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**Crazy nodules in a hazy field: miliary tuberculosis presenting with ground glass opacities in a diagnosed case of Henoch–Schönlein purpura**

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## **Abstract**

Tuberculosis is known for its atypical manifestations among the immunosuppressed. In this case report, we describe a rare radiological presentation of tuberculosis in a patient on treatment with steroids for Henoch–Schönlein Purpura (HSP). The patient presented with complaints of fever, dry cough, and breathlessness. Chest imaging revealed diffuse ground glass opacity in bilateral lung fields with innumerable random nodules and mediastinal lymphadenopathy. Fundus examination revealed choroid tubercles and was diagnosed as miliary tuberculosis. The patient was started on anti-tubercular therapy and the patient improved symptomatically. This case report necessitates clinicians to keep an eye open for the atypical manifestations of tuberculosis.

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## **Introduction**

Tuberculosis continues to be a major health burden worldwide with 10.6 million people suffering from tuberculosis each year and 26% of these cases were reported from India in 2021.<sup>1</sup> This illness is well known for its decoy presentations, making awareness of utmost importance in a country like India, with a high tuberculosis burden.

Miliary tuberculosis is seen in less than 2% of tuberculosis cases. It is due to the bloodborne and lymphatic spread of mycobacterium tuberculosis from a central focus and infiltration of other organs including the liver, bone marrow, spleen, lungs, and meninges, and forms small caseating granulomas of 1-3 mm diameter. Immunosuppressed patients often present with atypical clinical and radiological manifestations leading to diagnostic dilemma.<sup>2</sup>

Here we describe a case of miliary tuberculosis with rare and perplexing radiological findings in an immunosuppressed patient.

## **Case Report**

A 37-year-old Indian male presented with complaints of painless petechial rashes all over the body below the face and also bleeding from the nose. He had no history of fever, photosensitivity, ulcers in the mouth, nose, or genital areas, loss of weight, or any prolonged illness in the past. He also did not have any dyspnea, hemoptysis, hematemesis, or pleuritic symptoms. His routine blood investigations including coagulogram were within normal limits

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and no abnormalities were detected on his chest X-ray. However, a punch biopsy of the skin revealed leukocytoclastic vasculitis. Immunofluorescence revealed linear deposition of Immunoglobulin A (IgA) and IgC in the vessel wall, IgG and IgM were negative. A diagnosis of Henoch–Schönlein Purpura (HSP) was made and he was started on steroids. One month later, he presented with complaints of facial puffiness and bilateral pedal edema. The routine hemogram and liver functions were within normal limits. However, his blood urea was 47 mg/dL, and S. creatinine was 1.4 mg/dL. The urine microscopy showed a protein of 500 mg/dL, with urine albumin being 3+ with no pus cells or red blood cells, or casts in urine. Also, the 24-hour urinary protein value was 2900 mg/dL. Ultrasonography (USG) of the abdomen showed bilateral raised renal cortical echogenicity with grade I fatty liver and splenomegaly. Antinuclear Antibody (ANA), Perinuclear Anti-Neutrophil Cytoplasmic Antibodies (pANCA), and Anti-Neutrophil Cytoplasmic Antibodies (cANCA) were all negative. A left kidney biopsy revealed focal segmental glomerulosclerosis. A diagnosis of minimal change disease was made and the steroids were continued.

Three months later, the patient presented with complaints of dry cough of one month duration and fever and breathlessness of 15 days duration. His blood investigations revealed a normal hemogram and coagulogram with blood urea of 87 mg/dL, serum creatinine of 1.6 mg/dL, Serum Glutamic-Oxaloacetic Transaminase (SGOT) 86 IU/L, Serum Glutamate Pyruvate Transaminase (SGPT) 79 IU/L, Alkaline Phosphatase (ALP) 301 IU/L, total protein 5.9g/dL, serum albumin 2.6 g/dL, urine routine showed protein of 100 mg/dL with Red Blood Cell

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(RBC) count 12-15/hpf with no significant pus cells, epithelial cells or casts. Chest X-ray showed bilateral diffuse nodular infiltrates and Computed Tomography (CT) showed diffuse ground glass opacity in bilateral lung fields with innumerable random nodules scattered in both the lung fields and mediastinal lymphadenopathy. Sputum microscopy for acid-fast bacilli was negative. Sputum Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) for mycobacterium tuberculosis was also negative. The presence of diffuse ground glass opacities in a known case of HSP, raised the possibility of Diffuse Alveolar Hemorrhage (DAH) at first. As the patient was immunosuppressed and was from a country with a high tuberculosis burden, the possibility of tuberculosis was also considered. Fundus examination revealed choroid tubercles and a diagnosis of miliary tuberculosis was made on a clinicoradiological basis. The patient was started on anti-tubercular therapy, continued with the lower dose of corticosteroids and other supportive treatment, and improved symptomatically. In spite of not augmenting the immunosuppression, the patient improved. The chest X-ray infiltrates have resolved and the patient has improved clinically.

## **Discussion**

HSP, an IgA-mediated small vessel vasculitis, is a disease of children essentially; it can also be seen in adults but may be more severe.<sup>3</sup> The clinical tetrad of arthritis, abdominal pain, hematuria, and nonthrombocytopenic palpable purpura is essential for its diagnosis. Precipitating factors for HSP include malignancy, infections, environmental chemicals, toxins,

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physical trauma, and complement deficiency. Pulmonary involvement is unusual and is seen in adults primarily, of which, diffuse alveolar hemorrhage is the commonest manifestation.<sup>4</sup>

Deposition of the IgA immune complex in vessel walls of affected organs activates the complement pathway and recruits inflammatory cells causing diffuse alveolar hemorrhage which is associated with high mortality and requires treatment with aggressive immunosuppression. Other pulmonary manifestations include usual interstitial pneumonia and interstitial fibrosis.

Tuberculosis has infrequently been reported in adults with HSP in the literature, with variable clinical presentations. Also, it has been proposed that HSP may be triggered by tuberculosis or could be due to Anti-Tuberculosis Treatment (ATT).<sup>5-8</sup> A few case reports of pulmonary tuberculosis with HSP have been published (Table 1), of which miliary tuberculosis has been rarely reported.

Miliary tuberculosis, a life-threatening variant of disseminated tuberculosis, is classically characterized by the presence of uniform and discrete pulmonary opacities of diameter 3 mm or less radiologically and is seen in about 50% of cases. Other “non-classic” miliary patterns include asymmetrical nodular patterns, coalescence of nodules, mottled appearance, snow storm appearance, diffuse ground glass opacity obscuring background nodules, and air space consolidation.<sup>2</sup>

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Various respiratory diseases present with the finding of ground glass opacity on CT scans of the thorax. These hazes might result from the partial filling up of the alveoli or due to the thickening of the alveolar walls, septal interstitium, or both. This radiological picture on thoracic CT scan can be observed generally in alveolar hemorrhage, nonspecific interstitial pneumonia, pulmonary alveolar proteinosis, tuberculosis, and sarcoidosis.<sup>9-12</sup>

Miliary tuberculosis may occasionally present with a predominant ground glass opacity pattern or diffuse ground glassing with nodules. This ground glass attenuation is due to the small granulomas in the septal interstitium or alveolar wall thickening and the exudative and edematous changes in the lung causing diffuse alveolar damage in hematogeneously disseminated tuberculosis. This can even lead to acute respiratory distress syndrome.<sup>13,14</sup> However, this non-specific finding was superimposed with miliary nodules in our case.

In a study of 105 confirmed miliary tuberculosis patients, ground glass opacity was observed in 70 (67%) of patients.<sup>13</sup> Other smaller studies in 14 and 25 confirmed miliary tuberculosis patients demonstrated the presence of ground glass attenuation in 64% and 92% respectively.<sup>15,16</sup> Ji Lee *et al.*, in their study, found that miliary tuberculosis patients with a greater extent of ground glass opacities had a progressive disease.<sup>13</sup> Radiology plays a major role not only in diagnosing tuberculosis, but also gives an insight regarding disease progression.

Although DAH is the most common pulmonary manifestation of HSP, its classical features like hemoptysis, anemia or hypoxemia were lacking in this patient. Features of dissemination can provide clinical clues in diagnosis in cases with negative microbiology and atypical radiology.

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In this case, a negative Mantoux test further confounded our diagnosis. Fundus examination revealed choroid tubercles and ultrasound abdomen showed splenomegaly. The differential diagnosis of choroid tubercles includes hemangioma, amelanotic melanoma, foreign body, brucellosis, syphilis, and histoplasmosis. However, we considered tuberculosis primarily due to the clinical picture and high prevalence of the disease in our country. The resolution of symptoms and infiltrates on chest X-ray with anti-tubercular treatment, without further augmenting immunosuppression also confirmed our diagnosis retrospectively. A few studies have reported that active *Mycobacterium tuberculosis* can trigger HSP, however this requires more evidence for confirmation.

## **Conclusions**

This case is reported here to highlight that classical miliary nodules are not always observed in all patients. Tuberculosis is well known for its myriad of imaging patterns. Ground glass opacities are a frequent manifestation of miliary tuberculosis, especially in immunosuppressed patients. Through the implementation of various programs at both national and global levels, the incidence of tuberculosis is declining. However, the atypical and unfamiliar manifestations are increasing. Thus clinicians should always keep an eye open to the not-so-common manifestations of this common malady, to prevent its catastrophic complications.

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**Table 1.** Case reports of pulmonary tuberculosis with Henoch–Schönlein Purpura (HSP).

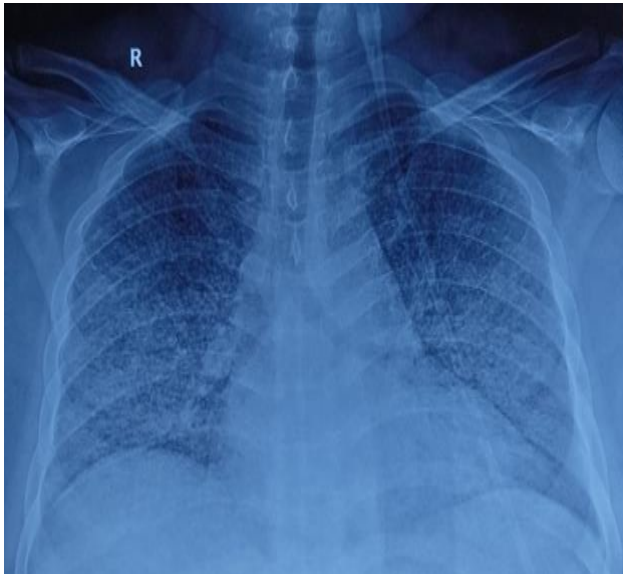
Serial No.	Author/year	Radiology	Treatment
1.	Mishima Y <i>et al.</i> (1994) <sup>6</sup>	Multiple cavities mainly on right lung	ATT followed by steroids
2.	Han BG <i>et al.</i> (1995) <sup>5</sup>	Diffuse scattered, ill defined nodules in entire both lung fields and patchy and confluent density in both upper lungs	ATT
3.	Islek I <i>et al.</i> (2002) <sup>9</sup>	Bilateral hilar adenopathy with perihilar infiltrate	ATT
4.	Kitamura H <i>et al.</i> (2007) <sup>10</sup>	Infiltration of both upper lobes	ATT followed by steroids
5.	Isobe Z <i>et al.</i> (2008) <sup>11</sup>	Consolidation in right upper lobe	ATT followed by steroids

ATT, Anti-Tuberculosis Treatment

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**Figure 1.** Chest X-ray showing bilateral diffuse nodular infiltrates predominantly in the middle and lower zones.

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**Figure 2.** High-Resolution Computed Tomography (HRCT) shows diffuse ground glass opacities in bilateral lung fields with innumerable random nodules scattered in both lung fields and mediastinal lymphadenopathy.

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**Figure 3.** A dilated funduscopy of the right eye revealed multiple choroid tubercles throughout the retina.

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