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Letter to the Editor

High incidence of ANCA-positive Interstitial Pneumonia after the 2011 Fukushima disaster



Dear Editor,

The Great East Japan Earthquake and tsunami on March 11, 2011, resulted in the Fukushima nuclear power plant accident, which consequently led to a massive emission of radioactive substances. Although there are many papers published on the relationship between the Fukushima disaster and the victims' health status,^{1–3} reports on lung diseases are limited.^{4,5} We investigated the effects of the disaster on the characteristics of patients with chronic interstitial pneumonia (CIP), who had been admitted to Fukushima Medical University Hospital, located 57 km away from the Fukushima Daiichi Nuclear Power Plant. Participants gave written informed consent and the Fukushima Medical University Ethics Committee approved this study.

The Great Hanshin Earthquake, which measured 7.2 on the Richter scale, hit Kobe in 1995 with a significantly high regional morbidity of myeloperoxidase (MPO)-antineutrophil cytoplasmic autoantibody (ANCA)-related angitis reported after the disaster. Although the cause(s) of the high morbidity of MPO-ANCA-related angitis in Kobe was not clarified, this fact suggests the possibility that the disaster triggered the induction of ANCA in such patients. This background prompted us to investigate whether the Fukushima disaster influenced the prevalence and clinical characteristics of patients with ANCA-positive CIP. We reviewed patients admitted to our department with CIP retrospectively, and the prevalence of ANCA was first evaluated in patients with CIP admitted before and after the Fukushima disaster. Patients with definite connective tissue diseases and granulomatosis with polyangiitis were excluded. Clinical characteristics such as laboratory data, pulmonary function tests, and the bronchoalveolar lavage (BAL) fluid findings of patients with ANCA-positive CIP were compared before and after the disaster.

Five years previous to the event, 26 out of 255 CIP patients had ANCA-positive CIP (10.2%, MPO-ANCA: $n = 24$, PR3-ANCA: $n = 2$). On the other hand, six months after the disaster, six out of 25 CIP patients (Table 1) had ANCA-positive CIP (24.0%, MPO-ANCA: $n = 5$, PR3-ANCA: $n = 1$), showing a significant increase in patients with ANCA-positive CIP ($p = 0.04$). Fig. 1 was analyzed at three-month intervals from March 2011, with a maximum of five patients with ANCA-positive CIP between June and September, accounting for 31.3% (5/13 patients) of CIP patients during the same period. The area that ANCA-positive CIP patients were residing in at the time of the earthquake was not considered as a determining factor.

We had nine patients with ANCA-positive CIP one year after the disaster. The clinical parameters in the nine patients were not different compared to those in the 26 ANCA-positive CIP patients before the disaster (data not shown). The incidence of microscopic polyangiitis (MPA) was also identical between patients before and after the earthquake (3/26 vs. 2/9 patients).

In a previous study, Yashiro *et al.* reported significantly high regional morbidity of MPO-ANCA-related angitis and nephritis with respiratory tract involvement after the Great Hanshin Earthquake.⁶ They hypothesized that the cause of increase in the number of MPO-ANCA-related nephritis patients was as follows: 1) Substances such as asbestos and silica in the environment of a damaged city after an earthquake may activate neutrophils releasing MPO, and induce autoimmunity to MPO. Silica aspirated through the airway may activate alveolar macrophages, not only inducing inflammatory reactions, but also resulting in chemotaxis of neutrophils, which are the source of MPO. 2) The increase may be due to an induction of antibodies by an unknown antigen that has cross-reactivity against MPO.

After the Great East Japan Earthquake, Ebisawa *et al.* reported an increase in the number of patients with diffuse alveolar hemorrhage (DAH).⁴ In post-earthquake DAH patients, clinical parameters suggestive of infectious diseases tended to be positive and serum IgE titers were significantly higher with a tendency of higher silica concentrations in BAL fluid. Interestingly, one of the DAH patients turned out to be MPO-ANCA positive. The results suggested the possibility of an infection- and/or dust-induced partially allergic form of DAH.

Our hospital is located on the inland side of northern Fukushima Prefecture and was not affected by the tsunami. There was little in terms of complete collapse of buildings; however, damage such as wall cracks and roof collapse was reported by many residents. The possibility that the disaster induced the onset of CIP might be low because there was no change in the annual number of CIP patients admitted to our department before and after the disaster. In nine ANCA-positive CIP patients who admitted after the disaster, four patients had been pointed out chest abnormal shadows before the disaster. In these patients, their respiratory symptoms or chest abnormal shadows were worsened after the disaster. These facts suggest the possibility that the disaster might induce ANCA production resulting in the disease worsening. In this study, we could not identify the exact cause(s) of the high incidence of ANCA-positive CIP patients. However, there are three possibilities. 1) Inhalation of dust such as silica may cause an increase in ANCA-positive CIP patients, although we did not measure silica concentrations in BAL fluid. 2) The Fukushima nuclear

Peer review under responsibility of Japanese Society of Allergy.

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Table 1
Characteristics of ANCA-positive Interstitial Pneumonia patients after the disaster.

	Age (yr)	Gender	Diagnosis	MPO-ANCA (EU)	PR3-ANCA (EU)	WBC (/mm ³)	LDH (IU/L)	CRP (mg/dl)	ESR (mm/h)	KL-6 (IU/L)	SP-D (ng/ml)
1	69	M	IPF	<10	16	6300	353	3.83	38	698	192.1
2	75	M	IPF	307	<10	10,100	264	0.81	17	1117	115.6
3	61	F	MPA	23	<10	9500	161	3.66	83	769	44.6
4	36	F	MPA	1300	<10	2800	319	8.41	34	365	123.5
5	75	F	IIP	79	<10	7900	234	1.04	77	790	70.2
6	80	M	IIP	72	<10	8400	255	1.28	41	935	133.8

MPO-ANCA, myeloperoxidase-antineutrophil cytoplasmic autoantibody; PR3-ANCA, proteinase 3 antineutrophil cytoplasmic autoantibody; WBC, white blood cells; LDH, lactate dehydrogenase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; KL-6, Krebs von den Lungen 6; SP-D, surfactant protein-D; IPF, idiopathic pulmonary fibrosis; MPA, microscopic polyangiitis; IIP, idiopathic interstitial pneumonia.

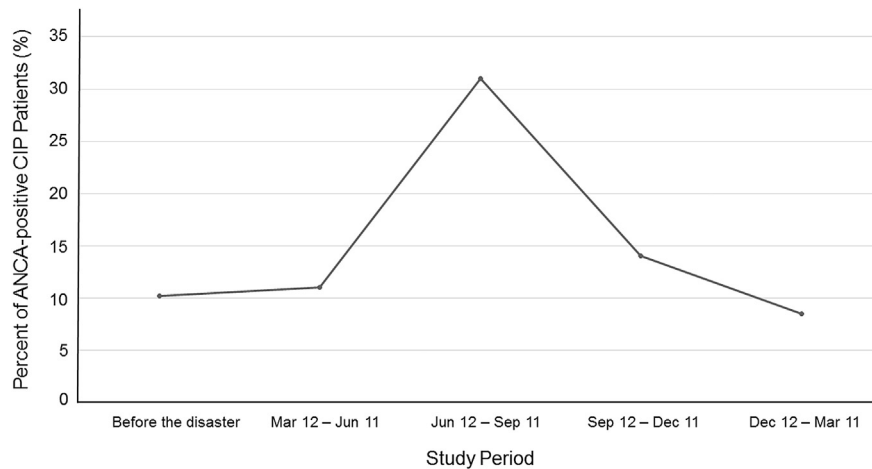


Fig. 1. Change in percent of ANCA-positive Interstitial Pneumonia patients before and after the disaster. Analysis of the number of ANCA-positive CIP at three-month intervals from March 12, 2011 showing a significant increase between June 12 and September 11. ANCA, antineutrophil cytoplasmic autoantibody; CIP, chronic interstitial pneumonia.

power plant accident caused uneasiness and mental stress in many people who lived in the neighborhood. Mental stress is reported to induce neutrophil activation,^{7,8} thus such stress due to the earthquake may have influenced ANCA production. 3) It has been reported that the circulating neutrophil count is affected after radiation exposure. Although Sakai *et al.* demonstrated no marked effects of radiation exposure on the distribution of white blood cell counts, including neutrophil and lymphocyte counts detected within one year after the disaster in the evacuation zone,⁹ the effect of radiation exposure on ANCA production cannot be completely excluded.

In summary, a significantly high incidence of ANCA-positive CIP was observed after the 2011 Great East Japan Earthquake and tsunami complex disaster here in Fukushima. We could not determine whether an increase in ANCA-positivity in CIP patients has any clinical impacts. However, it has been reported that CIP patients with MPO-ANCA developed MPA during follow-up,¹⁰ thus careful monitoring of patients to clarify the effect(s) of a complex disaster on respiratory diseases is necessary.

Acknowledgments

This study was partly supported by a grant to the Diffuse Lung Diseases Research Group from the Ministry of Health, Labour and Welfare, Japan.

Conflict of interest

The authors have no conflict of interest to declare.

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Received 10 July 2015

Received in revised form 25 August 2015

Accepted 14 September 2015

Available online 11 November 2015