Reversed Halo Sign on CT as a Presentation of Lymphocytic Interstitial Pneumonia

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Radiology Case. 2013 Oct; 7(10):51-56 :: DOI: 10.3941/jrcr.v7i10.1517

ABSTRACT

A 52 year-old African American female with a past medical history of symptomatic uterine fibroids and increasing abdominal circumference underwent abdominal computed tomography (CT) as part of her workup. Because of an abnormality in the left lower lobe, CT of the chest was subsequently performed and showed a focal region of discontinuous crescentic consolidation with central ground glass opacification in the right lower lobe, suggestive of the reversed halo sign. The patient underwent percutaneous CT-guided core biopsy of the lesion, which demonstrated lymphocytic interstitial pneumonia, a benign lymphoproliferative disease characterized histologically by small lymphocytes and plasma cells. This case report describes the first histologically confirmed presentation of lymphocytic interstitial pneumonia with the reversed halo sign on CT.

CASE REPORT

CASE REPORT

A 52-year-old African American female with a past medical history significant for symptomatic uterine fibroids presented to the emergency department with menorrhagia and increased abdominal girth. She underwent transvaginal ultrasound (TVUS), which demonstrated a large heterogeneous uterus with areas of calcification, suggestive of uterine fibroids. However, because of the patient's pelvic pain, rapidly increasing abdominal girth and weight loss, she underwent computed tomography (CT) of the abdomen, which showed incidental small nodules in the left lower lobe [Fig. 1]. A dedicated chest CT was later performed to better characterize the nodules and evaluate for additional pulmonary abnormalities.

CT of the chest was performed from the thoracic inlet to the upper abdomen, which revealed a focal region of discontinuous crescentic consolidation with central ground glass opacification and some normal appearing lung in the right lower lobe, suggestive of the reversed halo sign (RHS) [Fig. 2]. Given the RHS on CT, the differential diagnosis included cryptogenic organizing pneumonia (COP), bacterial pneumonia, sarcoidosis, non-specific interstitial pneumonia as well as other infectious or inflammatory processes. Although it was felt to be an unlikely diagnosis, given the presence of a markedly enlarged uterus in a patient being worked up for possible malignancy, atypical appearance of pulmonary metastases was also considered. To obtain a diagnosis, the patient underwent a CT-guided core biopsy of the right lower lobe lesion using a 15 cm long 18-guage SuperCore needle (Angiotech Pharmaceuticals, Inc., Vancouver, British Columbia, Canada) with a 2 cm long throw passed co-axially though a 17-guage introducer needle [Fig. 3]. The patient also underwent a supracervical hysterectomy.

The biopsy material received in the pathology laboratory consisted of 3 tan-pink cores of soft tissue, 0.3-0.5 cm in length and less than 0.1 cm in diameter. Microscopic examination showed lung parenchyma with prominent cellular infiltrate [Fig. 4A]. The cellular infiltrate occupied the interstitium of the lung, causing widening of the alveolar septae [Fig. 4B] and was characterized by lymphocytes, with some admixed histiocytes, plasma cells and very rare

eosinophils [Fig. 4C]. Focal fibroblastic foci were also seen. The findings were interpreted as consistent with lymphocytic interstitial pneumonia (LIP) pattern.

The final surgical pathologic diagnosis of the uterus displayed secretory endometrium and numerous leiomyomata, but no evidence of malignancy. According to clinic notes, the patient was doing well at one month following hospital discharge. She was not experiencing any pulmonary symptoms at the time of last documented clinic evaluation.

DISCUSSION

The reversed halo sign (RHS), also sometimes reported as the atoll sign, was first described in 1996 by Voloudaki et al. as a sign specific for cryptogentic organizing pneumonia (COP) [1]. It is a computed tomography (CT) pattern that represents an area of central ground-glass attenuation surrounded by a crescent or ring of consolidation. Since the initial report describing the RHS, this finding has been found to be associated with a variety of infectious and noninfectious processes [2]. According to Godoy et al., the RHS on CT is most commonly seen with COP, with this finding present on approximately 19% of all High Resolution Computed Tomography (HRCT) studies of the lungs in patients subsequently given this diagnosis pathologically. Subsequent to the initial report describing the RHS as specific for COP, this sign has also been described with invasive fungal pneumonia, paracoccidioidomycosis, Pneumocystis jirovecii pneumonia, tuberculosis, community-acquired pneumonia, Wegener granulomatosis, lipoid pneumonia, bacterial pneumonia, non-specific interstitial pneumonia, sarcoidosis, and pulmonary embolism [1-4]. Some lymphoproliferative conditions such as lymphomatoid granulomatosis or neoplasms like lung adenocarcinoma and metastatic disease may also manifest as the RHS on CT. Post-treatment changes from radiofrequency ablation and radiation therapy have also been associated with this CT sign [2, 3]. This case report describes the first histologically-confirmed presentation of lymphocytic interstitial pneumonia (LIP) with the RHS on CT.

LIP was first described by MacFarlane et al. in 1973 [5]. It is a benign lymphoproliferative disorder characterized by a diffuse and exquisitely interstitial proliferation of small lymphocytes and plasma cells [6, 7]. Patients with LIP often have an underlying systemic disease or connective tissue disorder. Conditions such as Sjogren syndrome, acquired immunodeficiency syndrome, Castleman syndrome and Epstein-Barr virus have been associated with LIP [8, 9, 10]. The patient described in this case report did not have any of these conditions.

According to Johkoh et al., the most common findings associated with LIP on HRCT are areas of ground glass attenuation, centrilobular nodules and subpleural small nodules, while on chest radiography, findings are usually bilateral reticular or reticulonodular opacities, predominantly in the lower lung zones. Other imaging findings associated with LIP include thickening of bronchovascular bundles, interlobular septal thickening, air cysts and absence of lymphadenopathy [8, 9, 11, 12].

To our knowledge, the RHS has not been described in the literature in association with LIP. We present a pathologically proven case of LIP with corresponding radiologic and histologic images. After reviewing this case report, radiologists can widen their differential diagnosis to include LIP when presented with the RHS on CT of the lungs.

TEACHING POINT

The reversed halo sign (RHS) is a nonspecific finding on High Resolution Computed Tomography. When the RHS is identified on Computed Tomography scanning, it is important to consider a broad differential diagnosis and also consider Lymphocytic Interstitial Pneumonia.

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FIGURES

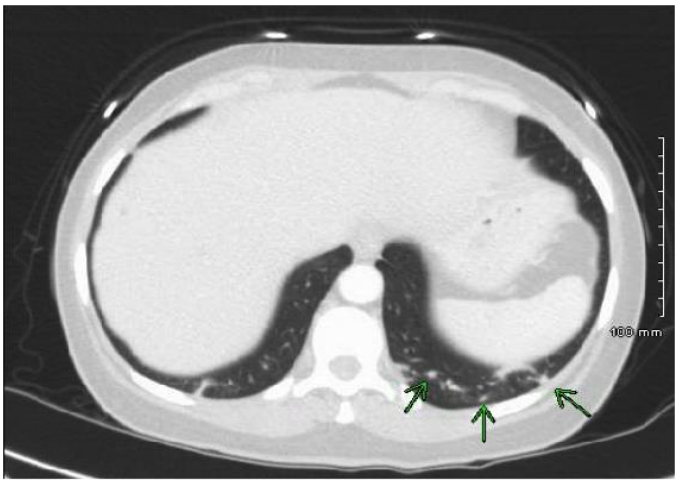

Figure 1: 52 year old female with lymphocytic interstitial pneumonia in the right lower lobe. Lung windowed axial Computed Tomography (CT) images of the lung bases on the patient's presenting CT abdomen/pelvis performed for pelvic pain, increasing abdominal girth and weight loss demonstrate nonspecific subcentimeter non-calcified solid pulmonary nodules in the left lower lobe (green arrows). (Protocol: Phillips Brilliance 64 slice CT scanner, 115 mA, 120 kvp, 3 mm slice thickness, CTDIvol 6.460 mGy, 120 mL Optiray 350 IV contrast at 2 mL/s)

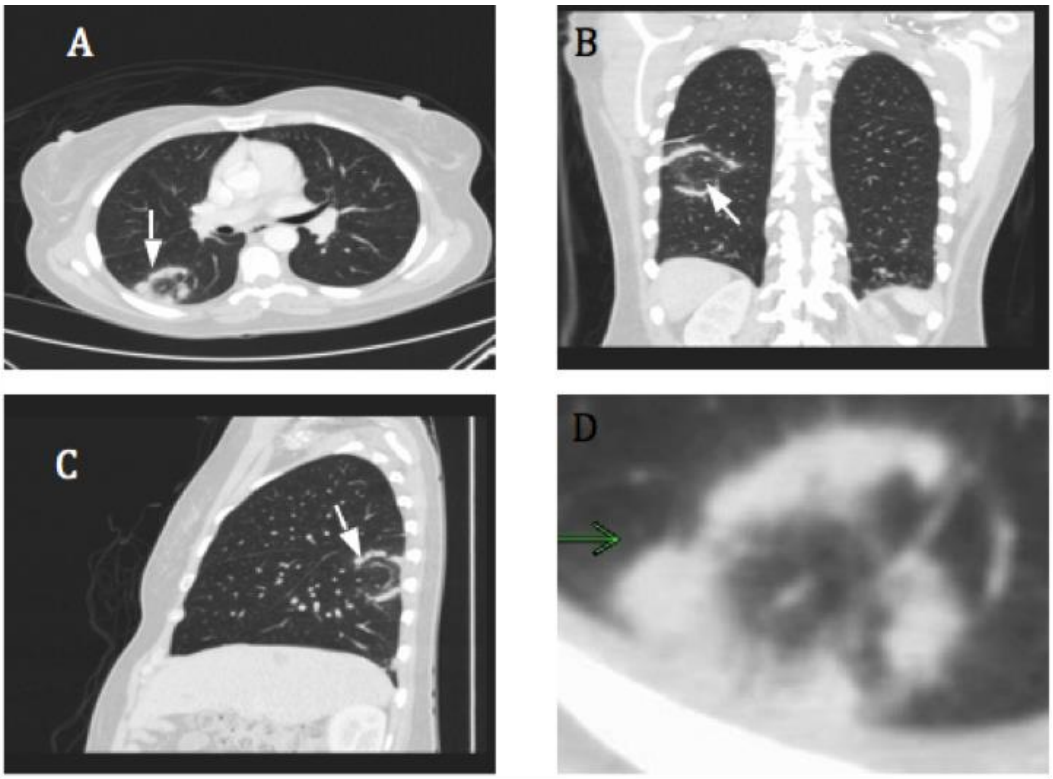

Figure 2: 52 year old female with lymphocytic interstitial pneumonia in the right lower lobe. Lung windowed axial (A), coronal (B), and sagittal (C) Computed Tomography images demonstrate a focal region of discontinuous crescentic consolidation with central ground glass opacification (arrows) and some normal appearing lung in the superior segment of the right lower lobe, consistent with the reversed halo sign. Coned-down image (D) of the reversed halo sign better illustrates the crescentic consolidation (green arrow) surrounding ground glass density admixed with normal lung parenchyma (white arrow). Protocol: Phillips Brilliance 64 slice CT scanner, 186 mA, 120 kvp, 3 mm slice thickness, CTDIvol, 9.135 mGy, 69mL Optiray 350 IV contrast at 2.2 mL/s)

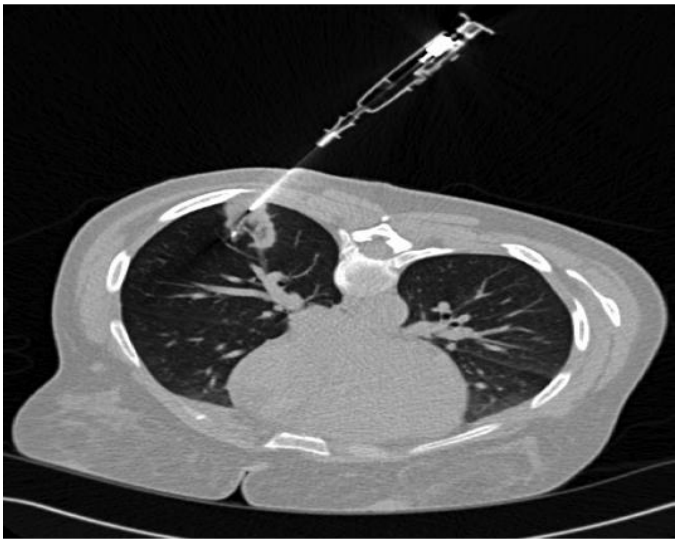

Figure 3: 52 year old female with lymphocytic interstitial pneumonia in the right lower lobe. Procedural image demonstrates Computed Tomography-guided trans-thoracic core biopsy of the crescentic consolidation with central ground glass density in the superior segment of the right lower lobe (Protocol: Siemens Volume 200m, 5 mm slices, 120 kvp 250 mA).

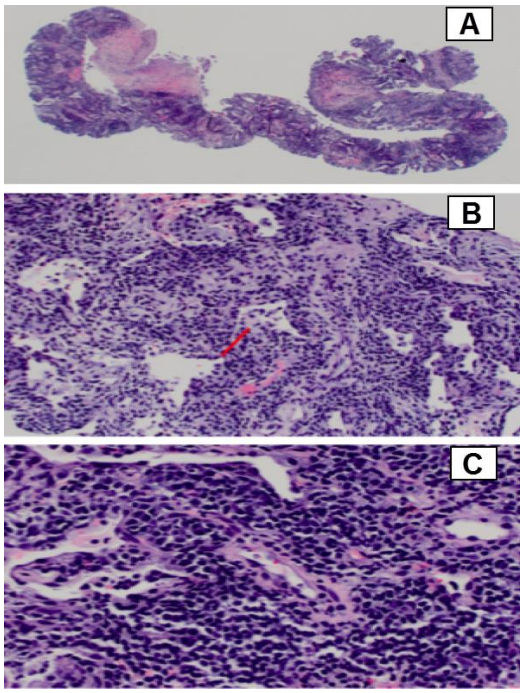

Figure 4: 52-year-old female with lymphocytic interstitial pneumonia in the right lower lobe. Histopathologic examination of the lung core biopsies stained with hematoxylin and eosin (H&E): (A) 20x magnification view shows prominent cellular infiltrate in the lung parenchyma; (B) 200x magnification view with marked widening of the alveolar septae (example indicated by red bar) by inflammatory infiltrate; (C) 400x magnification view - inflammatory infiltrate consists mostly of lymphocytes with some admixture of plasma cells, histiocytes and very rare eosinophils.

Etiology	• Reported as part of immune reconstitution syndrome • Mutations of the B-cell chronic lymphocytic leukemia/lymphoma 6 (BCL-6 or zinc finger protein 51) gene have shown association • Viruses such as Human immunodeficiency Virus-1 (HIV), Human T-Lymphotropic Virus-1 (HTLV) and Epstein Barr Virus (EBV) [11,12]
Incidence	• Exact incidence and prevalence unknown • 14% of patients with immunodeficiency states • 39% of patients with autoimmune disease [11,12]
Gender ratio	• Lymphocytic Interstitial Pneumonia (LIP) is more common in women when not associated with HIV infection[11, 12]
Age predilection	• Average age of 56 years • 4th and 7th decade of life in cases not associated with HIV [9,11,12]
Risk Factors	• Autoimmune disease • Systemic immunodeficiency states • EBV, HTLV-1, HIV-1 [6,8,9,11,12]
Treatment	• Corticosteroids are used if the patient is symptomatic and/or has physiologic compromise due to LIP • Alkylating agents for patients refractory to corticosteroids • Antibiotics are used for associated pulmonary infections. • LIP has been reported to improve with the use of zidovudine alone. Highly active antiretroviral therapy Highly Active Antiretroviral Therapy may result in improvement or resolution of LIP in some instances. • Bronchodilators may be used for associated wheezing [11, 12]
Prognosis	• Variable course with duration from 1 -11 years • Half of patients without HIV improve after treatment but relapses occur [11,12]
Findings on imaging Computed Tomography	• Ground glass opacities with diffuse distribution • Thin-walled perivascular/subpleural cysts and reticulation • Nodules follow lymphatics in centrilobular, subpleural and peribronchovascular distribution • Absence of Lymphadenopathy [6, 8,10,12]
Findings on Chest Radiograph	• Bilateral, predominantly lower zone, reticular or reticulonodular opacities [12]

Table 1: Summary table for Lymphocytic Interstitial Pneumonia

	Computed Tomography (CT) Findings	Chest Radiography (CXR) Findings
Invasive Fungal Pneumonia	• Reversed Halo Sign (RHS) • Air crescent sign • Ancillary findings: nodules >1 cm in diameter • Pleural effusion	• Patchy airspace nodules • Consolidation • Cavitations • Pleural effusion
Endemic Fungal Infections (Paracoccidioidomycosis, Histoplasmosis and Cryptococcosis)	• RHS • Air crescent sign • Ancillary findings: nodules >1 cm in diameter • Pleural effusion	• Patchy airspace nodules • Consolidation • Cavitations • Pleural effusion • Mediastinal adenopathy
Pneumocystis jiroveci pneumonia	• Patchy areas of ground glass attenuation with a background of interlobular septal thickening	• Diffuse bilateral airspace opacities extending from the perihilar region • Patchy asymmetric airspace opacities • Pneumatoceles • Pleural effusions • Intrathoracic adenopathy
Tuberculosis (TB)	• RHS • Centrilobular and pulmonary nodules • Subcarinal and left hilar lymphadenopathy • Areas of consolidation with cavitation	• Patchy or nodular airspace opacities • Cavity formation • Noncalcified round airspace opacities • Homogeneously calcified nodules (usually 5-20 mm) • Miliary TB - numerous small, nodular lesions that resemble millet seeds
Bacterial Pneumonia	• RHS • Nodular pattern • Linear pattern • Reticular pattern • Ground glass opacity • Consolidation	• Non-segmental homogeneous consolidation involving one or multiple lobes • Air bronchogram • Homogenous parenchymal lobar opacities
Organizing Pneumonia (Cryptogenic Organizing pneumonia)	• RHS • Airspace Consolidation with air bronchograms • Ground glass appearance or hazy opacities	• Patchy unilateral or bilateral consolidation • Small nodular opacities
Non-specific interstitial pneumonia	• RHS • Basal and peripheral predominance • Traction bronchiectasis	• Ground glass opacities • Reticular changes
Sarcoidosis	• Small nodules within ground glass area and outer areas of consolidation of the RHS • Large nodule in left upper lobe • Subpleural nodules along costal pleural surface and fissures • Hilar and/or paratracheal adenopathy with upper lobe predominance • Bilateral airspace opacities in a bronchovascular distribution • Calcified hilar or mediastinal lymph nodes in patients with longstanding disease	• Hilar and/or paratracheal adenopathy with upper lobe predominance • Bilateral airspace opacities • Pleural effusion (rare) • Egg shell calcifications
Lipoid Pneumonia	• Fat attenuation as low as –30 Hounsfield Unit within the consolidative opacities and nodules	• RHS • Opacities typically ground glass or consolidative, bilateral, and segmental or lobar in distribution and predominantly involve the middle and lower lobes • Poorly marginated nodules • Pneumatoceles • Pneumomediastinum • Pneumothorax (rare) • Pleural effusions

Table 2 (continued on next page): Differential diagnosis of Lymphocytic Interstitial Pneumonia

	Computed Tomography (CT) Findings	Chest Radiography (CXR) Findings
Wegener Granulomatosis	• RHS • Nodular opacities • Areas of consolidation • Cavitary lesion • Airspace Opacities	• Pulmonary nodules (solitary or multiple) • Both thick- and thin-walled cavities • Pneumothorax in association with cavitary nodules and subpleural blebs
Pulmonary Embolism	• RHS • Subpleural wedge-shaped consolidation • Pulmonary infarction	• Band atelectasis • Elevation of hemidiaphragm • Prominent central pulmonary artery • Oligemia at site of embolism
Lymphomatoid granulomatosis	• Pulmonary nodules or masses with peribronchovascular, subpleural, and lower lung zonal preponderance • Central low attenuation ground-glass halo • Peripheral enhancement of nodules and masses	• RHS • Bilateral nodules or masses in the lower and peripheral lung fields • Pleural effusions • Pneumonitis • Large mass like lesion • Cavitation of nodules • Pneumothorax
Lung Adenocarcinoma	• Areas of consolidation • Solitary or multiple pulmonary nodules • Solid nodules, mixed solid/ground glass nodules • Pure ground glass nodules • RHS present in tumor	• Variable • Solitary pulmonary nodule, mass • Pleural effusion • Lung collapse • Mediastinal or hilar fullness
Metastatic disease	• Multiple nodules in periphery of lungs • Cavitation • Calcification • Hemorrhage around nodules • Air-space pattern • RHS	• Large nodules frequently lobulated with irregular margins • Confluent nodules • Multinodular mass
Radiofrequency ablation of Pulmonary neoplasms	• RHS • Circumferential ground glass opacity surrounding lesion • Tumor cavitation • Bubble-like lucencies • Pleural thickening	• Non specific • Pneumonia • Pneumothorax
Radiation Therapy	• RHS • Ground glass opacities • Consolidation • Traction bronchiectasis • Volume loss	• Non-specific • Confined to the irradiation port • Airspace opacities • Pleural effusions or atelectasis

Table 2 (continued): Differential diagnosis of Lymphocytic Interstitial Pneumonia

ABBREVIATIONS

COP = Cryptogenic Organizing Pneumonia
CT = Computed Tomography
HRCT = High Resolution Computed Tomography
LIP = Lymphocytic Interstitial Pneumonia
RHS = Reversed Halo Sign
TVUS = Transvaginal Ultrasound

KEYWORDS

Reversed halo sign; Lymphocytic interstitial pneumonia, CT

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