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Case Report
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# Brain Stem Tubercular Reactivation Following Second Episode of SARS-CoV-2 Infection

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## Introduction

With the COVID-19 pandemic, newer clinical manifestations, and presentations secondary to the novel virus is creating a lot of diagnostic dilemmas amongst clinicians. Studies have established similarities between the immunopathology of COVID-19 and mycobacterial Immune Reconstitution Inflammatory Syndrome (IRIS). Innate immune component of both COVID-19 and IRIS centers on aberrant activation and signaling of macrophages and monocytes, by the immunomodulatory effects of cytokines produced, particularly interleukin-18 [1].

## Case Presentation

A 1-year 9-month-old boy presented with fever (100-102 F) for 10 days along with neck stiffness and extreme irritability. The caretaker of the child was diagnosed with tuberculosis two months back with sputum being positive for acid fast bacilli and GeneXpert detecting the presence of *Mycobacterium tuberculosis* sensitive to Rifampicin. Subsequently, the parents had recovered from COVID-19 about six weeks back. In view of baby having CNS symptoms along with history of contact with a patient of tuberculosis, the baby was suspected to have TB meningitis and relevant investigations were sent accordingly. Computed Tomography (CT) chest revealed necrotic mediastinal nodes. Magnetic Resonance Imaging (MRI) brain showed moderate communicating hydrocephalus with meningeal enhancement. Cerebrospinal Fluid (CSF) study revealed lymphocytic pleocytosis (Cell count- 640/cmm, lymphocytes 98% and neutrophils 2%) with elevated protein (1463 mg/100 ml) and normal glucose (75 mg/100 ml). CBNAAT from sputum and CSF was negative. In addition, COVID IgG antibody was positive. He was diagnosed as tubercular meningitis and started on 4 Anti-Tubercular Drugs (ATD) along with oral prednisolone. Baby was afebrile and playful within a week and repeat MRI brain after one month showed moderate communicating hydrocephalus with mild reduction in the ventricular size and regression of periventricular interstitial edema. Clinically the baby remained asymptomatic, ATD were continued, and steroid was gradually tapered off over next 4 weeks.

Six weeks after stoppage of prednisolone, the baby developed cough and was found to be COVID RT-PCR positive. Over the next 4 days he became lethargic, and sensorium deteriorated, with drooling of saliva, decreased urination and had to be hospitalized. Within a day, he developed left sided facial palsy and drowsiness increased. MRI Brain revealed (Figure 1, 2) multiple conglomerated rings enhancing lesions in the pontine and medullary regions with perifocal edema and meningeal enhancement along with an increase in the hydrocephalus.

He was started on intravenous dexamethasone (0.6 mg/kg/day in 4 divided doses) in view of immune reactivation and ATD were continued. Looking at the new onset lesions in the brain stem possibility of drug resistant TB was considered, the primary contact was traced, and she was found to have recovered. Thus, drug resistance seemed unlikely and initial therapy was continued along with steroids. Gradually over a period of 7 days, mentation improved along with the facial palsy and child was discharged with a plan of continuing oral prednisolone for another month. He remains asymptomatic on follow up.

## Discussion

We report a case of tubercular meningitis stable on 3 months of ATD that flared after second episode of COVID-19 infection presenting with new onset bulbar palsy and left sided facial palsy. MRI brain showed multiple new onset tuberculomas in the medulla and pons that raised the possibility of flaring up of TB post-COVID-19. The bulbar and facial palsy improved on administration of dexamethasone thus pointing towards an immune reactivation, best explained by an IRIS-type reaction.

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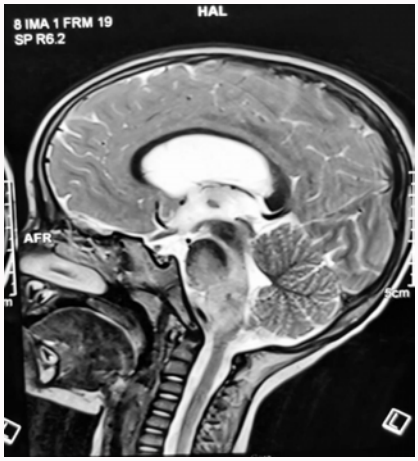


**Figure 1:** MRI Brain (T2 weighted sagittal plane) showing increased signal intensity in brainstem.

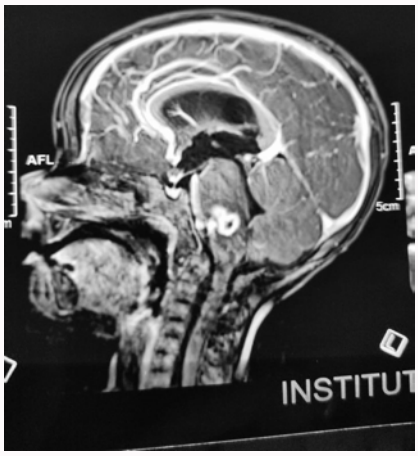


**Figure 2:** MRI Brain (post contrast T1 weighted sagittal plane) showing conglomerated ring like enhancing lesions in the pontine and medullary regions with perifocal edema, suggestive of granulomatous lesion. Meningeal enhancement is noted.

IRIS is a condition seen in response to rapid immune reconstitution [1]. Two forms have been described [2,3]. In unmasking IRIS, the immune reconstitution unmasks a previously undiagnosed infection. Paradoxical IRIS refers to the worsening of previous infection after the commencement of therapy. A typical feature of this syndrome is the recurrence of original lesions in a more pronounced version and rapid clinical improvement following corticosteroid therapy [4]. The radiological and clinical features of paradoxical IRIS were both present in our patient's presentation.

Previously Mertens et al. reported a case of steroid sensitive COVID-19 Immune Reconstitution Inflammatory Syndrome induced ARDS following COVID-19 infection in a 54-year-old male [5]. As per a study by Seddiki et al., COVID-19 and Mycobacterial IRIS share similar immunopathology and suppression of inflammatory response by corticosteroid therapy is effective in both cases. In addition, the study also established the central role of Interleukin-18 and hence should be investigated further as a possible therapeutic target [1].

Corticosteroids (prednisolone 1.5 mg/kg/day tapered over four to six weeks) are considered as the first line therapy for IRIS. Duration of therapy depends on severity and recurrence of symptoms but continuation beyond four-six months is discouraged. Biologics and immunomodulators including TNF-α inhibitors, thalidomide, IL-6 blockers have been used in various cases of refractory IRIS [2].

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