

SHORT PAPER

Hansen's disease in the era of COVID-19: An observation on a series of six patients with co-infection

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Abstract

Since the onset of the present pandemic, effect of the novel corona virus on other infectious conditions continues to be investigated. Although the immunological responses to SARS-Cov-2 infection have been elaborated extensively, they fail to explain, variations in its clinical manifestations and its interaction with other diseases. Hansen's disease is known to present as a complex immunological response to the lepra bacilli, resulting in its varied spectral manifestations. An interaction between these two infectious agents, hence, may affect Hansen's disease. We came across six cases of Hansen's disease who developed COVID19 co-infection. This series presents their clinical course and outcome, during the period of co-infection. All cases were followed up for a minimum eight-week period thereafter. In all these cases the active phase of coronavirus infection had no effect on Hansen's disease and those on prednisolone for their lepra reaction had a more favorable outcome, with two cases manifesting exacerbation of their lepra reactions in the follow period.

KEYWORDS

coronavirus disease, COVID19, Hansen's disease

1 | INTRODUCTION

The effect of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection on preexisting diseases is yet to be fully explored. The immune response to SARS-CoV-2 continues to be a riddle with variable clinical outcomes. This variability is bound to affect other immune responsive diseases such as Hansen's disease. We came across six such cases of Hansen's disease who developed SARS-CoV-2 co-infection. Their course during the period of this co-infection and follow up is elaborated and reported after institutional ethical committee review.

2 | OBSERVATIONS

Six cases of Hansen's disease with coexistent COVID19 infection were managed at the skin centre of a tertiary care hospital between

April 2020 to October 2020. The 04 cases reported with upper respiratory symptoms while 02 were screened following a recent exposure to a positive COVID19 case. Their COVID19 diagnosis was on the basis of a positive reverse transcriptase polymerase chain reaction test (RT-PCR) for SARS-Cov-2 (E and RdRp gene) sampled by a nasopharyngeal swab. The four cases were already on Multidrug Therapy (MDT) as per the standard WHO regimen for Hansen's disease¹ while two were diagnosed afresh and placed on treatment. The 02 cases, intolerant to dapsone were placed on modified MDT (rifampicin 600 mg once a month and clofazimine 50 mg daily), four were on prednisolone for lepra reactions, of which one was placed on thalidomide later.

They were managed at our institution's dedicated Coronavirus Disease (COVID19) facility, and declared free from infection once their SARS-CoV-2 RT-PCR tested negative (tested 10th day after initial detection or every 7 days thereafter in case of persistent positivity). During this period they underwent regular hematological and

TABLE 1 Summary of cases with COVID19 and Hansen's disease

Age	Duration of Hansen's disease up to diagnosis	Duration of MDT	Reason for COVID 19 screening	Spectrum of Hansen's disease	Comorbidity	Treatment	Course of Hansen's disease during COVID19 active phase ^a	Course of COVID19 illness	Status in follow up period
44	3 months	Fresh diagnosis	Screening	Pure Neuritic with Type I reaction with ulnar clawing left hand	Nil	MDT + prednisolone 60 mg/day	Persistent Type I reaction with no change in severity	Uneventful 17 days to RT PCR negativity	Unexplained febrile illness 16 weeks later.
31	2 months	16 weeks	URI	Borderline tuberculoid + Type I reaction with no deformity	Gilberts syndrome	Modified MDT + prednisolone 20 mg/day	Persistent Type I reaction with no change in severity	Uneventful 10 days to RT PCR negativity	Uneventful
32	4 months	8 weeks	Screening	Borderline lepromatous with Ulnar clawing right hand	Nil	MDT + prednisolone 40 mg/day	Uneventful	Uneventful 24 days to RT PCR negativity	Type I reaction 2 weeks later on tapering prednisolone to 20 mg
20	2 months	12 weeks	URI	Pure neuritic with no deformity	Nil	MDT	Uneventful	10 days to RT PCR negativity Desaturation treated with high flow oxygen, Tab Hydroxychloroquine 400 mg BD x 01 day, followed by 200 mg BD x 04 days Tab azithromycin 500 mg OD x 1 day, followed by 250 mg OD x 04 days	Uneventful
30	3 years	7 months	URI	Hansens LL + Type II reaction with no deformity	Nil	Modified MDT, Prednisolone 30 mg OD	Uneventful	Prolonged COVID 19 illness 35 days to RT PCR negativity • Anemia (Hb-6.4), Neutrophilic leucocytosis (92%). • Abnormal peripheral blood smear: Microcytic hypochromic RBCs, fragmented RBCs 2.3%, anisopoikilocytosis, toxic granules and vacuolation in neutrophils, Treatment: Tab Vitamin C 500 mg OD Tab Zinc 50 mg OD Packed RBC 01 unit	• Malaise and tiredness lasted for 4 weeks • Furunculosis • Exacerbation of Type II reaction
24	2 years	Fresh	URI	Pure neuritic with bilateral ulnar clawing	Nil	MDT	Uneventful	Uneventful	Uneventful

Abbreviation: MDT, multidrug therapy.

^aActive phase: time duration to RT PCR for SARS Cov2 negativity.

biochemical screening while radiological investigations were dictated by their clinical profile. All cases were followed up for a minimum period of 8 weeks once they were declared free from infection.

Their response to COVID19 and recovery was variable and is summarized in Table 1.

2.1 | Case 1

A 44-year-old male Hansen's disease-pure neuritic case diagnosed afresh, tested positive at screening for COVID19 following a high-risk exposure to an infected person. He was placed on MDT and exhibited an uneventful course during the next 2 weeks when he tested RTPCR negative. The 16 weeks later he developed an unexplained febrile illness with a normal biochemical, serological and radiological profile. His tests for other prevalent seasonal and endemic illnesses in our region: dengue, malaria, chikungunya was negative. He turned afebrile after 3 days and has remained so ever since.

2.2 | Case 2

A known case of Gilbert's syndrome with Hansen's disease borderline-tuberculoid and type-1-reaction, on modified-MDT and prednisolone for past 2 months (tapered from 60 mg daily to 20 mg daily), presented with symptoms of upper respiratory infection of 3 days. His course during COVID19 illness and follow up was uneventful.

2.3 | Case 3

A 32-year-old male symptomatic for 4 months with Hansen's disease borderline-lepromatous on MDT and type-I-lepra-reaction of 6 weeks duration on prednisolone tapered from 60 mg daily to 40 mg daily was detected positive upon screening post COVID19 high risk exposure. COVID illness and recovery except for a prolonged 24-day period of infectivity was uneventful. His lepra reaction exacerbated 2 weeks later, for which he was reinstated on 60 mg prednisolone daily and is now asymptomatic.

2.4 | Case 4

The 20 year old male with Hansen's disease pure-neuritic on MDT of 3 months duration was detected COVID19 positive following sudden onset febrile illness with cough and low oxygen saturation on room air (89%) which recovered on high flow oxygen. Hematological and biochemical parameters were normal except elevated lactate dehydrogenase (LDH) of 462 U/L. He turned afebrile in 3 days, recovered without sequelae in 10 days with normal LDH levels.

2.5 | Case 5

A case of Hansen's lepromatous-lepromatous on MDT for 7 months, manifested Type 2 reaction at 5 months of MDT, was on tapering doses of prednisolone at 30 mg when he became symptomatic with cough and nasal stuffiness.

He had a prolonged COVID19 illness along with microcytic hypochromic anemia (6.4 g%) and LDH 189 U/L but no lung involvement. He was managed symptomatically along with a single unit of packed red blood cells.

After a prolonged COVID 19 illness of 35 days, he continued to have persistent malaise and tiredness. In the immediate follow up period he had exacerbation of his lepra reaction and multiple furunculosis. He was managed with thalidomide 100 mg four times a day and withdrawal of prednisolone for his Type 2 lepra reaction; amoxicillin 625 mg with clavulanic acid 125 mg thrice daily for 5 days for furunculosis. He is now asymptomatic after 10 weeks on MDT and thalidomide.

2.6 | Case 6

A young 20-year-old male, pure-neuritic Hansen's disease case, symptomatic for past 2 years with mild bilateral ulnar clawing presented in the recovery period of his COVID19 illness. He had remained asymptomatic and recovered in 10 days.

3 | DISCUSSION

Mycobacterium leprae elicits a varied immune response; a specific Th1 and Th17 response preventing its multiplication (tuberculoid spectrum) and a specific Th2 response that allows its dissemination (lepromatous spectrum). Type IV hypersensitivity reaction involving both native and adaptive immune responses drives a switch from Th2 to Th1 manifesting as Type-1 lepra reaction, while a type III hypersensitivity reaction due to a poor cellular immune response and a brisk humoral response leads to Type-2 lepra reaction. The proinflammatory cytokines and chemokines along with complement activation in type 2 reactions result in its skin manifestations and neural damage.^{2,3} However which arm of these immune responses ultimately confer protection are still being explored and their effect on preexisting Hansen's disease is yet to be reported.

As in Hansen's disease, COVID19 illness is known to present with a variable inter-individual response. Studies in COVID-19 patients have demonstrated increased proinflammatory cytokines and chemokines,^{4,5} with an overwhelming initial Th1 response against the virus which forces a switch to Th2 response resulting in excessive organ damage.^{4,5} Some of these as mentioned above also regulate cell-mediated and humoral immune responses to *M. leprae*.^{6,7} It has thus been speculated that cytokine responses in COVID19 infection may alter the clinical picture of Hansen's disease.⁸

In this series patients showed no change in their Hansen's disease course during active COVID19 infection, however one (Case 3) developed a type I reaction on follow up period while another (Case 5) had an exacerbation of his preexisting type II reaction. This possibly reflects the cytokine shift in COVID19 illness, which may have an effect over an extended period of time. Of the four cases already on prednisolone, 3 had an uneventful COVID illness while one lepromatous-lepromatous case (Case 5) had a prolonged illness. Prednisolone as an immunosuppressive agent may be responsible for a suppressed cytokine response resulting in an uneventful COVID19 illness. Case 4 with severe illness had a higher LDH level, no lung involvement, subsiding to normal levels (<180u/l) within the active phase of the disease. Case 5 with severe disease had a marginally raised LDH with maximal rise of 189 u/l which also settled within 10 days to normal values. We are hence unable to comment on its significance in Hansen's disease despite its reported significance in COVID19.⁹ Unexplained short febrile illness in follow up period of case 1 cannot be attributed conclusively to COVID19 illness, unless a larger cohort with similar findings is examined.

4 | CONCLUSIONS

Although limited by a few cases our series brings forth few interesting findings.

Patients may have delayed reactions during the recovery phase despite turning RTPCR negative for SARS-CoV-2. Those on steroids apparently had a less stormy course and uneventful recovery. COVID19 infection caused no clinical effect on Hansen's disease during the active phase.

However, these observations are limited by the smaller number of cases, lack of defined treatment protocol for COVID19 and its coinfection in Hansen's disease. Immune modifying agents for COVID19 treatment may also affect Hansen's disease. Long term follow up of such cases may help in arriving at a definitive conclusion on the effect either of these infections have on the other.^{6,10,11}

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

AUTHORS CONTRIBUTIONS

Dr Sandeep Arora, Conception and design, acquisition of data, literature search, analysis and interpretation of data; and drafting the manuscript and revising it.

Dr Anuj Bhatnagar, Acquisition of data, literature search, analysis and interpretation of data; and drafting the manuscript and revising it.

Dr Gautam Kumar Singh, Acquisition of data, literature search, analysis and interpretation of data; and drafting the manuscript and revising it.

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Dr Amit Bahuguna, Literature search, analysis and interpretation of data; and drafting the manuscript and revising it.

Dr Pankaj Das, Literature search, analysis and interpretation of data; and drafting the manuscript and revising it.

Dr Prachi Verma, Literature search, analysis and interpretation of data; and drafting the manuscript and revising it.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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