Case Report

# Reversed halo sign in community acquired pneumonia

## A case report

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**Key words:**
- Reversed halo sign
- Atoll sign
- HRCT
- Ommunity acquired pneumonia

**SUMMARY**

**Reversed halo sign (RHS) is defined as central annular ground-glass opacity surrounded by a ring of denser consolidation at least 2mm thickness. It was first described by Voludaki et al. in a case report of two COP cases and later concluded that it was specific to cryptogenic organizing pneumonia. Since then, the RHS was associated with a wide range of pulmonary diseases: pulmonary fungal infections, tuberculosis, community – acquired pneumonia, sarcoidosis, pulmonary neoplasms, Wegener granulomatosis, pulmonary infraction and other diseases. We report a patient case of community-acquired pneumonia with of RHS on HRCT, and we review the literature on this radiological sign. We present a 70 years-old male, who was admitted to emergency department with lower tract respiratory infection symptoms, HRCT was performed and revealed multiple round ground-glass opacities fringed with peripheral consolidation in both lungs. The patient was diagnosed with community-acquired pneumonia and treated successfully with respiratory quinolone. Unfortunately, the infectious agent was not determined, as well as bronchoscopy with BAL was not helpful for diagnosis. At follow up, in 21 days and 4 months, the patient remained asymptomatic, and chest CT revealed a clear improvement. Finally, reversed halo sign has been reported in a wide range of conditions, and investigation of its aetiological factors is required.**

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### INTRODUCTION

Reversed halo sign, also known as atoll sign, is defined as central ground-glass opacity surrounded by denser consolidation of crescentinc or ring shape of at least 2mm thickness. It was first described on high-resolution CT (HRCT) as being specific for cryptogenic organizing pneumonia (COP).

Since then, the reversed halo sign was associated with a wide range of pulmonary diseases: pulmonary fungal infections, pneumonocystis pneumonia, tuberculosis, community – acquired pneumonia, lymphomatoid granulomatosis, Wegener granulomatosis, lipoid pneumonia, sarcoidosis, pulmonary neoplasms, pulmonary infraction and following radiation and radiofrequency therapy of pulmonary malignancies.

## CASE PRESENTATION

We are reporting a 70 years-old male patient who was admitted to our hospital with a one-week history of fever and non-productive cough. The patient also complained for anorexia and weight loss. He was treated with antibiotics (Amoxicillin/Clavulanic Acid Tb 875/125mg 1x2 + Clarithromycin Tb 500mg 1x2) five days before his admission by his general practitioner. Due to the persistence of fever he was referred to our clinic. His past medical history was unremarkable for any chronic medical illness. He was a smoker of 50 pack/years and denied ethanol, drug abuse and recent travel. No drug allergies were noted.

At presentation the patient's body temperature was 37.8°C, blood pressure was 120/75 mm Hg and percutaneous oxygen saturation was 97% in room air. His heart rate was 100 to 110 beats per minute with a sinus rhythm revealed on ECG. Respiratory rate was 18 to 20 breaths per minute. His heart sounds were normal with no murmurs or extra sounds. Auscultation revealed coarse crackles over the posterior right lung. There was no clubbing, cervical or axillary lymphadenopathy, skin lesions or joint swelling. Physical examinations of the rest systems did not provide any significant information.

The patient's white blood count was 5,760 cells/mm$^3$ (lymphocytes = 20%, neutrophils = 69%, and atypical = 8%). CRP level was 8.4 mg/L.

At presentation the chest X-ray showed a consolidative pattern in the right middle and lower lung fields. Chest computed tomography (CT) revealed multiple round ground-glass opacities fringed with consolidation in both lungs, namely the "reversed halo sign" (Figure 1).

Afterwards bronchoscopy with BAL was done and didn't reveal any remarkable endoscopic findings (bronchoalveolar lavage fluid (BALF) cell analysis: alveolar macrophages 84%, CD4+ 5%, CD8+ 3%, CD4+/CD8+ =1.6, neutrophils 5%, squamous epithelial cells 3%). Tests for antinuclear antibody (ANA) and anti neutrophil cytoplasmic antibody (ANCA) were negative. The Legionella and Pneumonococcal antigen urine testing were negative. Blood cultures were negative. Sputum cultures were

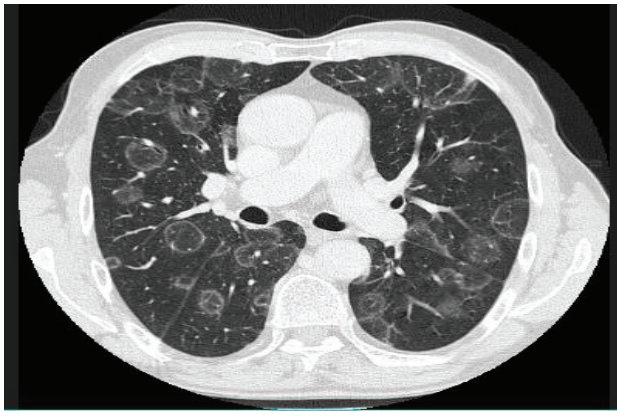

**FIGURE 1.** Multiple round ground-glass opacities fringed with consolidation in both lungs.

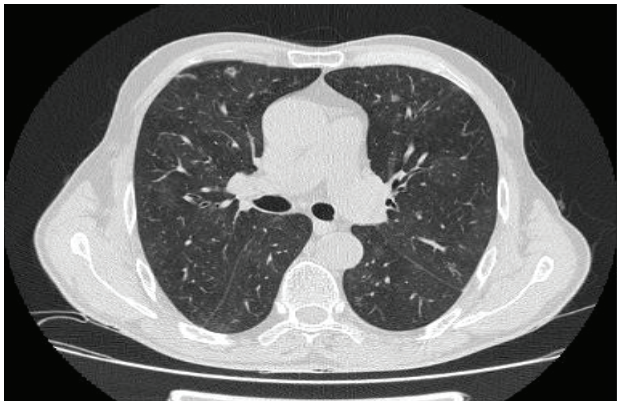

**FIGURE 2.** After 21 days.

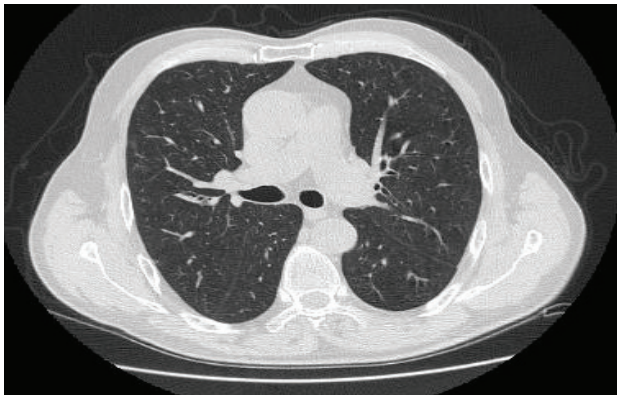

**FIGURE 3.** After 4 month.

not performed, since the patient had no expectoration.

The patient was diagnosed with community – acquired pneumonia and treated successfully with Moxifloxacin i.v. (400mg/d), without receiving corticosteroids. The symptoms were improved dramatically and he became afebrile within the fourth day. At follow up the patient remained afebrile. Computed tomography of the chest (after 21 days and 4 months) revealed a clear improvement (Figure 2, Figure 3).

## REVIEW

The reversed halo sign was first described and associated with **COP**[1], but it is not specific to this disease. A wide spectrum of conditions can manifest with the reversed halo sign on chest HRCT[2].

**The reversed halo sign** (RHS) is characterized by a focal area of ground-glass opacity surrounded by a more or less complete ring of consolidation on high-resolution CT (HRCT)[3].

Sometimes RHS can have specific **morphological** findings helpful in differential diagnosis as RHS with thickened rim and reticulation or "bird nest sign" and RHS with micronodules. The reticular RHS is linked with invasive fungal disease. RHS with micronodules is related to active granulomatous disease, mainly tuberculosis[4], but also paracoccidioidomycosis (PCM) or cryptococcosis and non-infectious granulomatous diseases such as sarcoidosis[5].

The presence of RHS on HRCT can be useful to narrow the differential diagnosis. Analyzing the patient's clinical history and additional CT findings is helpful for the final decision and treatment.

There is a spectrum of infectious, neoplastic, non-infectious/non-neoplastic diseases that may appear as RHS on HRCT. Various clinical situations that can guide the clinicians were described.

### Clinical signs and symptoms of pulmonary infection

In immunosuppressed patients **opportunistic fungal diseases** should be included in the differential diagnosis[5]. Opportunistic invasive fungal pneumonias (IFPs) have high morbidity and mortality. The most common IFP is an invasive pulmonary aspergilosis (IPA). Other angioinvasive moulds, such as Zygomycetes species are encountered in immunosuppressed patients[7,8]. In cases of IFP, the RHS is an early sign that results from pulmonary infarct. Other findings include nodules and pleural effusion[9].

The RHS has been described in up to 10% of patients with PCM[10]. PCM is frequent mycosis in Latin America. The HRCT findings of patients with pulmoparacoccidioidomycosis include ground-glass areas, small centrolobular nodules, cavitated nodules, and areas of emphysema[10].

In patients from areas with high rates of **Mycobacterium tuberculosis infection** (TB), pulmonary tuberculosis should always be included in the differential diagnosis. Additional CT findings can help the radiologist: centrilobular nodules and tree-in-bud opacities, as well as subcarinal and hilar lymphadenopathy, areas of consolidation with cavitation[11,12]. It is remarkable that areas of consolidation have usually upper lobe distribution in these cases.

**Pneumocystic Jiroveci Pneumonia** (PJP) is the most common opportunistic infection in HIV-positive patients. The RHS has been described in AIDS patients with pneumocystis pneumonia[13,6].

The RHS has been reported in cases of bacterial, pneumococcal[14], psittacosis or legionella **pneumonias**. Since infection can cause organizing pneumonia, it is possible that in some of the reported cases of bacterial pneumonia the RHS was a part of secondary organizing pneumonia, provoked by the inflammatory damage.

### Known primary neoplasm

The RHS has been described as an early secondary finding of **radiofrequency ablation** (RFA) of pulmonary nodules. The central GGO area is corresponded to an area of coagulative necrosis of the nodule, whereas peripheral consolidation is corresponded to fibrotic tissue[15].

**Radiation-induced lung disease** (RILD) is common following radiation therapy of the thorax. The RHS may be seen during the acute phase of RILD, in the first 4-12 weeks after treatment. It is probably related to inflammatory process or pulmonary necrosis related to radiation, or secondary organizing pneumonia triggered by radiation injury of the lung[2].

In patients under chemotherapy, multiple RHS lesions may correlate with non-specific interstitial pneumonia (NSIP) or organizing pneumonia linked with **drug-induced toxicity**[7].

In patients with a known primary malignancy RHS lesions may appear as atypical presentation of metastatic disease. The presence of new RHS lesions in these patients should be examined for lung **metastatic progression**[7].

### Patients with vascular or thromboembolic disease

Patients with **pulmonary embolism** (PE) may pres-

ent RHS on CT in case of pulmonary infarction. The RHS in patients with pulmonary infarction translates central coagulative necrosis with peripheral rim of collagen tissue produced by fibroblasts[16,17].

The RHS has been described in patient with **Wegener's granulomatosis**, in association with lung nodules, ground-glass opacities and cavitary lesions. RHS in this condition represent an intermediate stage that preceded cavitation[18].

## Asymptomatic patient or with subacute clinical symptoms

RHS has been described as an atypical manifestation in **sarcoidosis**. Sarcoidosis is a granulomatous disease. In 90% of cases lungs and intrathoracic lymph nodes are affected. RHS in sarcoidosis can represent either non-caseating granulomatous inflammation or secondary organizing pneumonia[7].

**Cryptogenic organizing pneumonia** (COP) is the most common lung disease described in immunocompetent patients with the RHS[1]. This sign can also be seen in cases of secondary organizing pneumonia. Histopathologically, the central ground-glass opacity of the RHS corresponds to alveolar septal inflammation; the peripheral consolidation represents organizing pneumonia within the alveolar ducts[6].

**Non-specific interstitial pneumonia** (NSIP) is an interstitial lung disease that may be idiopathic, but is more commonly associated with collagen vascular disease, hypersensitivity pneumonitis or drug toxicity[7]. The RHS correlates with interstitial inflammation that predominates in the middle and lower lung. HRCT in patient with NSIP reveal also reticular pattern, areas of consolidation and traction bronchiectasis.

The RHS has been described by Kanaji et al in case of exogenous **lipoid pneumonia** after inhaling spray paint. In this case RHS represented organizing pneumonia resulting from lipoid pneumonia[19].

**Pulmonary adenocarcinoma** may present as an area of consolidation, a single node or as multiple nodules. The RHS is an uncommon presentation of lung adenocarcinoma[7].

**Lymphomatoid granulomatosis** (LG) is associated with Epstein-Barr virus (EBV) which mainly affects the lungs. In this case, the RHS corresponds to area of aerated parenchyma with a peripheral ring of lymphomatoid vascular invasion[2].

## CONCLUSION

A wide variety of diseases, infectious and noninfectious, may present with the reversed halo sign on chest CT. The two most commonly associated diseases are the organizing pneumonia and invasive fungal pneumonia. The patient's history and clinical data in combination with the additional radiological findings should help to narrow the differential diagnosis. Although a biopsy is needed in many diseases with RHS on HRCT, it can be avoided in certain scenarios.

In the clinical case reported above, the RHS on chest CT was related with inflammatory process, provoked by infection. The diagnosis of CAP was based on clinical presentation, laboratory tests (acute phase protein), and clinical improvement after treatment with antibiotics only. Unfortunately, the infectious agent was not determined, as well as bronchoscopy with BAL was not helpful, since it was performed in the convalescent phase. Nevertheless, we assume that the causative agent provoked organizing pneumonia and persistent inflammation in lung parenchyma, causing prolonged symptoms.

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## ΠΕΡΙΛΗΨΗ

### Ανάστροφο σημείο της άλω στα πλαίσια πνευμονίας της κοινότητας

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Πνευμονολογικό Τμήμα, Γενικό Νοσοκομείο Σερρών

*Ανάστροφο σημείο της άλω ορίζεται ως δακτυλιοειδής σκίαση τύπου θολής υάλου περιβαλλόμενη από πυκνωτική περιφερική ζώνη πάχους τουλάχιστον 2 χλστ. Πρώτη φορά περιγράφτηκε από την Βολουδάκη και συνεργάτες σε 2 περιστατικά κρυπτογενούς οργανούμενης πνευμονίας και αρχικά θεωρήθηκε ως παθογνωμονικό σημείο της νόσου. Αργότερα ανάστροφο σημείο της άλω περιγράφτηκε σε διάφορα άλλα*

*πνευμονικά νοσήματα: μυκητιασικές πνευμονικές λοιμώξεις, φυματίωση, πνευμονία της κοινότητας, σαρκοείδωση, κοκκιωμάτωση Vegener, πνευμονικά έμφρακτα, νεοπλάσματα πνεύμονα κ.α. Στο παρόν άρθρο παρουσιάζεται περίπτωση ασθενούς με πνευμονία της κοινότητας με ακτινολογική εικόνα ανάστροφου σημείου της άλω στην αξονική τομογραφία υψηλής ευκρίνειας και γίνεται ανασκόπηση της βιβλιογραφίας. Πρόκειται για ασθενή ηλικίας 70 ετών που προσήλθε στο ΤΕΠ με συμπτώματα λοίμωξης κατώτερου αναπνευστικού, υπεβλήθη σε HRCT, η οποία ανέδειξε πολλαπλές δακτυλιοειδείς σκιάσεις τύπου θολής υάλου με πυκνωτική περιφερική ζώνη. Αντιμετωπίστηκε επιτυχώς με αναπνευστική κινολόνη, ως περιστατικό πνευμονίας της κοινότητας με μη ταυτοποιημένο αιτιολογικό παθογόνο, δεδομένου ότι ο εργαστηριακός έλεγχος δεν απομόνωσε υπεύθυνο μικροοργανισμό, όπως επίσης αργότερα η βρογχοσκόπηση με βρογχοκυψελιδικό έκπλυμα δεν ανέδειξε ιδιαιτέρα παθολογικά ευρήματα. Κατά την επανεκτίμηση σε 21 ημέρες και 4 μήνες ο ασθενής παρέμεινε ασυμπτωματικός με σαφώς βελτιωμένη ακτινολογική εικόνα. Συμπερασματικά, ακτινολογική εικόνα ανάστροφου σημείου της άλω στην HRCT δεν αποτελεί παθογνωμονικό σημείο μίας νόσου και συνιστάται να διερευνηθούν όλα τα αίτια εμφάνισης της RHS.*

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***Λέξεις - Κλειδιά:*** *Ανάστροφο σημείο της άλω, υψηλής ανάλυσης αξονική τομογραφία, πνευμονίας της κοινότητας*

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