CASE REPORT

Granulomatous interstitial pneumonia induced by the intake of rice bran pickles: a rare subtype of pulmonary manifestation associated with food allergy

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SUMMARY

Pulmonary manifestations associated with food allergy are rich in variety. We report the first case of food-induced granulomatous interstitial pneumonia mimicking hypersensitivity pneumonitis (HP). A 77-year-old woman with respiratory symptoms was referred to our hospital. We performed a surgical lung biopsy, which showed the features of granulomatous interstitial pneumonia. Her clinical history resembled those observed in HP. However, avoidance of exposure to the causative antigens did not improve her symptoms. Moreover, the patient had some features inconsistent with HP, such as elevated serum IgE levels, blood eosinophilia, intrathoracic lymphadenopathies and pleural effusion. Therefore, we pursued another extrinsic non-inhaled antigen as the cause of pulmonary involvements. We noted that she had been eating homemade rice bran pickles, and pulmonary involvements were induced by an ingestion challenge test. We suggest that granulomatous interstitial pneumonia may be a rare subtype of the pulmonary manifestations associated with food allergy.

BACKGROUND

Pulmonary manifestations associated with food allergy are rich in diversity and include anaphylaxis, asthma, rhinitis, serous otitis media and pulmonary haemosiderosis.¹ However, granulomatous interstitial pneumonia has not been reported as a manifestation of food allergy. We report a case of food-induced granulomatous interstitial pneumonia mimicking hypersensitivity pneumonitis (HP).

CASE PRESENTATION

A 77-year-old woman with a history of insomnia and osteoarthritis presented to our hospital with non-productive cough and dyspnoea. She was a non-smoker and had no obvious occupational exposures. She was being treated with mirtazapine, brotizolam, celecoxib, limaprost alfadex and rabeprazole sodium. At presentation, her vital signs were as follows: body temperature 37°C; respiratory rate 24/min; and oxygen saturation 88% on room air. Chest auscultation revealed bilateral expiratory rhonchi. Palpable superficial lymph nodes and skin rash were absent.

Laboratory test results were as follows: leucocytes 5900/μL, eosinophils 2050/μL, haemoglobin 10.4 g/dL, haematocrit 33%, platelets 27.0×10⁴/μL, C reactive protein 0.77 mg/dL, immunoglobulin (Ig) G

3300 IU/dL, IgE 10 900 IU/dL, ACE 20.1 U/L, *Trichosporon asahii* antibody negative, and KL-6 420 U/mL. Spirometry revealed a restrictive ventilatory pattern with a forced vital capacity of 1.39 L (68% of predicted) and forced expiratory volume in 1 s of 0.99 L (72% of forced vital capacity). A bronchodilator test with nebulised salbutamol was negative. Chest radiography showed bilateral ground-glass opacities, predominantly in the lower lobes (figure 1A). Chest CT showed bilateral mosaic attenuation, right lower lobe ground-glass opacities, mediastinal and bilateral hilar lymphadenopathies and right pleural effusion (figure 1B–D). We performed a surgical lung biopsy from right S8. The biopsy specimen showed interstitial cellular infiltrations and airspace aggregation of macrophages and lymphocytes (figure 2A). Small and poorly formed non-necrotising granulomas with a multinucleated giant cell were also seen in an interstitial location or within airspaces (figure 2A,B). Interstitial fibrosis and features of vasculitis were absent. These histological features were compatible with those observed in HP, but indistinguishable from sarcoidosis.

The patient's respiratory symptoms and radiographic findings improved during admission, without any medication, but recurred in the outpatient setting. These clinical features quite resembled those observed in HP. By the history taking of her environment, residential exposures to contaminated humidifiers and indoor moulds were suspected as the cause of pulmonary manifestations. We recommended improvement of the environment, after which her symptoms still did not improve. Moreover, she had some features inconsistent with HP, such as elevated serum IgE levels, blood eosinophilia, intrathoracic lymphadenopathies and pleural effusion. Therefore, we pursued another extrinsic non-inhaled antigen as the cause of pulmonary involvements. We noted that she had been eating homemade rice bran pickles, known as 'Nukazuke' in Japan, prepared using vegetables, salt and unheated rice bran, every day starting a month before her first visit. A lymphocyte stimulation test with unheated rice bran paste was positive. Next we performed a rice bran pickle ingestion challenge test in the inpatient setting to deny any involvement in inhaled antigens. As a result, symptoms of cough and dyspnoea developed on day 7, and bilateral ground-glass lung opacities were observed on day 11. We made the diagnosis of a

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Figure 1 Chest radiography showing bilateral ground-glass opacities, predominantly in the lower lobes (A). Chest CT showing bilateral mosaic perfusion (B), right lower lobe ground-glass opacities (C) and mediastinal and bilateral hilar lymphadenopathies with right pleural effusion (D).

food-induced granulomatous interstitial pneumonia on the basis of a positive challenge test result. Respiratory symptoms improved with oral prednisolone 15 mg daily. The patient is currently being followed up as an outpatient.

DISCUSSION

Histological patterns associated with pulmonary drug reactions include diffuse alveolar damage, non-specific interstitial pneumonia, organising pneumonia, eosinophilic pneumonia and granulomatous interstitial pneumonia.^{2–3} Granulomatous interstitial pneumonia has been described in patients who took certain drugs, such as acebutol, cocaine, cromolyn sodium, flutaxetine hydrochloride, methotrexate, nitrofurantoin, procabazine, pentazocine, sirolimus and tripeleminamine.^{2–3} Nukazuke is a type of Japanese rice bran pickle. In this case, we suspect that the unheated rice bran used in the preparation of Nukazuke may have caused the hypersensitivity reactions because the patient had never developed an allergic reaction after eating the vegetables used in Nukazuke. Rice can less frequently trigger

some allergic disorders including asthma, anaphylaxis and urticaria; proteins with molecular masses of 14–16, 26, 33 and 56 kDa have been demonstrated to be potentially allergenic.^{4–8} However, the patient had eaten cooked rice without any problems; a similar event has been reported in a patient who could eat cooked rice without problems, but experienced contact urticaria from raw rice.⁸ These discrepancy might be due to the heat instability of rice allergenic proteins, because 40% of rice allergenic proteins were reported to lose their antigenicity after heating at 100°C for 60 min.⁹ On the contrary, we could not perform an ingestion challenge test of pure rice bran. Therefore, it is possible that these hypersensitivity reactions were caused by the *Lactobacillus*-dominated microbiota that grows in aged rice bran paste or allergic substances produced by such microbiota.¹⁰

In the present case, the pathological findings and clinical course quite resembled those observed in HP. However, HP is defined as extrinsic allergic alveolitis caused by inhaled allergens.¹¹ Therefore, the present case is strictly different from HP. Pathological findings in the present case can be observed in

Figure 2 (A) Interstitial cellular infiltrations and airspace aggregation of macrophages and lymphocytes were seen. A multinucleated giant cell (arrow) was also seen (H&E; original magnification $\times 100$). (B) Small and poorly formed non-necrotising granulomas (arrow heads) were seen in an interstitial location or within airspaces (H&E; original magnification $\times 100$).

other diseases, such as sarcoidosis, silicosis and hard metal lung disease. Silicosis and hard metal lung disease were denied by her occupational history, but it was histopathologically difficult to distinguish from sarcoidosis. In this case, the patient also had some features inconsistent with HP, such as elevated serum IgE levels, blood eosinophilia, intrathoracic lymphadenopathies and pleural effusion. These abnormalities have sometimes been reported in patients with drug-induced granulomatous interstitial pneumonia.^{12–15} The present case demonstrates that careful and detailed history taking of drug or food may be required in cases mimicking, but with these inconsistent features of, HP. A further review of similar cases is required to clarify this hypothesis.

Learning points

- Pulmonary manifestations associated with food allergy are rich in diversity and include anaphylaxis, asthma, rhinitis, serous otitis media and pulmonary haemosiderosis.
- We report the first case of granulomatous interstitial pneumonia induced by food intake that was proven by an ingestion challenge.
- Careful and detailed history taking of drug or food may be required in cases mimicking, but with some features inconsistent with HP, such as elevated serum IgE levels, blood eosinophilia, intrathoracic lymphadenopathies and pleural effusion.

Competing interests None.

Patient consent Obtained.

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