



# Reversed Halo Sign in Hypersensitivity Pneumonia: A Diagnostic Difficulty

## *Hipersensitivite Pnömonisinde Ters Halo İşareti: Tanısal Güçlük*

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### **Abstract**

Herein is a case of histologically proven hypersensitivity pneumonia in a patient who presented initially with a focal, rounded area of ground glass opacity surrounded by a complete or nearly complete ring of consolidation known as reversed halo sign on high resolution computed tomography. To the best of our knowledge, this association has not been previously described.

**Key words:** *Reversed halo sign, hypersensitivity pneumonia, high resolution computed tomography.*

### **Özet**

Burada yüksek çözünürlüklü bilgisayarlı tomografi incelemede tam ya da tama yakın bir halkasal konsolidasyon alanı ile çevrelenmiş buzlu cam alanı odakları yani ters halo işareti şeklinde kendini gösteren ve histolojik olarak hipersensitivite pnömonisi almış bir olguyu sunduk. Hipersensitivite pnömonisi ve yüksek çözünürlüklü bilgisayarlı tomografide ters halo işareti arasındaki ilişki literatürde bu güne kadar tanımlanmamıştır.

**Anahtar Sözcükler:** *Ters halo işareti, hipersensitivite pnömonisi, yüksek çözünürlüklü bilgisayarlı tomografi.*

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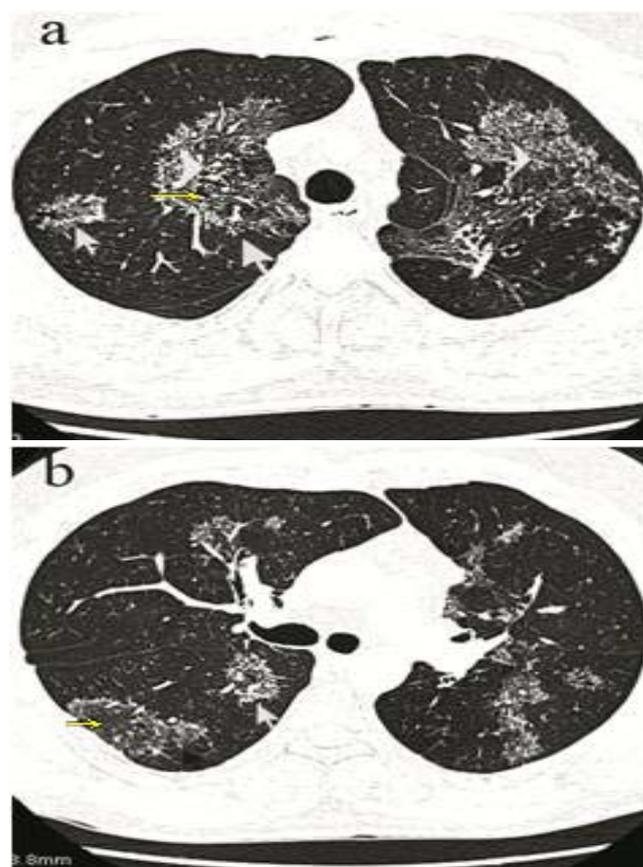


The reversed halo sign (RHS) is defined as a focal, rounded area of ground glass opacity surrounded by a complete or nearly complete ring of consolidation, as demonstrated on high-resolution CT (HRCT) scan of the chest (1). Initially it was reported to be specific for cryptogenic organizing pneumonia (COP) (2). Nevertheless, RHS has also been described in various diseases in several reports. The current study describes a case of histologically proven hypersensitivity pneumonia (HP) in a 54-year-old patient who exhibited RHS on chest HRCT. To our knowledge, RHS has not been reported in a patient with HP.

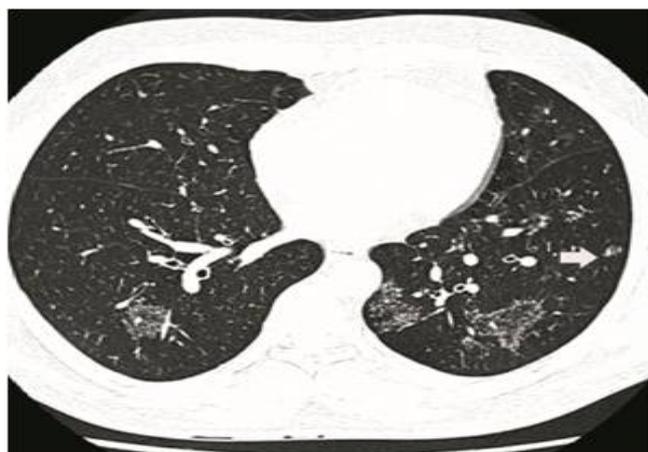
### CASE

A 54-year-old male patient admitted to our hospital with cough, sputum, and dyspnea of four weeks duration. Previous medical history revealed that he worked on a farm and coal mine at different periods in his life. He was ex-smoker for a month, but he had a 60 pack/year smoking history. Prior to referral, he initially presented to a government hospital. He was treated with antibiotics, but his clinical symptoms did not regress. On physical examination, his vital signs were normal. His lung fields were clear to auscultation. Laboratory investigations were unremarkable. High resolution computed tomography of the lungs was obtained in January 2011. High resolution computed tomography images were obtained at full inspiration with 1.25-mm slice thickness at 10-mm intervals. Peak voltage was 120 kVp, modulated tube current was 300 mA and reconstructed using a high-spatial frequency reconstruction algorithm. The images were reviewed using mediastinal (width, 250–450 HU; level, 40–50 HU) and lung (width, 1,500–1,700 HU; level, 600 to 700 HU) window settings. Chest HRCT revealed bilateral pulmonary opacities formed of central ground glass with peripheral areas of increased density, which affected all lobes and both the central and peripheral sections of the lungs with relative sparing the basis of the lungs (Figure 1). Some of the lesions of RHS had a reticular appearance and some had bronchiolectasis at the central ground glass opacity portion (Figure 1a). Centrilobular nodules were also seen in the lower lobes (Figure 2). Irregular linear opacities and traction bronchiectasis were also noted at the

left upper lobe apicoposterior segment (Figure 1a). On the basis of previous medical history and clinical, and HRCT findings, the differential diagnoses that was considered were farmer's lung (HP), simple coal workers pneumoconiosis (CWP), and COP. He underwent a video assisted lung biopsy. Histopathological examination of lung biopsy revealed patchy interstitial fibrosis and mononuclear inflammatory cell infiltration and several small granulomas without necrosis (Figure 3). The pathology results were consistent with HP. He was started on prednisone treatment. On clinical follow-up after seven months, the symptoms of the patient regressed and chest HRCT examination showed the complete resolution of the peripheral increased opacities and incomplete resolution of the central ground glass opacities of RHS (Figure 4). Also, the reticular appearance of the central ground glass portion had disappeared and bronchiolectasis regressed (Figure 4a).



**Figure 1a,b:** Axial HRCT images obtained at supraaortic level (a) and carina level (b) shows patchy opacities formed of centrally ground-glass opacity zone and periphery increased opacity of consolidation (white arrows) in both lungs. Note the reticular appearance and bronchiolectasis (yellow arrows) at the central zone formed of ground-glass opacity.



**Figure 2:** Axial HRCT image obtained at pulmonary vein level shows centrilobular nodules (arrow).

## DISCUSSION

The RHS was firstly defined as COP (2); however, it is not specific for this disease. Since then, it has been described in many diseases such as fungal infections (3,4), sarcoidosis (3,5), pulmonary embolism (3), edema (3), lung carcinoma (3), Wegener's granulomatosis (3,6), pneumocystis pneumonia (7), and tuberculosis (8). Marchiori et al. (3) reported this sign in secondary organizing pneumonia in patients with H1N1 infections, radiation therapy, drug reaction, collagen vascular diseases, and pneumococcal pneumonia. It is manifested as central ground glass opacity (corresponding to alveolar septal inflammation and cellular debris in the alveolar spaces) surrounded by a more solid ring- or crescent-shaped airspace consolidation (corresponding to granulomatous tissue in the peripheral air spaces) (8).

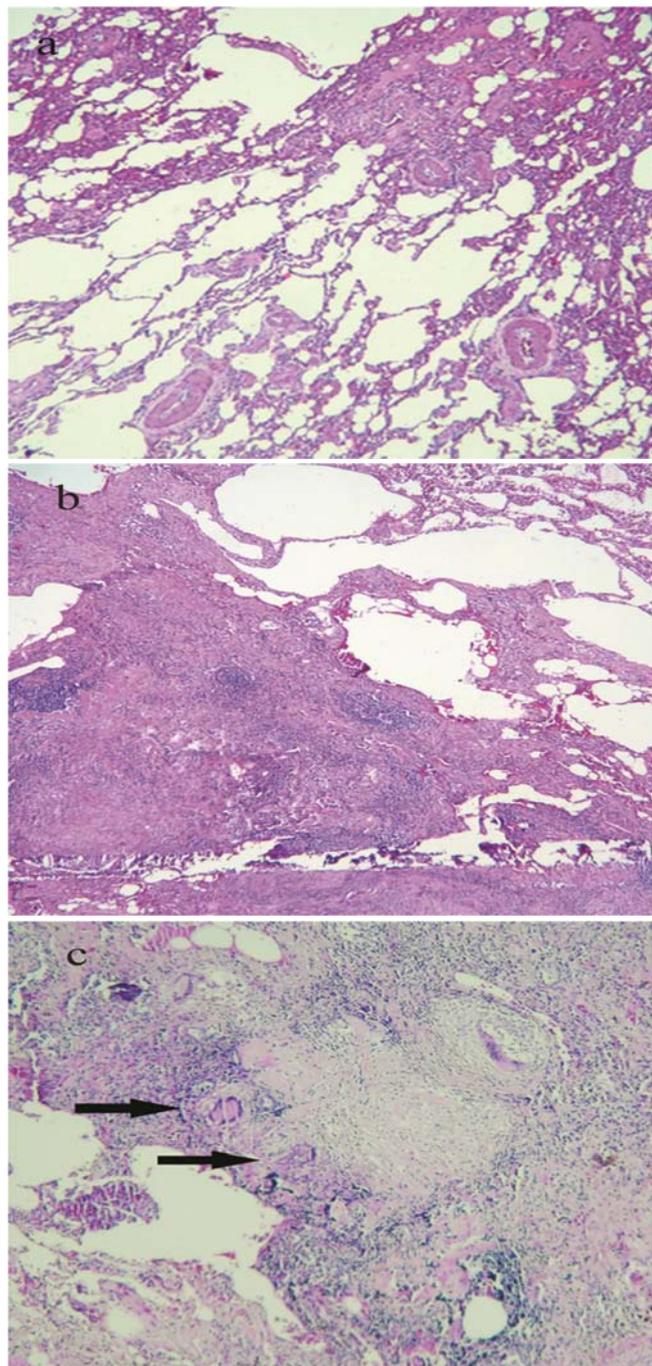
In the present case, differential diagnoses were farmer's lung, simple CWP, and COP. In HP HRCT appearance of recurrent and transient ground glass opacities or ill-defined consolidation superimposed with small nodules is considered typical and highly suggestive (9). Also, the characteristic HRCT signs in the patient were ground glass opacity and RHS with centrilobular sited nodules. Centrilobular nodules were found both on HP and CWP (9,10). In HP they were predominantly located in the middle and lower zones (9) as in the current patient. However, in CWP they were mostly located in the upper zones that coalesced to form conglomerate masses (10). Furthermore, ground glass opacity and reversed halo signs are not specific for simple CWP. Nevertheless, RHS, which was the major HRCT sign for this patient, was not

a characteristic sign for HP, although it was not reported in the literature. The reversed halo sign is characteristic for COP (2). Typical HRCT features of this entity include patchy consolidation, ground glass opacity, small nodules that may be peribronchial or peribronchiolar, and crazy paving appearance. Cryptogenic organizing pneumonia often involves the lower lung zones and subpleural distribution (11). In the current patient, the ground glass opacities and RHS were located all over the lung with relatively sparing the lung bases.

Histologically, the characteristic lesion for CWP is the coal macula, consisting of numerous pigment-laden macrophages that correspond to centrilobular or subpleural nodules on HRCT (12). In HP, small nodular appearances correlate with the presence of alveolitis, interstitial infiltrates, small granulomas, and cellular bronchiolitis (13). Cryptogenic organizing pneumonia is characterized by the presence of granulation tissue polyps within the lumina of the bronchioles and alveolar ducts and patchy areas of organizing pneumonia (14). The pathology results of the current patient were consistent with no pigment-laden macrophages, and granulation tissue polyps.

The HRCT findings of HP include ground glass opacity, centrilobular nodules, fibrosis, air trapping-mosaic pattern, and emphysema (9). The ground glass opacification may be patchy or diffuse with middle lung zone predominance (15). Ground glass attenuated centrilobular nodules are smaller than 5 mm in diameter and profuse throughout the lungs with middle and lower zone predominance. The irregular linear opacities, traction bronchiectasis, volume loss, and honeycombing are signs of fibrosis. These changes are most often found at the chronic stage and occasionally in the subacute stages with no zonal predominance (9,10). Radiologic evidence of emphysema was reported more commonly than fibrosis by some authors (16). According to the duration of the clinical status, HP is often divided into acute, subacute, and chronic phases. Centrilobular nodules, ground glass attenuation, and mosaic attenuation may all be found at any phase of the disease and may be the sole finding even in patients with clinically chron-

ic HP. Findings of fibrosis are usually found only in chronic HP (9).

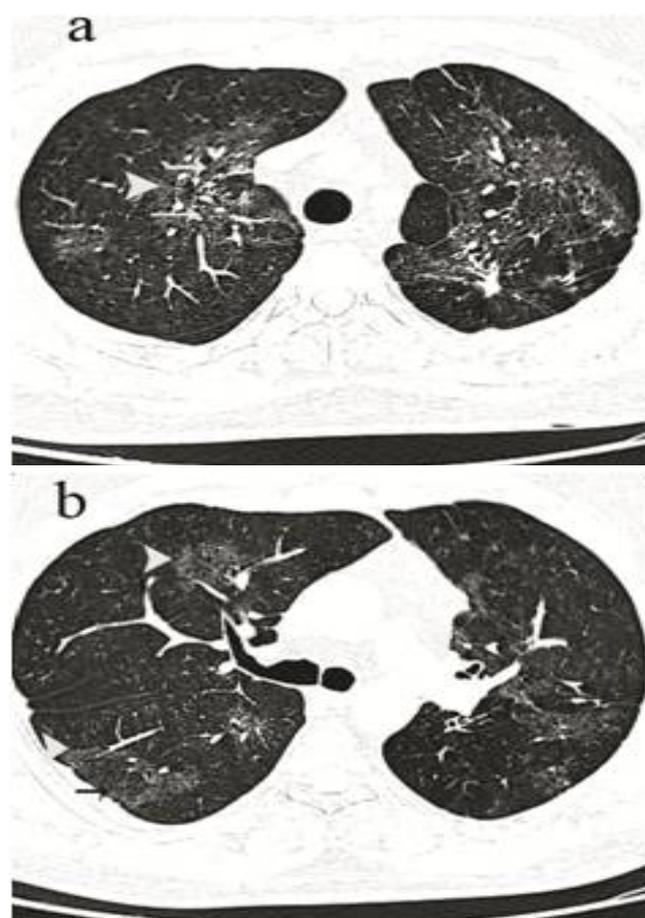


**Figure 3a,b,c:** Low power microscopically appearance of patchy fibrosis in the lung parenchyma (HE, X6). (a) Severe fibrosis areas with collagen accumulation and nodular aggregates of chronic inflammatory cell infiltration in interstitium of lung parenchyma (HE, X10). (b) Small non-necrotic granulomas with Langhans-type giant cells (arrows) in interstitial areas showing heavy fibrosis and chronic inflammatory infiltration (HE, X30) (c).

Marchiori et al. (3) stated that RHS should be considered a relatively nonspecific finding. Although the presence of the RHS could narrow the differential diagnosis,

the final diagnosis should be done with the clinical findings and the other HRCT findings (3). Hypersensitivity pneumonia might be presented in this form without the presence of classical HRCT findings.

Marchiori et al. (17) reported a reticular appearance of ground glass opacity in their patients with invasive pulmonary aspergillosis. Kim et al. (2) reported bronchiolectasis both in the ground glass opacity and consolidation zones in the study that was formed from the patients with COP. In the current case, the reticular appearance with bronchiectasis at the central ground glass opacity zone was also observed. Reversed halo sign with reticulation and bronchiolectasis at the central ground glass opacity zone should be investigated with further studies comprised of larger patient groups with the diagnosis of HP.



**Figure 4a,b:** Axial HRCT images obtained at supraaortic level (a) and carina level (b) corresponding to the same levels as Fig. 1 shows complete resolution of the peripheral increased opacities (arrow heads) and incomplete resolution of the central ground-glass opacities (arrows) of RHS. Also, the reticular appearance of the central ground-glass portion had disappeared and bronchiolectasis were regressed (a).

This study showed that RHS with reticulation and bronchiolectasis at the central ground glass opacity zone might be associated with HP. In conclusion, radiologist and clinicians should be aware that RHS can indicate many different diseases with different treatment options.

## CONFLICTS OF INTEREST

None declared.

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