate day. This oral medication regimen is to be continued for a further period of two years.

After six weeks follow-up, facial macules had significantly reduced and ear lobules appeared normal. The subcutaneous nodules had completely disappeared. Ocular examination showed that visual acuity had improved to 6/9 in the left eye, and remained 6/6 in the right eye. In the left eye, there was minimal perilimbal congestion, limbal leproma reduced in size and extent, conjunctival oedema disappeared corneal oedema reduced, and interstitial keratitis regressed from the pupillary area to the pupillary border with the presence of ghost vessels. His oral medications were continued with monthly reviews. The frequency of Gutt Fluoromthalone was reduced to four times a day for two weeks; then tapered to stop over a month time.

Leprosy is responsible for 5% of blindness worldwide [3]. It has the highest incidence of ocular involvement than any other single systemic disease [4]. Ocular involvement is reported to be as high as 85.5% [5], with the highest involvement in lepromatous leprosy [5,6]. The incidence of leproma of the eye is reported to be 0.75 to 1% among lepromatous leprosy patients. Most lepromas in the eye are reported to be in relation to the ciliary body with uveitis [7, 8] and infrequently cornea [9].

The ocular involvement in leprosy may be due to (a) primary infection of the ocular adenexa; (b) secondary to nerve involvement; (c) due to direct invasion of the anterior segment of the eye with gradual spread to conjunctiva and cornea; (d) sensitization of ocular tissues by the presence of mycobacteria either locally or elsewhere in the body. Primary ocular manifestations of leprosy include madarosis, lagophthalmos and ectropion of the lids, chronic conjunctivitis, corneal anaesthesia, corneal nerve thickening, interstitial keratitis, corneal ulcer, episcleritis and/or scleritis and uveitis. In general, the ocular clinical picture of leprosy is usually mixed, with multiple features involving several eye structures. In this case, the ocular presentation was confined to the limbus and cornea only, with no other ocular manifestations.

Prevalence of interstitial keratitis ranges between 3% to 20% among lepromatous leprosy patients [10,11]. The upper temporal quadrant of the cornea is the most common location for lepromatous interstitial keratitis and the condition is often bilateral [12]. In our case, the interstitial keratitis was the primary presentation; it was uniocular and located in the upper nasal quadrant in the left eye.

Histoid leprosy is a well-recognized rare expression of multi-bacillary leprosy with characteristic clinical and histopathological features. This condition was first described by Wade in 1963 [2]. It is characterized by multi-organ involvement namely, skin, eyes, nerves, bones, liver and muscles. The histoid lesions commonly appear as smooth, hemispherical, non-tender, soft to firm subcutaneous nodules on an otherwise normal looking skin. Histologically, these lesions are composed of abundance of histiocytes with copious amounts of acid-fast bacilli. The prevalence of the histoid variant of lepromatous leprosy is about 1.8% to 3.6% of all lepromatous leprosy cases [13,14]. It is mostly reported in patients who had received dapsone as monotherapy for the treatment of their leprosy. Some cases were reported several years after effective completion of multi-drug therapy, as a relapse [15]. Though extremely rare, it has also been reported in newly diagnosed patients who have not received any treatment [16]. Our patient developed histoid variant of lepromatous leprosy *de novo*, as he never had history of leprosy or contact with a known leprosy patient.

In Brunei, only 9 cases of leprosy were detected among citizens in the period from 1993 to 2010 [17]. This reflects the

rarity of leprosy in the country. This is the first reported case of leprosy presenting with ocular manifestations in Brunei.

In conclusion, leprosy should be considered in the differential diagnosis of interstitial keratitis and limbal masses, even in counties where leprosy is extremely rare. As the resistant lepra bacilli load is very high in these patients, they can form a potential reservoir of infection in the community, wherein leprosy is very sparse.

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