Indian J Lepr 2019, 91 : 47-54
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http://www.ijl.org.in

Original Article

Interesting and Unusual Presentation(s) of Leprosy Resulting in Delayed diagnosis

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Received : 24.08.2018 Accepted : 30.12.2018

In the post elimination phase of leprosy programme, it continues to be an important health problem in India. Further various atypical forms are seen resulting in delayed diagnosis. A retrospective analysis of 2 years (January 2016 to December 2017) records of all in and out patients of leprosy cases who were treated at a service hospital in northern India was done. At this hospital a total of 97 leprosy cases were seen during the study period out of which 18 (18.5%) cases where the diagnosis was missed due to various reasons resulting in delay in initiation of MDT were included. These cases were examined to describe the clinical presentation, delay in diagnosis and its significant outcome. 61% (11/18) were males while 39% (7/18) females. 22.2% (4/97) had Histoid Hansen's disease; 22.2% (4/18) had chronic symmetrical polyarthritis, there was no hypoaesthetic or anesthetic patches or enlarged nerves in these patients and these were initially diagnosed and managed as Rheumatoid arthritis. 16.6% (3/18) had spontaneous ulceration of extremities and had no skin infiltration or thickened nerve on examination. Interestingly two of these three patients had associated hypoaethesia of extremities which was not taken into consideration for making diagnosis as no suspicion of leprosy was made, one patient in this group had developed foot drop (L) and Right ulnar claw. 16.6% (3/18) had pure neuritic leprosy while greater auricular nerve thickening was seen in 11.1% (2/18) atypical cases. 5.5% (1/18) patient had swelling of upper lip but there no lesion on face or nerve and was managed by a Dentist. Lichenoid lesions were seen in 5.5% (1/18) cases. Out of 18 atypical cases 83.3% (15/18) were in multibacillary pole while 16.6% (3/18) were in paucibacillary pole. 27.7% (5/18) each were BL and LL while 22.2% (4/18) each were Pure neuritic and Histoid Hansen's. 83.3% (15/18) patients were Bacillary positive. Grade 2 deformity developed in 22.2% (4/18) of these cases. The total duration elapsed between presenting to the primary care giver and the dermatology center where the final diagnosis was made ranged from 2 weeks to 3 years. Increase in awareness about various presentations of leprosy in post-elimination era should be emphasized to the health care physicians as well as other workers involved in detection/diagnosis of leprosy.

Keywords: Hansen's disease, Health care workers, Delayed diagnosis, Multi drug therapy

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Introduction

Leprosy is a leading causes of disability all over the world. Delay in diagnosing and managing leprosy can result in progression of the disease into disability and its transmission. This delay in diagnosis can be a result of a reluctancy on the part of the patient or inability of the primary health care provider to correctly diagnose and manage leprosy.

All over the world, the classical presentation of leprosy like hypopigmented and hypoaethetic patch, enlarged nerves and demonstration of acid fast bacilli on slit skin smear or skin biopsy still remain the basis for diagnosing leprosy. Hence, the perplexing and atypical clinical presentation of leprosy pose a diagnostic challenge even to the most experienced dermatologists. Significant delay in the diagnosis of leprosy is reported up to 10 years or even longer worldwide (Das et al 2007). The prevalence of disability is known to increase in patients who have delay in treatment due to various reasons (Hotez et al 2008). A cross sectional observational study on in-patient and out-patients of our department was done to analyse the cases presenting with atypical clinical presentations and the outcome of delay in diagnosing and treating these cases.

Material and Methods

It was a retrospective analysis done over a period of 2 years between Jan 2016 to Jan 2017 at leprosy center of a tertiary care service hospital which caters for a large special population from northern India. Study included data of both in and out-patient department of this Leprosy center during the said period. Permission from the Institutional Ethical Committee was taken before analysing the data and no personal identifying information was included. Detailed history and examination findings including skin lesions, peripheral nerve thickening and tenderness, signs suggestive of lepra reaction were documented. Patients were classified as per Ridley-Jopling classification & IAL classification (Ridley & Jopling 1966, IAL 1982). The WHO classification was used for grading the disability (Brandsma & Brakel 2003). A total 97 patients reported to the hospital during the study period of 2 years. Patients who had classical numb patch, enlarged or tender nerve or weakness of extremities and were diagnosed clinically as leprosy and started on multiple drug therapy were excluded. 18.5% (18/97) patients of leprosy who either lacked classical presentation of leprosy or where despite signs and symptoms of leprosy, leprosy was not suspected by the concerned health care professionals, were included. The diagnosis of leprosy was made late in these patients after multiple referrals and investigations, hence resulting in delay in treatment. Till such time all these patients were unnecessarily given other drugs except Multi drug therapy. The total delay between the first presentation to the physician and the time when the final diagnosis of leprosy was made was analyzed. Resulting disabilities occurring as a result of delayed in diagnosis and management of these cases with atypical presentation were analyzed.

Results

A total of 97 cases of leprosy were seen during the said period of time in both in and out-patient department of leprosy center of a tertiary care service hospital in northern India. Out of these 97 cases, 18 (18.5%) patients with atypical presentations were included in the study. Of 18 cases 61% (11/18) were males and 39% (7/18) were females. Male to female ratio was 1.5. The age was ranging from 27 years to 57 years with mean age of 44.7. Of the total 18 patients 22.2% (4/18) had Histoid variant of Hansen's disease and presented with skin color to erythematous papules and nodules. One Histoid patient had

Table 1 : Details of cases where diagnosis of Histoid leprosy was missed

Atypical cases confirmed as Histoid				
	Case 1	**Case 2**	**Case 3**	**Case 4**
Initial Presentation	Skin colored papules and nodules	Erythematous to skin colored papules and nodules	Papules/ nodules along with constitutional symptoms	Umbilicated papules and nodules
Initial diagnosis & Management	No diagnosis given Oral & Topical Antibiotics	No diagnosis made Oral Antibiotics given	Bacterial infection Antibiotics	Fungal infection Antifungals
Modality of diagnosis	Clinical examination and skin biopsy	Skin biopsy	Clinical examination and skin biopsy	Clinical examination and skin biopsy
Time lapse between initial reporting & confirmation of diagnosis	2 months	2 month - 2 weeks	2 months	20 days

Table 2 : Cases with arthritis like presentation

Atypical cases presented as Arthritis				
	Case 1	**Case 2**	**Case 3**	**Case 4**
Initial presentation swelling	Pain small joints along with swelling	Pain large and small joints Intermittent swelling of joints	Pain joints and swelling	Pain and small and large joints
Initial diagnosis & Management	Rheumatoid Arthritis Methotrexate & HCQ	Reactive arthritis NSAIDs	Rheumatoid arthritis Methotrexate & HCQ	No diagnosis made NSAIDs
Modality of Diagnosis	Slit skin smear AFB (L)	Skin biopsy from erythematous skin	No response to medicines Trial of MDT successful	No response to NSAIDs
Time lapse between initial reporting & confirmation of diagnosis	3 years	8 months	7 months	1 years

umbilicated lesions and was treated with oral antifungals while others were getting on and off antibiotics with minimal response. Table 1 gives the detailed account of Histoid cases in terms of initial presentation, management, diagnosis and time lapse between initial presentation to a

Table 3 : Atypical Pure neuritic patients and Cases with painless Ulceration

Atypical Pure neuritic patients and Cases with painless Ulceration						
	Case 1	**Case 2**	**Case 3**	**Case 4**	**Case 5**	**Case 6**
Initial presentation	Tingling both lower limbs	Weakness and tingling of right forearm	Numbness of right forearms	Spontaneous bullae formation lower limbs and forearm	Non-healing ulcers both lower and right forearms	Bullous lesions left leg
Initial diagnosis & Management	No diagnosis made Given NSAIDs	No diagnosis Given Multi-vitamins	Vit B 12 def Given Vit B 12	Non healing ulcers Wound debridement and oral Antibiotics given	Diagnosed as Pyoderma Oral and topical antibiotics given topical antibiotics	No Diagnosis made Oral Antibiotics
Modality of Diagnosis	Clinical examination	Clinical examination	Clinical examination	Clinical examination Skin biopsy	Clinical examination Skin biopsy	Clinical examination Skin biopsy
Time lapse between initial reporting & confirmation of diagnosis	1 year 9 months	1 year 9 months	1 year 5 months	1 month 2 weeks	1 year 3 months	1 month 1 weeks

health care provider to the time final diagnosis was made. 22.2% (4/18) patients presented with complaints of chronic symmetrical polyarthritis and polyarthralgia resembling rheumatoid arthritis, pain and joint swelling for which they were managed as case of rheumatoid arthritis. There was no hypoaesthetic or anesthetic patches or enlarged nerves in these patients. 2 of them were also given methotrexate and hydroxychloroquine while other two were taking non-steroidal-anti-inflammatory drug due to which one developed acute renal failure requiring hospitalization while another developed foot drop (R).

Details of atypical cases presenting as rheumatoid arthritis like features is depicted in Table 2. Of the total 18 cases 16.6% (3/18) patients had spontaneous painless ulceration of lower or upper limbs or both and were treated as case of non-healing ulcer and were getting oral antibiotics and wound debridement. There was no skin infiltration or thickened nerve on examination in these patients. Interestingly two of these three patients had associated hypoaethesia of extremities for making diagnosis, one patient in this group had developed foot drop (L) and Right ulnar claw. 16.6% (3/18) patients had pure neuritic form of leprosy and presented with only tingling of upper or lower limbs without any skin lesions and were getting vitamin supplements.

Table 3 summarizes different atypical presentations and management of cases with pure

Table 4 : Details of other cases with missed/delayed diagnosis of leprosy

	Other Atypical Cases			
	Case 1	**Case 2**	**Case 3**	**Case 4**
Initial presentation	Painless Cord like thickening on neck	Painless Cord like thickening neck	Painless swelling of upper lip	Lichenoid eruptions in photo-distribution pattern
Initial diagnosis & Management	EJV thrombosis LMWH	No diagnosis Oral Antibiotics	No Diagnosis made Oral Antibiotics and NSAIDs	Polymorphous light eruptions Topical steroids
Diagnosis confirmed	Skin biopsy	When red patch on face appeared Skin biopsy	No response to medications Skin biopsy	Skin biopsy
Time lapse between initial reporting & confirmation of diagnosis	8 months	3 months	9 months	4 months

neuritic leprosy and ulcers. One patient had only one nerve involvement while other two had 2 nerve involvement each. One of the patients with pure neuritic leprosy was diagnosed to have Vit B 12 deficiency and was on supplements. One patient in pure neuritic group had already developed total claw (R) hand on first visit to a dermatologist as leprosy was never suspected by the first medical contact possibly due to absence of skin lesions and not examining nerves. 11.1% (2/18) patients had greater auricular thickening for which one of them was treated as a case of external jugular vein thrombosis and was on low molecular weight heparin. No confirmation of vascular blockage was done in this case as leprosy was not considered as a possibility. One of the two cases with cord like thickening was under treatment by Otorhinolaryngologist for pain referred to the ear. One of the patients with greater auricular nerve thickening developed red patch during treatment and was referred for dermatology opinion while other patient had no involvement of facial or neck skin. 5.5% (1/18) patient had painless swelling of upper lip which was managed by dentist with antibiotics and NSAIDs. 5.5% (1/18) patient had multiple lichenoid lesions in photo-distributed pattern and was treated as a case of polymorphous light eruption by a Dermatologist prior to further referral. The details of these cases are given in Table 4.

27.7% (5/18) of these patients were borderline lepromatous (BL), 27.7% (5/18) were lepromatous leprosy (LL), 22.2% (4/18) were pure neuritic against 22.2% (4/18) who had histoid leprosy. As per WHO classification 83.3% (15/18) patients were in multibacillary pole while 16.6% (3/18) were in paucibacillary pole. 22.2% (4/18) of 18 patients developed deformities in the form of foot drop (Right), total immobile claw (Right) and one patient had both foot & wrist drop (Left) - The total duration elapsed between presenting to the primary care giver and the dermatology center where the final diagnosis was made ranges from

2 weeks to 3 years. 3 patients who developed disabilities were in multibacillary pole as against 1 patient of pure neuritic leprosy who had paucibacillary leprosy.

Discussion

Leprosy is a leading cause of preventable disability all over the world. Despite the World Health Assembly's highly enthusiastic resolution to eliminate leprosy as a public health problem globally by the year 2020, it remains a cause of significant morbidity especially from the areas with high endemicity (Lockwood & Suneetha 2005) Introduction of Multi Drug Therapy (MDT) for leprosy elimination three decades ago was extremely successful in curing large number of cases and in reducing the prevalence of leprosy globally as well as in India.

The diagnosis of leprosy is based on its classical presentation like hypopigmented, hypoasthetic patches, thickened nerves and demonstration of acid-fast bacilli on histopathology and skin biopsy since decades, however, leprosy is a great imitator and unusual presentations are known to occur in almost all the poles of leprosy. In present study most of these patients with these presentations either reported to the primary health care providers in remote locations where only paramedical staff is available or other specialists who may not be having enough experience in diagnosing atypical cases of leprosy thereby leading to variable delay in diagnosis of leprosy.

Knowledge of leprosy manifestations and a good clinical examination is gradually becoming a forgotten art amongst young doctors and rapid urbanization of the medical facilities in present days. It is a challenge to keep the interest of undergraduates alive in leprosy till the time they actually work on ground especially with reduced prevalence of leprosy all across the globe.

Still, it will be an over simplification to commit that rare forms of leprosy are easily diagnosed by dermatologists. The end result of this delayed diagnosis is resulting disability and a possibility of transmission of the disease to the community. In this era when we have eliminated leprosy and its prevalence has declined globally too, occurrence of disability is an indicator of existing lacunae in its implementation of leprosy eradication programme in different settings.

Amongst the forms of leprosy which are often missed at various levels of health care is Pure neuritic form of leprosy. It is a well-recognized form which still remains an enigma due to its clinical and management ambiguities. World over, skin and nerve involvement is considered as a hallmark of leprosy, hence in such scenario it is highly possible for paramedical staff, the leprosy workers on whose shoulder the entire leprosy eradication programme is dependent upon and other specialists who are also not well aware with this clinical variant to over-look leprosy as a differential diagnosis (Kumar et al 2012). Clinically it presents as peripheral neuropathy with functional impairment of single or multiple nerves but lacks cardinal features of leprosy. It is easier to be missed as leprosy and emphasis is more on looking for a classical patch of leprosy. These patients are often diagnosed late and after receiving multiple medications other than MDT. The outcome of this delay can result in deformities and disabilities (WHO 1991). Studies have found that paralytic deformities are highest (26%) among neuritic leprosy patients (Zhang et al 1993). We also had 4 cases of pure neuritic leprosy with varying presentation who were diagnosed late out of which one had developed grade 2 deformity.

Spontaneous ulceration of extremities is often dealt by health care workers and at times go missed as leprosy due to lack of examination for hypoaesthesia of the limbs. 3 of the cases we observed during the study had this presentation,

out of which two had associated hypoaesthesia which was not evaluated. A significant 2 of these cases developed grade 2 deformity prior to further referral to a skin center. Although rarely, but rheumatologist can encounter leprosy as primary arthritis or a coexisting infection or complication of therapy as some form of joint involvement is known to occur in 75% cases of leprosy and at times may be the only presentation of leprosy (Rao & Suneetha 2016). We encountered four cases with joint involvement in our study. Although histoid variant of leprosy is a known variant of the disease, the lack of knowledge about it amongst the primary health care provider and patients can result in delay in diagnosis. Schreuder (1998) reported that multibacillary cases have a higher chance of developing disability which was observed in our study also.

Although leprosy is an ancient disease and is showing a consistent decline in prevalence globally and in India, the delay in the diagnosis is still very common. The occurrence of disability at the time of diagnosis of the disease suggest that further efforts are required at timely diagnosis and management of the disease, to avoid the long-term sequelae associated with nerve damage and possibility of disease transmission.

Unusual presentations of leprosy continue to be reported from time to time, these may pertain to Histoid leprosy (Vora et al 2014, Meena et al 2017), nerve thickening confused with jugular vein thrombosis (Ramesh et al 2007), granuloma annulare like lesions/erythema multiforme like lesions (Das et al 2007), arthritis as dominant symptoms (Chauhan et al 2010, Prasad et al 2013, Pruthi et al 2016), plaques on unusual sites/ resembling other dermatoses (Sajad et al 2015, Yang et al 2018), other atypical neurological manifestations (Tayshetye et al 2013). Health care workers and physicians including specialists belonging to different specialities need to be aware of such atypical presentations. Our study adds to that experience of initial care givers not been able to diagnose many of such cases. It is important to urgently evaluate and modify the case evaluation system currently in place and to assess the diagnostic suspicion of the first contact in these cases and to make these points as awareness points in imparting further knowledge to health care workers.

While carrying out this analysis we found that apart from lack of awareness of these forms in some cases, there was lack of proper efforts in examining and investigating some others. No documentation of sensations or muscle examination findings was made. We recommend that timely action is required to sensitize our young professionals, medical officers and paramedical staff in remote and peripheral locations to the rare forms of leprosy, role of good clinical examination and openness to refer the patient further in case of difficulty to arrive at a diagnosis after proper investigation.

Conclusion

This study emphasizes the importance of highlighting the atypical presentation(s) of leprosy which may be missed by heath care providers and result in delay in their diagnosis and management sometimes resulting in preventable long-term sequelae in terms of disability. Apart from this it also resulted in unnecessary treatment with drugs other than multi-drug therapy resulting in acute renal failure in one patient possibly due to NSAIDs. Furthermore, these cases in multibacillary pole will also have higher potential of transmission of the disease. Despite a decline in the prevalence of leprosy all through the world, it is highly recommended to expect an encounter with such forms of leprosy especially in endemic regions. Sensitization of medical students to suspect leprosy where other possibilities are

ruled out after careful clinical examination and investigation and seeking for opinion of a Dermatologist/medical professional trained in leprosy despite absence of hypoaesthetic patch may be a small step in this regard. Early diagnosis, prompt treatment and disability prevention are the road to avoid these consequences.

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How to cite this article : Saraswat N, Agarwal R, Chopra A et al (2019). Interesting and Unusual Presentation(s) of Leprosy Resulting in Delayed diagnosis. *Indian J Lepr.* **91**: 47-54.