A 52-year-old male was referred with chief complaints of pain in the upper abdomen for 6 months and fever for 4 months with weight loss. No history of any previous major ailments or intake of immunosuppressant medications was elicited. However, a family history of tuberculosis was revealed. Upper gastrointestinal endoscopy showed nodularity in the jejunal mucosa, which was histologically proven to be due to jejunal lymphangiectasia [Table 1]. Endoscopic ultrasound (EUS) of the abdomen revealed a space occupying hypoechoic circumscribed lesion measuring 4.3 × 1.7 cm in the left adrenal gland, with maintained fat plane and left kidney [Figure 1]. EUS-guided fine-needle aspirate cytology (FNAC) smears from the adrenal mass lesion showed few groups of adrenal cortical cells and bare nuclei in a background containing lipid vacuoles, along with intracellular and extracellular yeasts forms of *Histoplasma* [Figure 2a and b]. Ziehl–Neelsen (ZN) stain did not reveal any acid-fast organisms; however, negative shadows of *Histoplasma* in the methylene blue background [Figure 2c], as described by Ranjan et al. were seen.[1] The scanty hemorrhagic aspirate obtained through EUS has been utilized for cytology smears only, and culture was not possible.

HIV serology was nonreactive, while absolute lymphocyte count (406/µL), absolute CD3 cell count (297/µL), absolute CD4 cell count (122/µL), and CD4 (Helper T) cell percentage (constituting 30% of total T lymphocytes) were reduced. These values showed reversal to normal range after 6 weeks of antifungal therapy [absolute lymphocyte count (1407/µL), absolute CD3 cell count (1066/µL), absolute CD4 cell count (488/µL), and CD4 (Helper T) cell percentage (34.7% of total T lymphocytes)]. The patient was discharged with oral itraconazole for 6 months. At 9 months of follow-up he was afebrile with normal CD4 count and ultrasonographic evidence of resolution of the adrenal lesion [Figure 1d].

EUS-guided aspiration cytology has recently facilitated the accurate diagnosis of adrenal histoplasmosis.[2] Initial and follow-up CD4 counts are required in these patients to assess the immune status and rule out idiopathic CD4 T-lymphocytopenia (ICL). ICL is a rare immunodeficiency disorder of unknown aetiology characterized by gradual decline of CD4 T-cells, often with opportunistic infections, but a slower disease progression in comparison to AIDS. ICL is defined by (1) Absolute CD4 T-lymphocyte count <300/µL or <20% of total lymphocytes at two occasions minimum 6 weeks apart; (2) negative HIV serology; (3) absence of any primary immunodeficiency or immunosuppressant drug intake.[3] The case described...
here did not fulfil the diagnostic criteria for ICL as the CD4 cell count improved to normal range after antifungal treatment for 6 weeks.

Posttreatment reversal of CD4 lymphocytopenia has been described in tuberculosis, but only in two earlier reports of disseminated histoplasmosis.\(^4,5\) Pooling of CD4 T-lymphocytes at the sites of active infection or granulomatous response resulting in relative peripheral CD4 lymphocytopenia, or a cytokine-mediated suppressive effect, as described for tuberculosis,\(^6\) may also apply for another similar macrophage, CD4 T-lymphocyte, and interferon \(\gamma\)-mediated granulomatous infection such as histoplasmosis. Therapeutic regimes resulting in elimination of the microbes and clearing of granulomatous inflammation may correct the CD4 lymphocytopenia by redistribution of the peripheral blood CD4 T-lymphocytes [Figure 3]. CD4 cell counts may not be evaluated always in histoplasmosis in immunocompetent patients reported from Indian subcontinent.

Hence, possible association of histoplasmosis with reversible CD4 lymphocytopenia may often remain undetected.

Cytologically, *Histoplasma* is characterized by small capsulated, round-to-oval yeast forms, with budding, in groups and clusters, present intra or extracellularly. In addition to the characteristic cytomorphology, antigen detection in urine or serum, serology, and culture may help, but these are not free of limitations and overlap. *Blastomyces dermatitidis* have broad-based budding yeasts, *Cryptococcus* have narrow-based budding yeasts with thick capsule, whereas *Candida* produces both small budding yeasts and pseudohyphae.

Another interesting observation in this patient is the association of jejunal lymphangiectasia [Figure 2d] with adrenal histoplasmosis and reversible CD4 lymphocytopenia. Thickened jejunal loops with lymphangiectasia here may be an incidental finding or secondary to immune deregulation due to CD4 T-lymphocytopenia.\(^7\) Future documentation of similar observations may help to resolve this issue better.

![Flow chart depicting the pathogenesis of CD4 T-lymphocytopenia in relation to macrophage activation; histoplasmosis can be the cause and effect of CD4 lymphocytopenia](image-url)

**Figure 3**: Flow chart depicting the pathogenesis of CD4 T-lymphocytopenia in relation to macrophage activation; histoplasmosis can be the cause and effect of CD4 lymphocytopenia.
To conclude EUS-guided FNAC for adrenal lesions requires precision, but can be diagnostically rewarding. Reversible CD4 lymphocytopenia is a less explained entity, distinct from ICL or HIV infection. Immunopathogenesis of its association with histoplasmosis may be related to the pooling of CD4 T-lymphocytes at the sites of granulomatous inflammation, followed by peripheral redistribution of those cells after clearance of infection, as described in tuberculosis. To the best of our literature search, reversal of CD4 lymphocytopenia after antifungal treatment has been documented earlier in only two cases with disseminated histoplasmosis. Histoplasmosis may well be both the cause and effect of CD4 lymphocytopenia; hence, initial and follow-up CD4 counts are essential to assess the immunological profile. Associated lymphangiectasia described in this patient may be incidental or secondary to altered immunological milieu.

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Conflicts of interest
There are no conflicts of interest.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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