A case of diaminodiphenyl sulfone-induced eosinophilic pneumonia

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CASE REPORT

An 81-year-old woman being treated for chronic urticaria consulted our outpatient clinic with a two-week history of productive cough and fever. Six months prior to the consultation, she consulted a dermatologist and was treated with an antihistamine-1-receptor blocker against urticaria. Since her itching continued, diaminodiphenyl sulfone (DDS), 50 mg daily, was added. The chronic urticaria then gradually improved, and the DDS was continued. Two weeks prior to the consultation, she developed malaise and cough with whitish sputum. On thoracic computed tomography (CT), a bilateral upper lobe and subpleural lesion-dominant, multiple, nonsegmental, consolidative shadow was observed (Figure 1). The possibility of community-acquired pneumonia was highly suspected, and a combination of clarithromycin and ceftriaxone for one week was given at a family practice office. However, her symptoms and the infiltrative shadow on chest X-ray gradually worsened, and she consulted our outpatient clinic. On physical examination, auscultation of her chest showed early inspiratory crackles. Blood laboratory examination showed: white blood cell count 9150/µL, eosinophils 5.8% (531/µL), red blood cell count 2,800,000/µL, hemoglobin 8.8 g/dL, hematocrit 28.1%, platelet count 249,000/µL, total protein 6.8 g/dL, albumin 4.0 g/dL, AST 20 IU/mL, ALT 9 IU/mL, LDH 201 U/mL (normal range: 106–211 U/mL), Fe 76 µg/mL, ferritin 402 mg/mL, total iron-binding capacity 110 µg/mL, Na 145 mEq/L, K 4.0 mEq/L, Cl 110 mEq/L, C-reactive protein 8.3 mg/dL, CEA 1.1 ng/mL, and KL-6 197 U/mL (normal range: 0–499 U/mL). The Coombs test was negative. A bronchofiberscopic examination was also performed. Bronchoalveolar lavage (BAL) cells showed elevated eosinophils (34.1%) and total cell count (2.67 × 10⁵/mL). The CD4/CD8-ratio of BAL cells was 3.56 (normal range: 1.0–2.0). No specific pathogen was recognized in the BAL fluid. A diagnosis of eosinophilic pneumonia was made, and the possibility of an adverse effect of DDS as the cause of eosinophilic pneumonia was suspected. Prednisolone, 25 mg daily (0.5 mg/kg/day), was then started, and DDS was discontinued immediately. Her productive cough and fever resolved, and the infiltrative shadow on chest X-ray and thoracic CT also improved gradually (Figure 2). Anemia and eosinophilia were also improved, with eosinophils of 0.2% (22/µL) and hemoglobin of 11.3 g/dL. After three months of treatment with tapering of prednisolone, the prednisolone was discontinued. Two years later, there was no recurrence of eosinophilic pneumonia.

DISCUSSION

Drug-induced pneumonia is known as one of the major adverse effects of allergic disease and malignant
Diaminodiphenyl sulfone is widely used for the treatment of chronic allergic skin diseases [2, 3]. Although drug eruptions are well known adverse effects of DDS [2, 3], there was no drug eruption in the present case. When looking retrospectively, the increased circulating eosinophil count and advanced anemia were the signs for early detection of this case. Computed tomography imaging and BAL cell findings in this case were similar to those of chronic eosinophilic pneumonia (CEP) [4]. Generally, circulating eosinophil cells are not increased in the early phase of CEP cases, but they are elevated in the delayed phase [4]. In this respect, the present case was not consistent with previous reports.

From the point of view of CT findings, both CEP and bronchiolitis obliterans with organizing pneumonia (BOOP)/cryptogenic organizing pneumonia (COP) were considered in the differential diagnosis of this case. Although transbronchial lung biopsy was not performed, the present case was compatible with the criteria for eosinophilic pneumonia showing an increased number of eosinophilic cells (more than 25.0%) and an increased CD4/CD8-ratio with BAL cells [4, 5]. The present case also did not have episodes of bronchial asthma as seen in CEP. According to the previous case reports of DDS-induced eosinophilic pneumonia, an upper lobe-dominant infiltrative shadow and nonsegmental, multiple, consolidative shadows were common [2, 3]. In this regard, the present case was compatible with previous reports. The reversed halo sign on thoracic CT imaging is also known as one of the specific findings of BOOP/COP and CEP, but it was not confirmed in the present case [6].

Although a challenge test (trying readministration of DDS) was not performed, no recurrence was seen after discontinuation of DDS. Furthermore, her anemia and eosinophilia were also improved after corticosteroid administration. Therefore, this case was diagnosed as DDS-induced eosinophilic pneumonia. The DDS-induced lymphocyte stimulation test was negative, which supported the possibility that the eosinophilic pneumonia in the present case was not mediated by a type IV allergic reaction, though it would not suggest that the present case was not DDS-induced eosinophilic pneumonia.

CONCLUSION

A rare case of DDS-induced eosinophilic pneumonia was reported. When finding a nonresolving pneumonia shadow on chest X-ray during treatment with DDS, the possibility of an adverse effect of DDS should be considered. An upper lobe-dominant infiltrative shadow and nonsegmental, multiple, consolidative shadows were characteristic findings in the present case. An increased circulating eosinophil count and advanced anemia were also useful for early diagnosis in this case.

Keywords: Diaminodiphenyl sulfone, Eosinophil, Eosinophilic pneumonia

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