CASE REPORT

Reversed halo sign on thin-section CT in a patient with non-specific interstitial pneumonia

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ABSTRACT. We present a case of non-specific interstitial pneumonia (NSIP) with reversed halo sign on thin-section CT. A 52-year-old female presented with a cough and New York Heart Association (NYHA) class 2 dyspnoea of 4 months duration. A chest radiograph showed poorly defined, patchy ground-glass opacities in both lungs. Thin-section CT demonstrated the reversed halo sign, which is a central ground-glass opacity surrounded by crescent or ring-shaped areas of consolidation in multifocal areas. Multifocal patchy ground-glass opacity and consolidation and enlarged paratracheal, hilar and subcarinal lymph nodes were also shown. Video-assisted thoracic surgical (VATS) lung biopsy was performed, and histopathology revealed cellular NSIP.

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Case report

A 52-year-old woman was referred to our institution complaining of a cough and New York Heart Association (NYHA) class 2 dyspnoea of 4 months duration. She was a non-smoker and had no significant medical history except chronic gastritis and intermittent knee pain. She had no other environmental risk factors for respiratory disease. Physical examination revealed decreased breath sounds with crackles on both lower lung fields. Laboratory examination revealed a white blood cell count of $5000 \mu\text{l}^{-1}$ (within normal limits) and an elevated erythrocyte sedimentation rate (ESR) level of 40 mm h^{-1} (normal range, $<20 \text{ mm h}^{-1}$). The patient had visited a local hospital 2 months prior to referral and was diagnosed with pneumonia. She was treated with amoxicillin/clavulanate for 2 weeks, but there was no improvement in either her clinical symptoms or her follow-up chest radiographs. A subsequent enhanced chest CT scan was performed at our institution and multifocal patchy ground-glass opacities and consolidations were observed in both lungs, predominantly in the subpleural and lower lung zones, and some of them in both lower lung zones were shown along the broncho-vascular bundle. The reversed halo sign, a central ground-glass opacity surrounded by crescent or ring-shaped areas of consolidation, was seen in multifocal areas of both lungs predominantly in the peripheral lung zone (Figure 1a,b). Bilateral paratracheal, hilar and subcarinal lymph nodes were enlarged. The presumptive diagnosis was diffuse interstitial lung disease, and cryptogenic organising pneumonia (COP) was thought more likely than non-specific interstitial pneumonia

(NSIP) because of the reversed halo sign. However, the specimen from video-assisted thoracic surgical (VATS) lung biopsy of the left upper lobe lingular segment and left lower lobe basal segment showed homogeneous septal thickening with preserved pulmonary architecture and diffuse interstitial infiltration of lymphoplasmacytic cells and histiocytes (Figure 1c,d). Cellular NSIP was diagnosed.

This suggested the possibility of collagen vascular disorder associated with interstitial pneumonitis. As a result, a patient history was obtained and laboratory examination undertaken. The patient complained of dry eyes, dry mouth, knee arthralgia, digit swelling and Raynaud's phenomenon. Laboratory examination revealed serum Sjögren's syndrome antigen A (SSA) ++, Sjögren's syndrome antigen B (SSB) $\pm$, Jo-1 +, centromere B+, and a fluorescent anti-nuclear antibody (FANA) titre of 1:80. Therefore, Sjögren's syndrome and limited-type systemic sclerosis with combined NSIP was diagnosed.

The patient was started on bolus intravenous methylprednisolone for three consecutive days followed by oral prednisolone. After 6 days of steroid therapy, the patient responded in her clinical symptoms and follow-up chest radiographs, and thin-section CT scan showed improvement (Figure 1e). Thereafter, oral steroid therapy was continued and after 6 months follow-up thin-section CT scan showed further improvement (Figure 1f).

Discussion

The reversed halo sign was described by Kim et al [1] as a central ground-glass opacity surrounded by a denser consolidation of crescent or ring shape that is at least 2 mm in thickness.

The central area of the ground-glass attenuation corresponds histopathologically to alveolar septal inflammation

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Figure 1. (a,b) Thin-section CT images show a central ground-glass opacity surrounded by crescent or ring-shaped areas of consolidation, showing the “reversed halo sign”. Multifocal patchy ground-glass opacity and consolidation are also seen in both lungs, predominantly in the subpleural and lower lung zones. Photomicrograph (haematoxylin-eosin stain, $\times 1$) of the video-assisted thoracoscopic surgery (VATS) lung biopsy specimen (haematoxylin-eosin stain; original magnification, (c) $\times 1$ and (d) $\times 40$) shows the diffuse homogeneous septal thickening with preserved pulmonary architecture, characteristic of cellular non-specific interstitial pneumonia (NSIP). A few scattered lymphoid follicles are observed, too. Diffuse interstitial infiltration of lymphoplasmacytic cells and histiocytes and occasional intra-alveolar fibrous plugs (Masson bodies) are also shown. Follow-up thin-section CT scan after (e) 6 days and (f) 6 months of steroid therapy, both showed improvement.

and cellular debris in alveolar spaces and the crescent or ring-shaped peripheral air-space consolidation corresponds to granulomatous tissue within the distal air spaces [2]. The sign was reported as a relatively specific finding for COP. The sign was previously described by Voloudaki et al [2] and by Zompatori et al [3]. However, recently this sign has also been described in various diseases, including pulmonary paracoccidioidomycosis [4], pulmonary zygomycosis, invasive pulmonary aspergillosis [5], lymphomatoid granulomatosis [6], Wegener’s granulomatosis [7], lipoid pneumonia [8], pulmonary sarcoidosis [9], drug-induced interstitial pneumonitis [10] and cellular NSIP [11]. In the reversed halo sign of paracoccidioidomycosis and lymphomatoid granulomatosis, the central area of ground-glass opacity consisted of an inflammatory infiltrate involving mainly the alveolar septa, and the peripheral consolidation consisted of dense and homogeneous intra-alveolar inflammatory infiltrates. There was no evidence of organising pneumonia [4, 6]. In pulmonary zygomycosis and invasive pulmonary aspergillosis, the reversed halo sign was attributable to an infarcted lung with a greater amount of haemorrhage in the peripheral consolidation than in the central ground-glass opacity [5]. In lipoid pneumonia, chronic inflammation with granulomatous organising lesions may lead to the reversed halo sign [8]. In pulmonary sarcoidosis, the sign consists of non-caseating granuloma with no evidence of organising pneumonia [9]. In these several cases, we assume that the reversed halo sign is mainly attributable to various stages of inflammation.

Thin-section CT features of NSIP tend to predominate in the middle and lower lungs. The most common manifestation is ground-glass attenuation. This finding is frequently associated with irregular linear or reticular densities and traction bronchiectasis [12]. The prevalence of honeycombing and consolidation range from 0% [13] to 30% [14] and from 16% [14] to 80% [13], respectively. However, the reversed halo sign is not a typical CT manifestation of NSIP.

The reversed halo sign in NSIP was first reported in Japan in 2007 by Ueda et al [11]. To our knowledge, the present case is the first report in the English language literature of cellular NSIP showing the reversed halo sign. In this case, the reversed halo sign consisted histopathologically of an inflammatory infiltrate in the alveolar septa, which was composed of lymphocytes, plasma cells and macrophages with preserved pulmonary architecture. Occasionally, Masson bodies and an organising pneumonia pattern were also seen. Although we could not perform direct histopathological and radiological correlation because of the limited VATS biopsy specimen, the finding of various inflammatory cells rendering the reversed halo sign in NSIP is consistent with previous reports.

Conclusion

Our case shows that the reversed halo sign can be seen in patients with cellular NSIP. When a thin-section CT

scan shows patchy ground-glass opacity and consolidation predominantly distributed in the peripheral and lower lung fields, NSIP and COP is usually included in the differential diagnosis. When a combined, reversed halo sign is seen on thin-section CT, the radiologist should avoid making a hasty diagnosis of COP and recognise that the reversed halo sign is not a specific finding of COP. The reversed halo sign can be seen in various diseases, including COP, pulmonary paracoccidioidomycosis, pulmonary zygomycosis, invasive pulmonary aspergillosis, lymphomatoid granulomatosis, Wegener's granulomatosis, lipoid pneumonia, pulmonary sarcoidosis, drug-induced interstitial pneumonitis and cellular NSIP.

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