

Hiccups as an unusual manifestation of tuberculosis-associated immune reconstitution inflammatory syndrome

Tuberculosis-associated immune reconstitution inflammatory syndrome (TB-IRIS) in HIV is the paradoxical worsening of an existing lesion or condition after initiation of highly active antiretroviral therapy (HAART) due to dysregulated augmentation of immune responses, despite an effective virological suppression.¹ The incidence has risen to nearly 54% with concomitant treatment of both diseases.² Persistent hiccups, as a manifestation of TB-IRIS is extremely rare, and we present probably the first case reported from India.

A 38-year-old man with HIV-1 presented with fever and productive cough of 3 months duration with no other important medical history. Physical examination revealed few crepitations at the right infrascapular region. Chest X-ray showed minimal bilateral hilar node enlargement. A sputum smear examination revealed acid-fast bacilli and cultures grew *Mycobacterium tuberculosis* (Mtb) sensitive to antituberculosis drugs. Random plasma sugar, liver and renal

function tests, and abdominal ultrasonogram were within normal limits. His baseline CD4 count was 69 cells/cmm and HIV plasma viral load was 438 000 copies/ml.

He was started on four drug antituberculosis therapy (ATT) daily under supervision, along with HAART after 20 days, as per the national guidelines.³ On day 16 post-HAART, he complained of hiccups as the sole symptom without any overt abnormality on physical examination. Pantoprazole, metoclopramide and antacids were administered orally. Two days later he was febrile (38.5 °C) and X-ray chest showed minimal mediastinal enlargement. Quantitative buffy coat analysis for malarial parasite and urine cultures were negative. Compared to the baseline values, there was a 2.3-times log₁₀ decline in plasma HIV viral load, an increase in CD4/CD8 ratio and elevated levels of interleukin-6 and C-reactive protein (Table I). He became afebrile after 3 days of receiving acetaminophen, but the hiccups persisted, warranting hospitalization.

Baclofen 10 mg (oral) twice a day was added. Ultrasonogram (repeated) revealed multiple enlarged abdominal lymph nodes (Fig. 1). Cytopathological examination of a left cervical node, that appeared

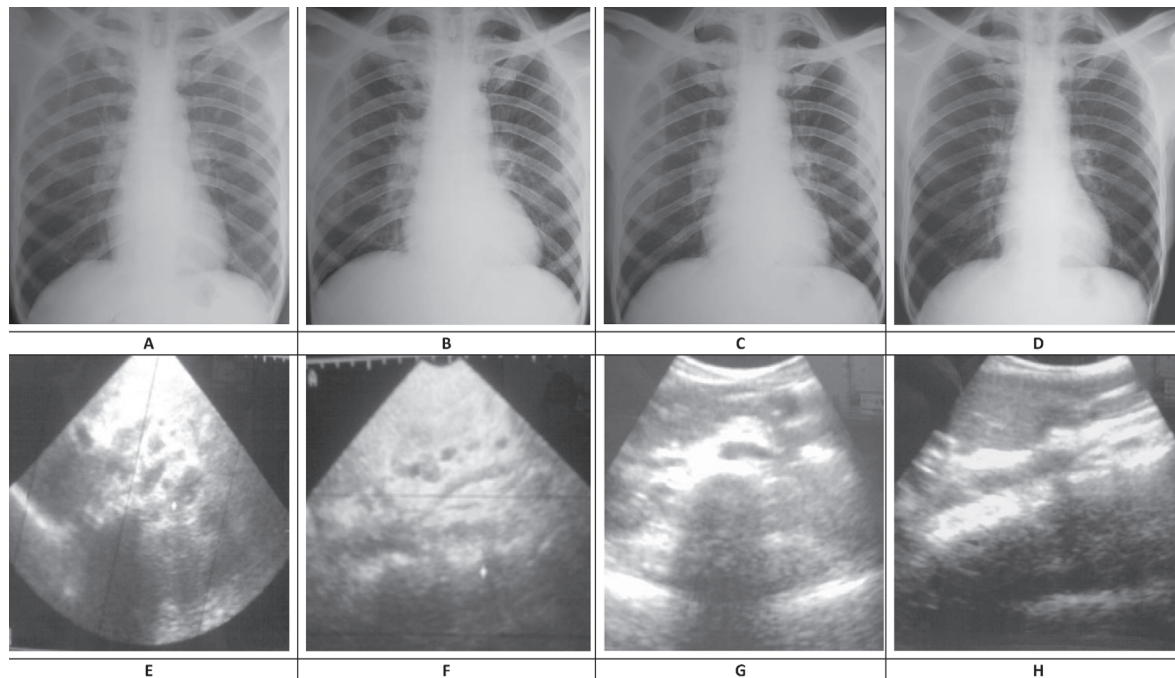


FIG 1. Chest X-ray (A-D) and ultrasonogram abdomen (E-H). A: Before starting antitubercular therapy (ATT); B: Day 3 of immune reconstitution inflammatory syndrome (IRIS) event; C: Day 25 of IRIS event; D: End of ATT; E and F: Day 9 after IRIS event; E: Extensive mesenteric adenitis; F: enlargement of lymph nodes along the portal vein; G and H: End of ATT after steroid therapy showing clearance; G: mesenteric and para-aortic region; H: along the portal vein.

TABLE I. Haematological parameters serially evaluated (including immune markers)

Parameter	Pre-ART	Antitubercular therapy				
	15/07/2011	IRIS episode 29/08/2011	2nd month 19/09/2011	6th month 20/01/2012	12th month 27/07/12	18th month 11/01/13
Haemoglobin (g/dl)	9.2	8.3	9	10.2	12.2	14.1
Red blood cells (cells/ml)	3.55	2.9	3.21	3.26	3.63	4.13
White blood cells (cells/ml)	6400	5300	6000	5000	3300	3200
Packed cell volume (%)	26.4	24.2	27.4	30.4	33.0	39.8
Platelets ($\times 10^3$ /ml)	156	200	186	368	179	264
CD4 (cells/ml)	69	50	66	107	142	174
CD8 (cells/ml)	1096	226	409	528	305	344
CD4/CD8 ratio	0.06	0.22	0.16	0.2	0.47	0.51
Viral load (copies/ml)	438 000	1973	<400	<400	Not done	Not done
C-reactive protein (mg/L)	25.4	86.5	20.1	2.3	Not done	Not done
Interleukin-6 (pg/ml)	12.6	35.7	18.1	1.5	Not done	Not done

ART antiretroviral treatment IRIS immune reconstitution inflammatory syndrome

simultaneously, revealed granulomatous lymphadenitis that was culture negative for Mtb. A diagnosis of IRIS was made by an independent panel of doctors (CC, SSe, SSw) based on the INSHI criteria (International Network for the Study of HIV associated IRIS).¹

He was started on steroids and his hiccups resolved in 5 days even though the abdominal nodes persisted on the ultrasonogram for several weeks. HAART and ATT were continued uninterrupted. At the end of ATT (month 6), ultrasonogram of the abdomen and X-ray chest were normal.

TB-IRIS presenting as hiccups is extremely rare with few cases reported with sarcoidosis,⁴ histoplasmosis⁵ and after steroid therapy in patients with lymphoma.⁶ That steroids alleviated hiccups, rather than aggravating it, aided in diagnosing IRIS.⁶ Resolution of hiccups (that correlated with decreases in levels of immune markers) despite persistent abdominal nodes signified an inflammatory pathology rather than mere physical compression.⁷ The importance of recognizing IRIS does not end solely with appropriate medication, but requires continued reassurance in the wake of frustrating symptoms, thus ensuring patient's compliance to life-long therapy of HAART.

ACKNOWLEDGEMENTS

Written informed consents both for publication and for using his radiographic images in the case report have been obtained from the patient. The study was supported by the ICMR Ad-Hoc grant (partly). Dr Andrade was supported by the Division of Intramural Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, USA. The content of this publication does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the US Government. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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Erratum

In the Correspondence titled 'Team-based learning in a medical centre in Malaysia: Perspectives of the faculty' by Salam *et al.* (*Natl Med J India* 2014;**27**:350), the Acknowledgement should read: 'We received UKM ethics committee grant PTS-2013-161 for this research' and not '... grant PTS-2012-161. . .'. We regret the error.—Editor