**Abstract.** – The “reversed halo” sign (RHS) is a distinct radiological sign representing a focal rounded area of ground-glass opacity surrounded by a more or less complete ring of consolidation. Initially, it was reported in two cases of cryptogenic organizing pneumonia and was considered to be relatively specific of the disease. Since then, it has been reported in a wide variety of clinical entities, thus reducing its specificity. We describe the reversed halo sign in a case of pneumococcal pneumonia. To the best of our knowledge, this is the first report in English literature. The presence of the “reversed halo” sign during the resolution phase of pneumococcal pneumonia has serious implications. First, it further reduces its specificity. Second, it opens new areas of research regarding its significance in cases of cryptogenic organizing pneumonia.

**Key Words:** Reversed halo sign (RHS), Pneumococcal pneumonia, Cryptogenic organizing pneumonia (COP).

**Case Report**

A 57 year old Caucasian woman presented with a 7-days history of fever and non productive cough. She has been receiving clarithromycin (500 mg b.i.d.) by her general practitioner. Due to the persistence of fever she was referred to our clinic. At presentation the patient was febrile. She reported progressive dyspnea on exertion, a pleuritic pain in the lower right hemithorax and constitutional symptoms as malaise and anorexia. She denied headaches, nausea, vomiting, diarrhea, dysuria, night sweats, and weight loss.

She was currently retired and worked as a teacher. She was a non smoker and denied ethanol, drug abuse, exposure to domestic animals and recent travel. No drug allergies were noted.

The patient was febrile with a temperature of 38.5°C (101.3°F). Her 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. She was hemodynamically stable with a blood pressure of 115/70 mm Hg. Auscultation of the lungs revealed crackles in the right lung base.

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.

At presentation the chest X-ray showed a consolidative pattern in the right middle and lower lung fields. A computed tomography of the chest showed extensive areas of consolidation with air-bronchogram in the lateral segment of the middle lobe and the right lower lung. A right sided pleural effusion was also noted (Figure 1).

The patient was treated with moxifloxacin i.v. (400 mg q.d.). She became afebrile during the fourth day.

Sputum and blood cultures were negative, but the *Streptococcus pneumoniae* rapid urinary antigen test was positive.

At follow up the patient remained afebrile. Computed tomography of the chest revealed a clear improvement. In the posterior segment of the right lower lobe there was a ring shaped opacity surrounding an area of ground glass attenuation, thus creating the “reversed halo” sign (RHS) (Figure 2).

After 3 months a chest X-ray revealed minimal residual abnormalities (mild elevation of the
right hemidiaphragm and a linear opacity in the right lower lung field) (Figure 3).

It must be stressed that the patient never received corticosteroids. To the best of our knowledge this is the first time in English literature that the reversed halo sign is described in *pneumococcal pneumonia*.

The “reversed halo” sign is a focal rounded area of ground-glass opacity surrounded by a more or less complete ring of consolidation. Initially it was reported in the context of cryptogenic organizing pneumonia and was considered to be characteristic of this disease. However, the reversed halo sign has been described in a variety of diseases. Its evaluation should be made with extreme caution taking into account history, clinical examination and other radiological findings.

### Review

#### Non Infectious, non Neoplastic Causes

**Cryptogenic Organizing Pneumonia (COP)**

Classically, the reversed halo sign was correlated with Cryptogenic Organizing Pneumonia (COP). COP is one of the seven Idiopathic Interstitial Pneumonias. Formerly known as Bronchiolitis Obliterans Organizing Pneumonia (BOOP) the ATS/ERS consensus of the Idiopathic Interstitial Pneumonias clearly encourages the embracement of the term COP. The latter term is preferred in order to avoid confusion with airway diseases such as constrictive bronchiolitis. Although relatively rare, COP has become a well characterized clinical entity with a specific pathological background in the context of a negative aetiological investigation. The histological hallmark is the presence of intraluminal buds of connective tissue within alveolar ducts and alveoli. These can extend from one alveolus to the next through the pores of Kohn, thus creating a “butterfly” pattern. Organization of connective tissue can be seen within bronchioles in the form of proliferative bronchiolitis but this is not obligatory. Alveolar epithelial injury is believed to be the triggering event and the primary damage takes place on the alveolar level. Lung architecture is usually preserved. Giant cell, granuloma or hyaline membranes are absent.
The RHS in COP was first reported by Voloudaki et al. in two patients. This paper is very important because it also offers CT-pathologic correlation. The central area of ground glass attenuation corresponded to alveolar septal inflammation and cellular debris while the ring of consolidation corresponded to the above mentioned histological pattern of Organizing Pneumonia.

The Authors concluded that since these features had not been described in any other disease, they might be characteristic features of COP.

The actual term “reversed halo” sign was proposed by Kim et al. The purpose of his study was to evaluate its value in the diagnosis of COP. 31 patients with COP were examined. Patients with associated collagen vascular diseases or other known causes of Organizing Pneumonia were excluded. The RHS was identified in 6 patients (19%). It was not seen in any patients with Wegener’s granulomatosis (14 patients), diffuse bronchoalveolar carcinoma (10 patients), chronic eosinophilic pneumonia (5 patients) or Churg-Strauss syndrome (1 patient). Therefore, the Authors concluded that the reversed halo sign was relatively specific for a diagnosis of COP and can be considered another diagnostic adjunct.

Since then several reports in medical literature, correlate the reversed halo sign with other clinical entities thus questioning its diagnostic specificity regarding COP.

The RHS is also reported in a case of minocycline induced Organizing Pneumonia.

Non Specific Interstitial Pneumonia (NSIP)

Ueda et al. reported a case of a 39 year old male who presented with chest discomfort, dry cough and dyspnea. High resolution CT showed ground glass opacities with bibasilar distribution. Loss of lung volume was indicative of a fibrotic disorder. The RHS was also observed. A biopsy specimen was obtained during video assisted thoracic surgery, which established the diagnosis of NSIP.

Sarcoidosis

Marlow et al. were the first to report the RHS in sarcoidosis. They used the term “fairy ring” sign based on Celtic mythology. CT findings included multiple thick rings of consolidation while the central areas of the lesions comprised of normal appearing lung parenchyma. Diagnosis was established with transbronchial lung biopsy which showed noncaseating granulomas with stains and cultures negative for fungi and acid fast bacilli.

Recently, Kumazoe et al. also reported the RHS in a case of biopsy proven sarcoidosis (transbronchial). In this case it is important that besides the RHS there were also nodules with perilymphatic distribution (subpleural, perifissural) which are considered characteristic of sarcoidosis.

Exogenous Lipoid Pneumonia

Kanaji et al. reported the RHS in a patient with exogenous lipid pneumonia due to inhalation of paint spray. Initially, CT revealed multiple, bilateral nodules. After 5 months some of the nodules exhibited the RHS.

Wegener’s Granulomatosis

Agarwal et al. described the RHS in a patient with Wegener’s granulomatosis. It is important that high resolution CT besides the RHS also revealed a cavitating mass. Hence, it seems that the RHS was present at an intermediate stage before the development of cavitation.

Infectious Causes

Fungal Infections

Paracoccidioidomycosis

Paracoccidioidomycosis, also known as South American blastomycosis, is a frequent endemic mycosis in Latin America, especially in farm workers. Gasparetto et al. reviewed the high resolution CT findings in 148 patients with proven paracoccidioidomycosis. Besides the known findings of interlobular septal thickening, parenchymal bands, ground-glass opacities, centrilobular nodules, the reversed halo sign was recognized in 15 patients (10%). There was no zone predilection and in 2 cases the reversed halo sign was the only finding. 3 patients underwent surgical lung biopsy and a CT-pathologic correlation was possible. The central area of the lesions consisted of alveolar septa inflammation composed of macrophages, lymphocytes, plasma cells and some giant cells, with relative preservation of the alveolar spaces. The periphery of the lesion (i.e. the peripheral rim of consolidation seen on high resolution CT) consisted of dense intraalveolar cellular infiltrate without any signs of organizing pneumonia. This paper is very im-
important for two reasons. First, it questioned the specificity of the RHS for COP. Second, it suggested that this sign can be seen in patients with active infection and without organizing pneumonia. Since then there have been more reports of the RHS in infectious diseases.

**Zygomycosis, Aspergillosis**

In a study by Wahba et al., 15, 189 patients with proven and probable fungal pneumonia were examined (132 with invasive pulmonary aspergillosis, 37 with zygomycosis and 20 with fusariosis). The RHS was recognized in 8 patients (4%). Most of them (7) suffered from hematological malignancies. Although the majority of the patients had invasive pulmonary aspergillosis, the RHS was found almost exclusively in patients with zygomycosis (7 patients with zygomycosis and 1 patient with invasive pulmonary aspergillosis). Thus, the frequency of the RHS reached 10.8% in zygomycosis. Long-term follow up in 7 patients showed that the reversed halo sign evolved into cavitation in 5 of them (after a mean period of 32.6 days).

In conclusion, the presence of the RHS in an immunocompromised patient susceptible to opportunistic infection is compatible with fungal infection. In such cases due to the greater possibility of zygomycosis the administration of amphotericin B based therapy is preferred, since voriconazole although the drug of choice in invasive aspergillosis is not active against Zygomycetes species\(^{16,17}\).

Of course the radiological findings cannot be a substitute for bronchoalveolar lavage or tissue confirmation.

**Tuberculosis**

Ahuja et al.\(^ {18}\) reported the RHS in a 15 year old male with tuberculosis. High resolution CT also showed centrilobular nodules, subcarinal and left hilar lymphadenopathy.

**Neoplastic Causes**

**Lymphomatoid Granulomatosis**

Lymphomatoid granulomatosis (LYG) is a rare EBV related T-cell rich, B-cell lymphoproliferative disorder. Grade I, II and III are described. Grade III equals to angiocentric lymphoma. High resolution CT findings include areas of consolidation, thin walled cysts, interlobular septal thickenings, pleural effusion and nodules. Nodules in LYG are usually multiple with bilateral distribution. They can cavitate (20-40%) or exhibit the “halo sign”. Benamore et al.\(^ {19}\) reported a case of histological proven LYG exhibiting the RHS. The patient initially presented with the more typical nodular opacities (as described before), which progressed into the RHS.

**Discussion**

The RHS can be seen in a variety of diseases (Table I). The interpretation should be based on information from history, clinical examination and other radiological findings (Table II). The clinical context of the patient is crucial. Immuno-compromised patients (especially with hematological malignancies) are considered to have an infection until proven otherwise. A recent travel to areas with a high incidence of paracoccidioidomycosis or tuberculosis is significant. The RHS loses part of its significance if other radiological signs are present (i.e. centrilobular or perilymphatic nodules, tree in bud pattern, cavitation, and mediastinal lymphadenopathy). The RHS can be seen in COP but it cannot obviate the need for tissue confirmation. In cases where steroid treatment is initiated without a biopsy (patient desire or poor status) the clinician should reconsider the diagnosis if a prompt improvement is not achieved or if a relapse occurs while the patient is still on a high steroid dosage (i.e.

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**Table I.** Diseases exhibiting the “reversed halo” sign.

<table>
<thead>
<tr>
<th>A. Non infectious, non neoplastic diseases</th>
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<tbody>
<tr>
<td>1) Cryptogenic Organizing Pneumonia (COP)(^ {14,15})</td>
</tr>
<tr>
<td>2) Non Specific Interstitial Pneumonia (NSIP)(^ 7)</td>
</tr>
<tr>
<td>3) Sarcoïdosis(^ {8,9})</td>
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<tr>
<td>4) Exogenous lipid pneumonia(^ {11})</td>
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<td>5) Wegener’s granulomatosis(^ {12})</td>
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<tr>
<th>B. Infectious diseases</th>
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<tbody>
<tr>
<td>1) Fungal infections</td>
</tr>
<tr>
<td>1a Paracoccidioidomycosis(^ {14,15})</td>
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<tr>
<td>1b Zygomycosis(^ {16})</td>
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<tr>
<td>1c Invasive aspergillosis(^ {17})</td>
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<tr>
<td>2) Tuberculosis(^ {18})</td>
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<td>3) Pneumococcal pneumonia</td>
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<th>C. Neoplastic diseases</th>
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<td>1) Lymphomatoid granulomatosis(^ {19})</td>
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*Papers referring not just in case reports but to a series of patients.*
more than 20 mg of prednisolone per day). Any extrapulmonary symptoms are not compatible with COP and should point to other diagnoses (Table III).

To the best of our knowledge this is the first time in English literature that the reversed halo sign is described in pneumonococcal pneumonia. The diagnosis was based on the Streptococcus pneumoniae rapid urinary antigen test which is a sensitive and specific method. Pneumonococcal pneumonia is a recognized cause of Organizing Pneumonia. Hence, we recognize the possibility that the infection could have triggered an uncontrolled inflammatory process that persisted after the aetiological agent had disappeared.

There are also reports of spontaneous improvement as well as improvement with macrolides in patients with COP. We did not proceed to tissue sampling because it was thought to be unethical, since the patient had improved and was asymptomatic.

It is very important that the RHS was seen during the resolution phase. Potentially the RHS represents a phase during the resolution procedure. It is possible that in the context of COP, the RHS signifies the initiation of an effective healing process. Hence, studies should take place trying to address the following questions: (1) Is steroid therapy mandatory in patients with COP presenting the RHS or is spontaneous resolution possible? (2) Do patients with COP exhibiting the RHS have a smaller rate of relapses? It is known that COP is characterized by a high rate of relapses (ranging from 9% to 58%) Such studies could shed light into the pathogenesis of COP and explain the impressive improvement under steroid therapy.

In conclusion the RHS is seen on a wide variety of diseases. It cannot support a specific diagnosis. Its evaluation is directly related to the clinical context in which it has developed.

**References**


