Should we persist with the term Lazarine leprosy? A historical perspective

Neelakandhan Asokan, Vijesh Valsalan

Department of Dermatology & Venereology, Government Medical College, Thrissur, Kerala, India.

Introduction

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*. The clinical spectrum varies from tuberculoid to lepromatous depending on host immunity. Lazarine leprosy constitutes an unusual presentation of leprosy.[1]

The term 'Lazarine' is derived from the name of a beggar, Lazarus in the Bible. According to medieval tradition, he suffered from leprosy, although not mentioned so in the Bible.[2] The literature concerning Lazarine leprosy is confusing as there is considerable overlap between the use of terms Lazarine leprosy and Lucio phenomenon. Additionally, the term Lazarine leprosy has been used to describe other ulcerative phenomena in leprosy, especially in malnourished patients, and as a manifestation of type 1 and type 2 lepra reactions. In this narrative review, we explore the context and clinical scenarios in which the term 'Lazarine leprosy' has been used in the literature. The articles were initially retrieved by PubMed search using the term 'Lazarine leprosy'. More articles were accessed using cross-references of the retrieved articles. After analysing these sources, we present our opinions on the relevance of the term 'Lazarine leprosy'.

Lucio phenomenon described as Lazarine leprosy

Ladislao de la Pascua (1844) is credited with describing Lazarine leprosy or the 'spotted disease' for the first time.[3] In 1852, Lucio and Alvarado described it as a form of ulcerating disease occurring in diffuse non-nodular leprosy.[4] Frequent reactional episodes occurred with scarlet spots that subsequently darkened and ulcerated, leaving atrophic and hypochromic scars with a hyperpigmented border. In 1948, Latapi and Zamora added some more features to the original description by Lucio and Alvarado and renamed it as Lucio phenomenon occurring in pure primitive diffuse leprosy.[5,6]

What Lucio and Alvarado described as the "disease of St. Lazarus" was probably renamed as Lucio phenomenon later. This probably resulted in the interchangeable use of the terms 'Lazarine leprosy' and 'Lucio phenomenon' by several subsequent authors.

Lazarine leprosy in malnourished patients

Skinsnes and Higa (1976) suggested that severe ulcerative phenomena occurring in lepromatous leprosy may be triggered by an infection in the presence of protein malnutrition with resultant immunological breakdown.[2] Protein malnutrition was suggested as the major cause of ulceration in these patients. Hypoproteinemia impairs both cellular and humoral immunity, increasing the susceptibility to infections by pathogens, such as streptococci and staphylococci. Intense tissue oedema secondary to reduced osmotic pressure increases the probability of ulceration. Strobel *et al.* (1979) reported cases of lepromatous leprosy with extensive ulceration and cachexia and suggested the use of the terms 'Lucio phenomenon' or 'Lazarine leprosy' for such cases.[7] Ramu and Dharmendra (1978) sought to differentiate Lazarine leprosy from Lucio phenomenon.[8] They suggested that Lazarine leprosy occurs near the tuberculoid end of borderline leprosy in debilitated patients.

Ulcerated type 1 reaction reported as Lazarine leprosy

In 1930, at the fifth international congress of leprosy, it was concluded that Lazarine leprosy may occur in the tuberculoid pole because of high inflammation and in the lepromatous pole because of high bacillary load.[9] Bhat *et al.* (2013) reported a case of ulcerating type 1 lepra reaction in a HIV+ patient with immune reconstitution inflammatory syndrome, mimicking Lazarine leprosy.[10] Sunandini *et al.* (2015) reported two cases of

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Corresponding author: Dr. Neelakandhan Asokan, Department of Dermatology & Venereology, Government Medical College, Thrissur, Kerala, India. asokann65@gmail.com

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Table 1: A summary of different clinical conditions described as 'Lazarine leprosy'

Clinical conditions	Authors	Year	Country	Patient details	Remarks
Lucio phenomenon	Lucio, Alvarado[4]	1852	Mexico	Not available	Described as 'spotted disease'
Ulcerated type 1 lepra reaction	Bhat *et al.*[10]	2013	India	The patient on HAART developed BT lesions which subsequently ulcerated.	As a part of immune reconstitution inflammatory syndrome in HIV
	Sunandini *et al.*[11]	2015	India	One patient in BT, and another in BL	Two cases of Type 1 reaction with ulceration
	Tripathy *et al.*[12]	2018	India	BT patient with facial lesions	Facial Lazarine leprosy in an immunocompetent patient without underlying malnutrition
	Wankhade *et al.*[13]	2020	India	BT patient with features of Type 1 reaction and intense ulceration	Nil
In malnourished patients	Skinsnes and Higa[2]	1976	China	An experimental study in rats	Suggested that severe ulcerative phenomenon occurring in lepromatous leprosy may be caused by malnutrition
	Strobel *et al.*[7]	1979	France	In patients of lepromatous leprosy with cachexia	Nil
Ulcerated type 2 lepra reaction	Strobel *et al.*[16]	1981	France	One patient with ulcerating erythema *nodosum* leprosum	Used the term Lazarine leprosy as an alternative term for ulcerating ENL
Other clinical presentations in leprosy	Nanda *et al.*[17]	2004	India	Two patients in BT spectrum	Both had BI 2 +, and tissue oedema; One patient was poorly nourished; No evidence of severe malnutrition, infection, or defence breakdown in both

HAART: Highly active antiretroviral therapy; BT: Borderline tuberculoid leprosy; HIV: Human immunodeficiency virus disease; BL: Borderline lepromatous leprosy; ENL: Erythema nodosum leprosum; BI: Bacteriological index

ulcerating type 1 reaction (one in borderline tuberculoid leprosy, and another in borderline lepromatous leprosy) as Lazarine leprosy.[11] Both had no underlying debilitating conditions.

Tripathi *et al.* (2018) described a case of severe ulcerated type 1 reaction on the face of a lady as Lazarine leprosy. They sought to differentiate it from the Lucio phenomenon, another condition described as Lazarine leprosy in previous literature.[12] Wankhade *et al.* (2020) reported a case of severe ulcerative type 1 reaction as Lazarine leprosy.[13] In their discussion, they mentioned about the Lucio phenomenon being reported earlier as Lazarine leprosy and the role of protein malnutrition as postulated by Skinses and Higa (1976).

Ulcerated type 2 reaction reported as Lazarine leprosy

Cochrane described Lazarine leprosy as a chronic progressive form of ulcerating erythema nodosum leprosum associated with severe systemic illness.[14] After a detailed discussion, Dharmendra and Desikan (1985) acknowledged that reports on Lazarine leprosy are conflicting, but most of the reported cases represent severe ulcerated erythema nodosum leprosum.[15] Strobel *et al.* (1981) reported a case of ulcerated erythema nodosum leprosum as Lazarine leprosy.[16] Fogagnolo (2007) pointed out the inappropriate use of the term Lucio phenomenon for ulcerating erythema nodosum leprosum and described the differentiating features between these two conditions.[6]

Use of the term Lazarine leprosy in other situations

In 2004, Nanda *et al.* reported two cases of borderline tuberculoid leprosy both with two skin lesions each and a bacteriological index of 2 +, who developed spontaneous ulceration of the existing lesions without any other features of lepra reactions, during multibacillary multidrug therapy for leprosy.[17] They described these cases as unique in that they were not in the lepromatous spectrum with high bacillary load; did not display features of lepra reactions, including the Lucio phenomenon; nor had marked malnutrition. A summary of different clinical conditions described as Lazarine leprosy is given in Table 1.

Discussion

There are two characters mentioned as Lazarus (a beggar having sores [Luke 16:19–31] and the Lazarus of Bethany [John 11:1–44]) in the Bible, with occasional conflation between the two.[18] Interestingly, even after several centuries, a similar conflation exists in medical literature too, regarding Lazarine leprosy.

Skinsnes and Higa (1976) had described how the use of term 'disease of St. Lazarus' by Lucio and Alvarado in their paper, resulted in the interchangeable use of the terms 'Lazarine leprosy' and 'Lucio phenomenon' by subsequent authors.[2] After analysing the paper by Lucio and Alvarado, they inferred that the former used the term 'spotted form' to denote the Lucio phenomenon, and used 'the disease of St. Lazarus' to denote leprosy in a general sense. But, unfortunately, subsequent papers probably missed this distinction and used the term Lazarine leprosy for Lucio phenomenon and for several other ulcerative phenomena in leprosy including type 1 and type 2 lepra reactions. Skinsnes and Higa quoted Pardo-Castello and Pineyro (1948) and Wade (1949) who opined against the use of the term Lazarine leprosy.[2,19,20] Despite this,

there has been continued use of the term 'Lazarine leprosy' to describe a variety of ulcerative phenomena - except trophic ulcers - in leprosy, which differ widely in their pathogenesis, clinical features and management. The only common feature among all these reports is marked 'leprous' ulceration.

Thapa (2005) opined that spontaneous ulceration may occur in histoid lesions or lesions with high bacillary load, even in the absence of features denoting type 1 or type 2 lepra reactions or the Lucio phenomenon.[21] He postulated that acute exacerbation of the disease, in which bacterial multiplication surpassed the macrophage population is the likely pathogenesis in such cases.[22] Thapa suggested to refrain from using the term 'Lazarine leprosy' even for such cases.[21]

Recently, an increasing number of ulcerated type 1 lepra reactions are being reported as Lazarine leprosy.[10–13] However, all leprous ulcers are not termed 'Lazarine'. There are several reports of Lucio phenomenon, without describing them as Lazarine leprosy.[23–28] Similarly, several articles do not refer to cases of ulcerating type 1 or type 2 lepra reactions as Lazarine leprosy.

Conclusion

Given the considerable discordance in the nomenclature, it is better to restrict the use of term Lazarine leprosy to describe those rare instances of spontaneous ulceration in leprosy associated with malnutrition, as suggested by Skinsnes and Higa (1976).[2] Ulcerating type 1 lepra reaction, ulcerating type 2 lepra reaction and Lucio phenomenon occurring in Lucio leprosy may better be described as such, instead of as Lazarine leprosy, as they possess distinct pathogenetic and clinical features.

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Conflict of interest
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