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Letter to Editor

Response to letter/ correspondence titled, "Hidden Invader or Hidden Errors? A Critical Review of a Case Report"

G Bashir[1], M Aman[2], AS Malik[3], S Wani[4], T Qayoom[5], IN Ahangar[6]

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We are highly thankful to Herlekar et al for their keen reading and reviewing our case report (Bashir et al, 2025, titled "A new case of Leprosy with Atypical Morphotype on Slit Skin Smear-Unmasking a Hidden Invader").

To summarize, the patient was a young male with history of nonhealing ulcer left foot with osteomyelitis and fracture of 1st and 2nd metatarsals and hypo-aesthetic lesions on back with decreased right ulnar nerve sensations with bilateral sural nerve palsy. Skin slit smear showed broken AFB resembling *Mycobacterium leprae.* The patient was discharged from this hospital as a case of leprosy and attached to dermatology for further management. Follow up report from dermatology OPD: The patient was attached to leprosy clinic of his native district for enrolment and for MDT collection as a case of BT leprosy, not in reaction, with an advice to start on MDT (MB).

Our response to observations of Herlekar et al is as follows:

Comments of Herlekar et al	**Reply**
The title of the case report having new words like "atypical morphotype" and "hidden invader" related to leprosy attracted our attention.	The title of the case report has been formulated to catch attention of readers, and we are really delighted that the title has invited your attention.
1.The case report mentions a young male presenting with a non-healing ulcer on the left foot for several years and several hypopigmented lesions over the back. While the authors are right in suspecting Hansen's disease- the subsequent case description	The case report being published from the Department of Microbiology of a tertiary care hospital, highlights the microbiological aspect of the case. **Clinical history and presentation of the case:** **On 05/06/2024:** The patient was admitted in the Department of Medicine under unit of Rheumatology of this hospital: the patient presented as case of non-healing ulcer left foot.

[1] Gulnaz Bashir, MBBS, MD, Professor
[2] Munaza Aman, MBBS, MD, Senior Resident
[3] Amir Sayed Malik, MBBS, MD, Senior Resident
[4] Sayam Wani, MBBS, MD, Senior Resident
[5] Tabish Qayoom, MBBS, Postgraduate scholar
[6] Irfan Nisar Ahangar, PhD (Microbiology), Tutor
Department of Microbiology, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, Jammu & Kashmir-190011, India
Corresponding Author: Dr Munaza Aman, **Email:** drmunaza27aman@gmail.com

is incomplete. There is no mention of neurological complaints / deficit in the patient, no neurological examination to elicit hypoesthesia/ anaesthesia, nerve thickening, tenderness etc. including the area around the ulcer and also any motor deficit.	**Medical history: The** patient was apparently alright two years back when patient noticed vesicular lesion on sole of left foot. The lesion was painful, non-erythematous and over next few days the vesicle cleared with non-healing defect at base of lesion. The defect at base of lesion persisted for 2 to 3 months, and patient availed medical advice from local practitioners of his native village. The patient was treated with multiple antibiotics (records not available with the patient) and ASD was applied. The lesion appeared to heal, however, after resuming activity the lesion worsened. 5 - 6 months later the patient noticed swelling in left foot and was diagnosed as case of arthritis, was on treatment for same (no medical record available). In 2023 MRI left foot revealed fracture of left 1st and 2nd metatarsal. Second MRI (March 2024) revealed septic arthritis 1st and 2nd metatarsophalangeal joint of left foot. There is history of fascial nerve palsy left side LMN type (June 2023). **Physical examination summary:** On examination**:** Patient was conscious, oriented, cooperative, afebrile, all vitals – within normal limits. **Local examination:** Hypopigmented, non-tender, non-pruritic lesions on back with decreased pain, touch, temperature sensation in centre. Bilaterally thickened ulnar nerves. Decreased sensation in the dermatome innervated by right ulnar nerve. Bilateral sural nerve palsy. Vasculitis was ruled out. Rest of physical examination was unremarkable. **On evaluation:** multiple investigations were ordered including microbiological sample collection for AFB (Slit Skin Smear). Investigations including ANA, C-ANCA, P-ANCA, RF, anti CCP were negative. HRCT chest -normal.

	After catching attention on smear microscopy for AFB- (morphologically characteristic acid-fast broken bacilli), skin biopsy from edge of lesion was ordered which revealed superficial perivascular lymphoid infiltrate on histopathological examination by a national reference laboratory (LPL-National Reference Lab, New Delhi) suggestive of indeterminate Hansen's- on histopathology examination**.** **Case summary:** Young male with h/o nonhealing ulcer left foot with osteomyelitis and fracture of 1st and 2nd metatarsals with hypo-aesthetic lesions on back and decreased right ulnar nerve sensations with B/L sural nerve palsy, skin slit smear showing broken AFB resembling *Mycobacterium leprae* discharged from this hospital as a case of leprosy on 16/06/2024 and attached to dermatology for further management. Follow up report from dermatology OPD: The patient was attached to leprosy clinic of his native district for enrolment and for MDT collection as case of BT leprosy, not in reaction, with an advice to start on MDT (MB).
2. The authors have mentioned in the history about the treatment of arthritis in the past with no further details. Joint involvement in a young person is a serious disease and can be seen in many diseases and also in the whole spectrum of leprosy, with acute involvement in episodes of reaction. No details about diagnosis or treatment are given.	This is a case of 20-year-old male, presented with history of non-healing ulcer left foot. The subjective medical history of patient revealed treatment for arthritis in past, rest was insignificant with no history of intake of anti-leprosy drugs, trauma, comorbidity, fever or myalgias.
3.The authors provide extensive details about the slit skin smear-its methodology and staining etc. which are well known and well described in the existing guidelines. But the authors missed on their readings and interpretation. Terms like 'a few AFB seen' is not the accepted protocol to describe it. That is why probably, the actual bacteriological (BI) and morphological index (MI) in this patient has not been given. Scientific terms like 'solid' 'granular' and 'fragmented' bacilli should have been used.	An extensive detail about the slit skin smear-its methodology has been described to catch attention of the practitioners/ clinicians for proper smear making as the results depend on properly collected sample. The procedure being invasive should be done very meticulously. The case report being published from the Department of Microbiology highlights the microbiological aspect of the case. The readings (very few bacilli) and interpretations have been done as per guidelines given in reference no. 5 of our manuscript (HRSA 2024).

4.The patient has been labelled as a case of 'indeterminate leprosy' primarily on the basis of histopathological findings of 'superficial perivascular lymphoid infiltrate' which alone does not indicate any form of leprosy. Presence of multiple hypopigmented lesions on the back, presence of AFB in the skin smear (even though the picture is of a very poor quality) and a trophic ulcer on the left foot have been totally ignored. Presence of AFB in the skin smear is sufficient to classify the disease as multibacillary, according to revised WHO classification. The wrong classification has put the patient in risk of getting no treatment (observation only) or inadequate treatment, which will be a disaster.	Presence of multiple hypopigmented lesions on the back, and a non-healing ulcer on the left foot have actually prompted for SSS. Presence of broken AFB in the SSS encouraged to advise for HPE which showed 'superficial perivascular lymphoid infiltrate'. Hansen's disease was definitely diagnosed on the bases of microbiological, HPE and clinical records available. After catching attention on smear microscopy for AFB (broken bacilli) the patient was attached to dermatology and leprosy clinic for the proper treatment and follow up as per recommended guidelines. The dermatologists and the treating physicians at leprosy clinic are aware of the latest classification and treatment protocol and **had put the patient on MDT.** In the discussion part of the case report, the patient has been discussed as per WHO guidelines as multibacillary case. As WHO guidelines state: **Multibacillary (MB) case:** A case of leprosy with more than five skin lesions; or with nerve involvement (pure neuritis, or any number of skin lesions and neuritis); or with the demonstrated presence of bacilli in a slit-skin smear, irrespective of the number of skin lesions (WHO 2018). The patient has not been labelled as a case of 'indeterminate leprosy'. However, the HPE report has directly been quoted under sub-heading "*mycobacteriological examination*" in case report.
5.In the context of a non-endemic region (stressed too often) it would have been valuable to describe whether contact tracing was attempted. Examination of close contacts is essential both for early detection and preventing transmission and development of complications / deformities.	After catching attention on smear microscopy for AFB (broken bacilli) the patient was attached to leprosy clinic and for dermatological consultation for proper treatment and contact tracing.

6.The central issue is about the terms used as in the title of the case report- "atypical morphotype" and "hidden invader". The authors have expressed great concern about 'broken AFBs' in the SSS, "it being an uncommon microbiological picture, which should not be overlooked". This observation even made them to state "hence to diagnose a new case of borderline leprosy with a picture of atypical morphotype of *Mycobacterium leprae* (broken AFB) on SSS in this non endemic area is a great challenge"- a totally unacceptable statement.	In this case all the bacilli were broken/fragmented which can be overlooked on microscopy as there were no solid staining bacilli. The stress has been made upon 'broken AFBs' in the SSS, being an uncommon microbiological picture, from an area where the cases of leprosy are not very common. And hence a message that such a picture should not be overlooked. The statement "hence to diagnose a new case of borderline leprosy with a picture of atypical morphotype of *Mycobacterium leprae* (broken AFB) on SSS in this non endemic area is a great challenge" has been written to highlight the case being suffering from an unhealed ulcer since many years and the attention towards leprosy as a differential diagnosis has been made now. Hence giving a clue to clinicians that there could be cases of leprosy more than the number we are predicting. Hence stressing upon not to miss such a picture on SSS.
7.The authors seem to be fascinated / intrigued by the presence of granular, fragmented, broken bacilli and it made them to label these with such new terms as 'atypical morphotypes' and 'silent invaders. They further warn of the great repercussions on the patient and society especially because these 'hidden invaders' can remain in the 'sub clinical form for decades. They again sound an alarm to the microbiologists to explore the 'hidden invader' with atypical morphotype.	The terms as 'atypical morphotypes' and 'silent invaders have been used in the title of the case report to make it catchy and attention seeking so as to make all healthcare workers and the ones especially working at ground level not to miss this picture of broken bacilli on SSS.
8.To justify their theorization/ presumption about the presence of these 'broken bacilli' – they cite the role of medication for arthritis which may have included TNF-α inhibitors, the antibiotics which the patient may have been prescribed for his non healing ulcer (no details however are given) to cause immunosuppression and partially affecting the AFBs to cause their disruption i.e. brokenness.	Literature has well explained the potential of many drugs like minocycline, ofloxacin, moxifloxacin, levofloxacin and clarithromycin against this bacillus (Ji et al 1991, Cogen et al 2020, already cited in our publication – Bashir et al).

9.The authors probably because of lack of complete technical information have imagined all this without realizing that- 'granular' and 'fragmented' bacilli are present normally in all slit skin smears-irrespective of treatment. Reading about morphological index (MI) would have saved the authors a lot of trouble.	We have highlighted the picture of granular and fragmented bacilli can be present even after treatment with non-leprosy drugs. Morphological index- Solid Bacilli/Total Bacilli (broken + solid). Since all bacilli were broken, so MI was zero.

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