REVIEW ARTICLE

The reversed halo sign: update and differential diagnosis

¹M C B GODOY, MD, PhD, ¹C VISWANATHAN, MD, ²E MARCHIORI, MD, PhD, ¹M T TRUONG, MD, ¹M F BENVENISTE, MD, ³S ROSSI, MD and ¹E M MAROM, MD

¹Department of Diagnostic Radiology, University of Texas M D Anderson Cancer Center, Houston, TX, USA, ²Federal University of Rio de Janeiro, Rio de Janeiro, Brazil, and ³Centro de Diagnostico Dr Enrique Rossi, Buenos Aires, Argentina

ABSTRACT. The reversed halo sign is characterised by a central ground-glass opacity surrounded by denser air–space consolidation in the shape of a crescent or a ring. It was first described on high-resolution CT as being specific for cryptogenic organising pneumonia. Since then, the reversed halo sign has been reported in association with a wide range of pulmonary diseases, including invasive pulmonary fungal infections, paracoccidioidomycosis, pneumocystis pneumonia, tuberculosis, community-acquired pneumonia, lymphomatoid granulomatosis, Wegener granulomatosis, lipoid pneumonia and sarcoidosis. It is also seen in pulmonary neoplasms and infarction, and following radiation therapy and radiofrequency ablation of pulmonary malignancies. In this article, we present the spectrum of neoplastic and non-neoplastic diseases that may show the reversed halo sign and offer helpful clues for assisting in the differential diagnosis. By integrating the patient's clinical history with the presence of the reversed halo sign and other accompanying radiological findings, the radiologist should be able to narrow the differential diagnosis substantially, and may be able to provide a presumptive final diagnosis, which may obviate the need for biopsy in selected cases, especially in the immunosuppressed population.

Received 3 October 2011
Revised 14 December 2011
Accepted 3 January 2012

DOI: 10.1259/bjr/54532316

© 2012 The British Institute of
Radiology

The reversed halo sign (RHS) is characterised by a central ground-glass opacity surrounded by a more or less complete ring of consolidation on high-resolution CT (HRCT) [1]. It has also been described as the “atoll sign” because of its resemblance to a coral atoll [2]. First reported in cryptogenic organising pneumonia, it was initially thought to be specific for this disease [3], but was subsequently described in a variety of pulmonary diseases [4, 5]. Despite being no longer considered specific, its presence in association with ancillary CT findings and the clinical history can be useful in narrowing the differential diagnosis. In this article, we present the spectrum of neoplastic and non-neoplastic diseases that may show the RHS and present clues that are helpful in the differential diagnosis. When the RHS is recognised on CT, by integrating the ancillary radiological and clinical data, the radiologist should be able to reach a succinct differential diagnosis to guide clinical decision making and/or determine treatment options.

Infectious diseases

Invasive fungal pneumonia

Opportunistic invasive fungal pneumonias (IFPs) have high morbidity and mortality rates. Although invasive

pulmonary aspergillosis (IPA) is the most common type of invasive fungal pneumonia, other angioinvasive moulds, such as *Zygomycetes* species (including *Rhizopus* and *Mucor*), are increasingly encountered in immunosuppressed hosts [6]. Early institution of high-dose antifungal therapy is associated with improved outcomes, and it is important to differentiate between IPA and pulmonary zygomycosis (PZ) because the therapy for presumed fungal pneumonia in this population is often aimed at the more prevalent aspergillosis, and the preferred antifungal agent for IPA is voriconazole, which is not effective against PZ. The clinical findings for PZ are similar to those for IPA. High suspicion for PZ should be raised in immunosuppressed patients with CT scan showing RHS, especially in the context of concomitant sinusitis and voriconazole prophylaxis [6], although the RHS can also be seen in patients with IPA [7].

In cases of IFP, the RHS is an early sign that results from pulmonary infarct. During the subacute phase an air-crescent sign is usually seen (Figure 1). Ancillary findings include nodules >1 cm in diameter and pleural effusion [8] (Figure 2).

Endemic fungal infections

The RHS has been described in up to 10% of the cases of paracoccidioidomycosis (South American blastomycosis) [9]. Paracoccidioidomycosis is the most common endemic systemic fungal infection in Latin America, particularly in Brazil. The lungs are affected in 80% of

Address correspondence to: Dr Myrna Godoy, Department of Diagnostic Radiology, University of Texas M D Anderson Cancer Center, 1515 Holcombe Boulevard, Unit 371, Houston, TX 77030, USA. E-mail: mgodoy@mdanderson.org

Figure 1. Pulmonary zygomycosis in a 22-year-old male with precursor B-cell acute lymphocytic leukaemia. (a) CT image shows the reversed halo sign (RHS) in the left upper lobe (arrows). (b) CT scan performed 2 months later shows interval development of cavitation (air crescent sign). The presence of RHS in an immunosuppressed patient is highly suggestive of pulmonary zygomycosis, especially if the patient is receiving prophylaxis for aspergillosis.

cases, and residual fibrotic lesions have been observed in approximately 60% of cases (Figure 3) [10]. Surgical lung biopsy specimens showed that the central ground-glass area of the RHS on CT scan corresponded to inflammatory infiltrate involving mainly the alveolar septa, whereas the peripheral ring of consolidation consisted of dense and homogeneous intra-alveolar inflammatory infiltrate [9].

The RHS has also been sporadically reported in patients with histoplasmosis and cryptococcosis [11, 12].

Pneumocystis jiroveci pneumonia

Pneumocystis pneumonia remains the most prevalent opportunistic infection in patients with acquired immunodeficiency syndrome (AIDS), although its prevalence has decreased since the introduction of highly active antiretroviral therapy [13]. The RHS was been rarely reported in human immunodeficiency virus

(HIV)-positive patients with *pneumocystis pneumonia* [14, 15].

Tuberculosis

After a steady decline of the prevalence of tuberculosis, since the mid-1980s there has been a resurgence due to the HIV epidemic and development of multidrug-resistant strains of *Mycobacterium tuberculosis*. Ahuja et al [16] described the first case of pulmonary tuberculosis with the RHS in a 15-year-old male. Additional findings included centrilobular nodules and subcarinal and left hilar lymphadenopathy [16]. In another case of tuberculosis with the RHS in an adult female, the associated CT findings included pulmonary nodules and areas of consolidation with cavitation [17]. A peculiarity reported in a patient with active tuberculosis and the RHS, and also mentioned in other granulomatous infectious processes including schistosomiasis and cryptococcosis,

Figure 2. Invasive pulmonary aspergillosis in a 54-year-old female with multiple myeloma and secondary plasma cell leukaemia who had undergone chemotherapy. (a) High-resolution CT image at the lung base shows a right lower-lobe pulmonary nodule (arrow) and the reversed halo sign (RHS) in the left lower lobe (curved arrow) with adjacent ground-glass opacities. (b) CT image with mediastinal window settings shows the peripheral consolidation of the RHS (asterisks). Note a small right pleural effusion.

Figure 3. Paracoccidioidomycosis in a 49-year-old male, resident of a rural area in Brazil. CT image shows reversed halo sign (RHS) lesions (arrows) and bilateral small poorly margined pulmonary nodules. The presence of RHS in a patient from an endemic region for fungal infection should raise concern for that specific fungal infection.

is the nodular appearance of the ring in the RHS, which has been histologically proven to correlate to granulomas, therefore assisting in the differentiation of active granulomatous disease *vs* organising pneumonia (Figure 4) [12, 18].

Bacterial pneumonia

The RHS has been sporadically reported in cases of community-acquired pneumonia, including pneumococcal pneumonia [4], psittacosis [19] and Legionnaire's pneumonia [20]. From the few reports describing the RHS with bacterial infection, it appears that the RHS is seen as a later manifestation of bacterial pneumonia, during the resolution phase. In this setting, the RHS is not helpful in treatment selection, which differs substantially from the RHS seen with invasive fungal infections, in which it is useful for antifungal medication selection.

Because infection can cause organising pneumonia histologically identical to that seen with cryptogenic organising pneumonia (COP), it is possible that in some of the reported cases of RHS associated with bacterial pneumonia in immune-competent individuals, in which open lung biopsy or complete resection were not obtained, the RHS may have represented secondary organising pneumonia that was triggered by the infection rather than a direct manifestation of the infectious process itself.

Non-infectious, non-neoplastic diseases

Organising pneumonia

Cryptogenic organising pneumonia is the most common condition described in immunocompetent patients with the RHS [2, 3, 21–23]. In one study, the RHS was found in 19% of HRCT scans of patients with COP [21]. This sign can also be seen in patients with secondary organising pneumonia (Figure 5) [22]. Histopathological

Figure 4. Tuberculosis in a 59-year-old female. High-resolution CT image shows bilateral small centrilobular nodules, tree-in-bud opacities and areas of reversed halo sign (RHS). Note the nodular appearance of the ring of consolidation of the RHS lesions (arrows), which may be helpful in the differentiation between active granulomatous disease and cryptogenic organising pneumonia. The presence of associated centrilobular nodules and tree-in-bud opacities should raise suspicion of tuberculosis.

correlation in the first two reports of COP with the RHS showed that the central ground-glass opacity of the RHS corresponded to alveolar septal inflammation and cellular debris; the peripheral consolidation represented organising pneumonia within the alveolar ducts [3].

Figure 5. Organising pneumonia in a 53-year-old male with graft-vs-host disease after stem cell transplantation for treatment of acute myelogenous leukaemia. CT scan shows bilateral peripheral and peribronchovascular consolidative opacities with the reversed halo sign (arrows). Open-lung biopsy showed organising pneumonia. The patient was treated with steroids with resolution of the lesions.

Non-specific interstitial pneumonia

Non-specific interstitial pneumonia (NSIP) is a chronic interstitial lung disease that may be idiopathic, but is more commonly associated with collagen vascular disease, hypersensitivity pneumonitis or drug toxicity [24]. The spectrum of the disease ranges from predominant interstitial inflammation (cellular NSIP) to predominant fibrosis (fibrotic NSIP), the latter having a worse prognosis [24, 25]. The RHS has been sporadically reported in cases of cellular NSIP [26, 27].

Sarcoidosis

Sarcoidosis is a multisystem granulomatous disease of unknown aetiology that affects the lungs and intrathoracic lymph nodes in more than 90% of patients [28]. The RHS is an atypical manifestation of the disease that has been reported in a few patients (Figure 6) [29–31]. As reported in granulomatous infections, Kumazoe et al [30] described the presence of small nodules within the ground-glass area and around the outer areas of consolidation of the RHS in a patient with sarcoidosis. Associated CT findings included a large nodule in the left upper lobe, small subpleural nodules along the costal pleural surface and fissures, and mediastinal lymphadenopathy. Histological correlation from the RHS showed non-caseating granuloma with no evidence of organising pneumonia. Fujii et al [29], however, described a patient with sarcoidosis with the RHS in which the histopathologic correlation showed organising pneumonia. Therefore the RHS in sarcoidosis can be a result of either non-caseating granulomatous inflammation or secondary organising pneumonia. The presence of associated small nodules within the RHS should lead to the presumptive diagnosis of a granulomatous process over organising pneumonia [31].

Figure 6. Sarcoidosis in a 44-year-old female. High-resolution CT image shows bilateral nodular opacities with the reversed halo sign (RHS) (arrows) and small pulmonary nodules with predominant perilymphatic distribution. The presence of the RHS associated with nodules in perilymphatic distribution and mediastinal and hilar lymphadenopathy (not shown) should raise suspicion of sarcoidosis.

Lipoid pneumonia

Lipoid pneumonia is an uncommon condition that results from accumulation of lipids in the alveoli. Exogenous lipoid pneumonia is caused by inhalation or aspiration of animal fat or vegetable or mineral oil, whereas endogenous lipoid pneumonia is usually associated with bronchial obstruction [32]. Kanaji et al [33] reported a case of exogenous lipoid pneumonia caused by chronic paint spray inhalation that presented with bilateral irregular pulmonary nodules. 5 months after the diagnosis, the RHS was noted on HRCT scan. Given the time lag between diagnosis by video-assisted thoracic surgery and identification of the RHS on HRCT scan, it is possible that the RHS represented organising pneumonia resulting from lipoid pneumonia.

Wegener granulomatosis

Wegener granulomatosis is an uncommon necrotising vasculitis associated with elevation of cytoplasmic antineutrophil cytoplasmic antibody titres. The upper respiratory tract is affected in almost all patients, and the lungs and kidneys are involved in 90% and 80% of patients, respectively [34]. Agarwal et al [35] described a patient with Wegener granulomatosis who presented with weight loss, epistaxis, fever, cough and chest pain. The patient had proteinuria due to glomerulonephritis. The HRCT scan showed the RHS, associated with nodular opacities, ground-glass opacities, areas of consolidation and a cavitory lesion. In this case, the RHS may have represented an intermediate stage that preceded cavitation, such as that seen in patients with invasive fungal pneumonia [7] and pulmonary infarction.

Pulmonary embolism

Acute pulmonary embolism (PE) is a common condition associated with substantial morbidity and mortality. In the USA, the incidence is estimated at 1 case per 1000 persons per year, and as many as 50 000–100 000 deaths annually are attributed to PE [36]. Pulmonary infarction occurs in 10% of cases of documented PE, usually presenting as a subpleural wedge-shaped consolidation on CT scan [37]. The RHS may be present and may precede cavitation (Figure 7).

Neoplastic diseases

Lymphomatoid granulomatosis

Lymphomatoid granulomatosis, also known as angiocentric lymphoma or angiocentric immunoproliferative lesion, is a rare Epstein-Barr virus-associated systemic lymphoproliferative disease. Progression to lymphoma has been reported in 12–47% of patients [38]. Benamore et al [39] reported a patient with lymphomatoid granulomatosis who presented with pulmonary nodules that subsequently appeared as the RHS.

Figure 7. Acute pulmonary embolism with pulmonary infarction in a 64-year-old female. (a) CT image shows the reversed halo sign in the superior segment of the right lower lobe. (b) CT image (mediastinal window settings) shows a clot in the distal right main pulmonary artery extending to the superior segmental branch of the right lower lobe pulmonary artery. (c) 2 month follow-up CT scan shows cavitation of the infarcted pulmonary parenchyma.

Lung adenocarcinoma

Lung adenocarcinoma may present on CT as an area of consolidation or as solitary or multiple pulmonary nodules, including solid nodules, mixed solid/ground-glass nodules and pure ground-glass nodules. Predominant ground-glass components within the nodules tend to correlate with slow growth and tend to correspond with lepidic pattern of tumour on histopathology [40, 41], which includes the spectrum from adenocarcinoma *in situ* to lepidic predominant invasive adenocarcinoma, previously termed, respectively, bronchioloalveolar cell carcinoma (BAC) and mixed subtype adenocarcinoma with BAC features [42]. The RHS can be seen in these

tumours when the ground-glass component of the nodule is present in the centre of the lesion (Figure 8).

Metastatic disease

The typical CT findings for pulmonary metastases are multiple round variable-sized nodules, predominantly in the periphery of the lungs. However, atypical findings are not uncommon, including cavitation, calcification, haemorrhage around the nodules and air-space pattern

Figure 8. Multifocal pulmonary adenocarcinoma in a 70-year-old female. CT image shows bilateral pulmonary nodules with the reversed halo sign (black arrows) and ground-glass pulmonary nodules (white arrows).

Figure 9. Metastatic renal cell carcinoma in a 73-year-old male. The CT scan shows multiple bilateral lesions with reversed halo sign (RHS), biopsy proven to represent metastatic renal cell carcinoma in a background of fibrosis and necrosis. In patients with a known primary malignancy, RHS lesions may represent atypical presentation of metastatic disease. The main differential diagnosis is organising pneumonia, which can be related to drug toxicity if the patient is receiving chemotherapy.

Figure 10. Reversed halo sign (RHS) following radiofrequency ablation (RFA) of a pulmonary adenocarcinoma in a 64-year-old female. (a) CT image shows the adenocarcinoma in the left lower lobe. (b) CT scan performed 1 month after RFA of the tumour shows development of the RHS. When present shortly after RFA, the RHS should not be confused with recurrence of disease.

[43]. The RHS is another atypical manifestation of pulmonary metastatic disease (Figure 9).

Post-treatment changes

Radiofrequency ablation

A spectrum of CT features have been described following radiofrequency ablation (RFA) of pulmonary neoplasms, including circumferential ground-glass opacity surrounding the treated lesion immediately following RFA, tumour cavitation, bubble-like lucencies and pleural thickening in the region of the pleura traversed by the radiofrequency electrode [44]. CT scan following RFA enables assessment of effectiveness of tumour treatment and detection of recurrence. Pulmonary neoplasms treated with RFA frequently increase in size from baseline until 1–3 months following RFA, then remain stable or decrease in size [44]. Mango et al report an RHS seen 6 weeks after RFA of a lung neoplasm in an 80-year-old male, which resolved on follow-up imaging [44]. The authors postulated that the central ground-glass opacity of the RHS corresponded to coagulation necrosis of

the tumour and adjacent pulmonary parenchyma. When present in a patient shortly after RFA, the RHS should not be confused with recurrence of disease (Figure 10).

Radiation therapy

Radiation-induced lung disease (RILD) is common following radiation therapy of the thorax. The typical CT findings include ground-glass opacities and/or consolidation in the acute phase, which usually occurs within 4–12 weeks after completion of radiotherapy. Traction bronchiectasis, volume loss and consolidation (radiation fibrosis) are typically seen during the late phase, which usually develops within 6–12 months after completion of radiation therapy, and can progress for up to 2 years before stability occurs [45]. The RHS may be seen during the acute phase of RILD (Figures 11 and 12). When it appears at the location of the tumour, it is probably due to tumour necrosis (Figure 11). When seen within the radiation field, but outside the location of the radiated tumour, it is probably related to inflammatory process or pulmonary necrosis related to radiation, or secondary organising pneumonia triggered by radiation injury to the lung (Figure 12) [46].

Figure 11. Reversed halo sign (RHS) following proton radiation therapy for a poorly differentiated squamous cell carcinoma in a 71-year-old male. (a) CT image shows the primary tumour in the left peri-hilar region. (b) CT scan performed 4 months after radiation therapy shows development of the RHS in the region of the tumour consistent with necrosis.

Figure 12. Reversed halo sign (RHS) following radiation therapy for a metastatic non-small cell lung cancer in a 59-year-old female. (a) CT image shows the primary tumour in the left upper lobe. (b) Positron emission tomography CT axial fusion image shows fludeoxyglucose (FDG) avid metastasis in the left scapula (arrow). (c) CT scan 1 month after chemotherapy and palliative radiation therapy to the left scapula shows development of the RHS in the left lung apex (arrow) adjacent to the primary tumour, consistent with radiation pneumonitis. (d) A follow-up CT scan performed 4 months after (c) shows development of cavitation in the region of the RHS. When present within the radiation field shortly after radiation therapy, the RHS should not be confused with infection or recurrence or disease.

Clinical application of the reversed halo sign

The RHS is not as specific as initially reported [3]. However, when combined with the patient's clinical data and ancillary radiological data, the radiologist should be able to narrow the differential diagnosis substantially, as summarised in Figure 13. The importance of this sign is perhaps greatest when imaging the severely immunocompromised host. Severely immunocompromised hosts include those with prolonged neutropaenia of less than 500 neutrophils per millimetre cubed for longer than 10 days, patients treated aggressively for leukaemia or lymphoma, or patients with graft-*vs*-host disease [47]. The presence of the RHS in such patients should be considered invasive fungal pneumonia until proven otherwise [48]. The diagnosis of invasive fungal infection heavily relies on CT findings and any delay in treatment results in a significant increase in mortality. When the RHS is encountered in such a scenario, fungal disease (and especially PZ) should be suspected. Knowledge of this sign and its aetiologies is useful in guiding appropriate antifungal coverage.

In the context of AIDS, the possibility of *Pneumocystis jiroveci* infection should be considered, especially when associated with ground-glass opacities on CT.

Tuberculosis should be suspected when the RHS has a nodular appearance and is associated with centrilobular nodules and pattern of endobronchial spread, especially if seen in an individual with increased risk, such as a patient with AIDS, an immigrant or a prison inmate.

When the RHS is encountered in patients with known extrapulmonary malignancy, it probably represents metastatic disease. However, because organising pneumonia may be triggered by chemotherapy, a new lesion with RHS that develops after starting chemotherapy should raise suspicion for organising pneumonia. When encountered as the primary cancer, as can be seen with pulmonary adenocarcinoma with lepidic growth, it is the timing of disease, with slow progression typical for this tumour, that should raise the suspicion that malignancy is the diagnosis and lead to biopsy.

In the setting of post-treatment changes, the RHS probably represents pulmonary infarction or inflammation. With the correct clinical history and timing after therapy, a biopsy can be avoided.

In conclusion, since its original description, the RHS has been reported in a variety of conditions. Although a biopsy is frequently needed to establish the diagnosis of many of the diseases that can be encountered with the RHS, by combining the clinical history and additional CT

Figure 13. Differential diagnosis of the reversed halo sign (RHS). AIA, angioinvasive aspergillosis; AIS, adenocarcinoma *in situ*; COP, cryptogenic organising pneumonia; LPA, lepidic predominant adenocarcinoma; N, no; NSIP, non-specific interstitial pneumonia; OP, organising pneumonia; PJP, *Pneumocystis jirovecii* pneumonia; PZ, pulmonary zygomycosis; RFA, radiofrequency ablation; Y, yes. *Includes immunosuppression, close contact with a person with tuberculosis, residence in or immigration from country where tuberculosis is common, residence in nursing home or prison, homelessness. **Includes cavitory lesions, lobular consolidation, centrilobular nodules and tree-in-bud opacities, as well as nodularity of the wall of the RHS and small nodules inside the RHS. ***Suspected in patients with acquired immunodeficiency syndrome. *Upper respiratory tract disease and non-specific glomerulonephritis, and elevation of cytoplasmic antineutrophil cytoplasmic antibody titres. ††Nodularity of the wall of the RHS and small nodules inside the RHS, possibly associated with symmetrical bilateral hilar and right paratracheal lymphadenopathy and small nodules with perilymphatic distribution. †Associated with connective tissue diseases, aspiration, drug toxicity, hypersensitivity pneumonitis, infection or radiation therapy. ††Less likely.

findings, in certain scenarios a biopsy can be avoided. Knowledge of the various manifestations of the reversed halo sign and its aetiologies is useful in avoiding misinterpretation, and can lead to appropriate, timely clinical management.

References

- Hansell DM, Bankier AA, MacMahon H, McLoud TC, Muller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. *Radiology* 2008;246:697–722.
- Zompatori M, Poletti V, Battista G, Diegoli M. Bronchiolitis obliterans with organizing pneumonia (BOOP), presenting as a ring-shaped opacity at HRCT (the atoll sign). A case report. *Radiol Med* 1999;97:308–10.
- Voloudaki AE, Bouros DE, Froudarakis ME, Datseris GE, Apostolaki EG, Gourtsoyiannis NC. Crescentic and ring-shaped opacities. CT features in two cases of bronchiolitis obliterans organizing pneumonia (BOOP). *Acta Radiol* 1996;37:889–92.
- Tzilas V BA, Provata A, Koti A, Tzouda V, Tsoukalas G. The “reversed halo” sign in pneumococcal pneumonia: a review with a case report. *Eur Rev Med Pharmacol Sci* 2010;14:481–86.
- Marchiori E, Zanetti G, Escuissato DL, Souza AS Jr, Meirelles GD, Fagundes J, et al. Reversed halo sign: high-resolution CT findings in 79 patients. *Chest* 2012;141:1260–6.

6. Chamilos G, Marom EM, Lewis RE, Lionakis MS, Kontoyiannis DP. Predictors of pulmonary zygomycosis versus invasive pulmonary aspergillosis in patients with cancer. *Clin Infect Dis* 2005;41:60–6.
7. Wahba H, Truong MT, Lei X, Kontoyiannis DP, Marom EM. Reversed halo sign in invasive pulmonary fungal infections. *Clin Infect Dis* 2008;46:1733–7.
8. Marom EM, Kontoyiannis DP. Imaging studies for diagnosing invasive fungal pneumonia in immunocompromised patients. *Curr Opin Infect Dis* 2011;24:309–14.
9. Gasparetto EL, Escuissato DL, Davaus T, de Cerqueira EM, Souza AS Jr, Marchiori E, et al. Reversed halo sign in pulmonary paracoccidioidomycosis. *AJR Am J Roentgenol* 2005;184:1932–4.
10. Tobon AM, Agudelo CA, Osorio ML, Alvarez DL, Arango M, Cano LE, et al. Residual pulmonary abnormalities in adult patients with chronic paracoccidioidomycosis: prolonged follow-up after itraconazole therapy. *Clin Infect Dis* 2003;37:898–904.
11. Marchiori E, Melo SM, Vianna FG, Melo BS, Melo SS, Zanetti G. Pulmonary histoplasmosis presenting with the reversed halo sign on high-resolution CT scan. *Chest* 2011;140:789–91.
12. Marchiori E, Zanetti G, Hochhegger B, Irion KL. Re: Reversed halo sign: nodular wall as criterion for differentiation between cryptogenic organizing pneumonia and active granulomatous diseases. *Clin Radiol* 2010;65:770–1.
13. Thomas CF Jr, Limper AH. Pneumocystis pneumonia. *N Engl J Med* 2004;350:2487–98.
14. Otera H, Tada K, Sakurai T, Hashimoto K, Ikeda A. Reversed halo sign in pneumocystis pneumonia: a case report. *BMC Med Imaging* 2010;10:26.
15. Marchiori E, Zanetti G, Meirelles GS, Escuissato DL, Souza AS Jr, Hochhegger B. The reversed halo sign on high-resolution CT in infectious and noninfectious pulmonary diseases. *AJR Am J Roentgenol* 2011;197:W69–75.
16. Ahuja A, Gothi D, Joshi JM. A 15-year-old boy with “reversed halo”. *Indian J Chest Dis Allied Sci* 2007;49:99–101.
17. Marchiori E, Grando RD, Simoes Dos Santos CE, Maffazzoli Santos Balzan L, Zanetti G, Mano CM, et al. Pulmonary tuberculosis associated with the reversed halo sign on high-resolution CT. *Br J Radiol* 2010;83:e58–60.
18. Marchiori E, Zanetti G, Irion KL, Nobre LF, Hochhegger B, Mancano AD, et al. Reversed halo sign in active pulmonary tuberculosis: criteria for differentiation from cryptogenic organizing pneumonia. *AJR Am J Roentgenol* 2011;197:1324–7.
19. Okubo T, Miyazaki E, Ueo M, Okubo F, Ando M, Fukami T, et al. A case of psittacosis with wandering infiltrates developing to acute respiratory distress syndrome. [In Japanese.] *Nihon Kokyuki Gakkai Zasshi* 2007;45:419–23.
20. Sakai F, Tokuda H, Goto H, Tateda K, Johkoh T, Nakamura H, et al. Computed tomographic features of Legionella pneumophila pneumonia in 38 cases. *J Comput Assist Tomogr* 2007;31:125–31.
21. Kim SJ, Lee KS, Ryu YH, Yoon YC, Choe KO, Kim TS, et al. Reversed halo sign on high-resolution CT of cryptogenic organizing pneumonia: diagnostic implications. *AJR Am J Roentgenol* 2003;180:1251–4.
22. Tokuyasu H, Isowa N, Shimizu E, Yamadori I. Reversed halo sign associated with dermatomyositis. *Intern Med* 2010;49:1677–8.
23. Walsh SL, Robertson BJ. Images in thorax. The atoll sign. *Thorax* 2010;65:1029–30.
24. Silva CI, Muller NL. Idiopathic interstitial pneumonias. *J Thorac Imaging* 2009;24:260–73.
25. American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. This joint statement of the American Thoracic Society (ATS), and the European Respiratory Society (ERS) was adopted by the ATS board of directors, June 2001 and by the ERS Executive Committee, June 2001. *Am J Respir Crit Care Med* 2002;165:277–304.
26. Ueda S, Inoue R, Tanaka K, Mizumori Y, Kawamura T, Nakahara Y, et al. A case of nonspecific interstitial pneumonia with reversed halo sign on chest HRCT. [In Japanese.] *Nihon Kokyuki Gakkai Zasshi* 2007;45:248–52.
27. Hong SH, Kang EY, Shin BK, Shim JJ. Reversed halo sign on thin-section CT in a patient with non-specific interstitial pneumonia. *Br J Radiol* 2011;84:e103–5.
28. Kuhlman JE, Fishman EK, Hamper UM, Knowles M, Siegelman SS. The computed tomographic spectrum of thoracic sarcoidosis. *Radiographics* 1989;9:449–66.
29. Fujii M, Ida M, Enomoto N, Nogimura H, Nakamura Y, Chida K, et al. A case of sarcoidosis manifesting as annular opacities after multiple nodular shadows. [In Japanese.] *Nihon Kokyuki Gakkai Zasshi* 2002;40:970–4.
30. Kumazoe H, Matsunaga K, Nagata N, Komori M, Wakamatsu K, Kajiki A, et al. “Reversed halo sign” of high-resolution computed tomography in pulmonary sarcoidosis. *J Thorac Imaging* 2009;24:66–8.
31. Marchiori E, Zanetti G, Mano CM, Hochhegger B, Irion KL. The reversed halo sign: another atypical manifestation of sarcoidosis. *Korean J Radiol* 2010;11:251–2.
32. Betancourt SL, Martinez-Jimenez S, Rossi SE, Truong MT, Carrillo J, Erasmus JJ. Lipoid pneumonia: spectrum of clinical and radiologic manifestations. *AJR Am J Roentgenol* 2010;194:103–9.
33. Kanaji N, Bandoh S, Nagamura N, Chang SS, Ishikawa S, Yokomise H, et al. Lipoid pneumonia showing multiple pulmonary nodules and reversed halo sign. *Respiratory Medicine Extra* 2007;3:98–101.
34. Ananthakrishnan L, Sharma N, Kanne JP. Wegener’s granulomatosis in the chest: high-resolution CT findings. *AJR Am J Roentgenol* 2009;192:676–82.
35. Agarwal R, Aggarwal A, Gupta D. Another cause of reverse halo sign: Wegener’s granulomatosis. *Br J Radiol* 2007;80:849–50.
36. Horlander KT, Mannino DM, Leeper KV. Pulmonary embolism mortality in the United States, 1979–1998: an analysis using multiple-cause mortality data. *Arch Intern Med* 2003;163:1711–17.
37. Greaves SM, Hart EM, Brown K, Young DA, Batra P, Aberle DR. Pulmonary thromboembolism: spectrum of findings on CT. *AJR Am J Roentgenol* 1995;165:1359–63.
38. Lee JS, Tuder R, Lynch DA. Lymphomatoid granulomatosis: radiologic features and pathologic correlations. *AJR Am J Roentgenol* 2000;175:1335–9.
39. Benamore RE, Weisbrod GL, Hwang DM, Bailey DJ, Pierre AF, Lazar NM, et al. Reversed halo sign in lymphomatoid granulomatosis. *Br J Radiol* 2007;80:e162–6.
40. Godoy MC, Naidich DP. Subsolid pulmonary nodules and the spectrum of peripheral adenocarcinomas of the lung: recommended interim guidelines for assessment and management. *Radiology* 2009;253:606–22.
41. Yabuuchi H, Murayama S, Murakami J, Hashiguchi N, Soeda H, Sugio K, et al. High-resolution CT characteristics of poorly differentiated adenocarcinoma of the peripheral lung: comparison with well differentiated adenocarcinoma. *Radiat Med* 2000;18:343–7.
42. Travis WD, Brambilla E, Noguchi M, Nicholson AG, Geisinger KR, Yatabe Y, et al. International Association for the study of Lung Cancer/American Thoracic Society/European Respiratory Society international multidisciplinary classification of lung adenocarcinoma. *J Thorac Oncol* 2011;6:244–85.
43. Seo JB, Im JG, Goo JM, Chung MJ, Kim MY. Atypical pulmonary metastases: spectrum of radiologic findings. *Radiographics* 2001;21:403–17.

44. Mango VL, Naidich DP, Godoy MC. Reversed halo sign after radiofrequency ablation of a lung nodule. *J Thorac Imaging* 2011;26:W150–2.
45. Choi YW, Munden RF, Erasmus JJ, Park KJ, Chung WK, Jeon SC, et al. Effects of radiation therapy on the lung: radiologic appearances and differential diagnosis. *RadioGraphics* 2004;24:985–97; discussion: 98.
46. Mukai N, Tokuyasu H, Izumi H, Takeda K, Hikino H, Shimizu E. A case of organizing pneumonia with a reversed halo sign following postoperative irradiation for breast cancer. [In Japanese.] *Nihon Kokyuki Gakkai Zasshi* 2011;49: 393–8.
47. Ascioglu S, Rex JH, de Pauw B, Bennett JE, Bille J, Crokaert F, et al. Defining opportunistic invasive fungal infections in immunocompromised patients with cancer and hematopoietic stem cell transplants: an international consensus. *Clin Infect Dis* 2002;34:7–14.
48. Georgiadou SP, Sipsas NV, Marom EM, Kontoyiannis DP. The diagnostic value of halo and reversed halo signs for invasive mold infections in compromised hosts. *Clin Infect Dis* 2011;25:1144–55.