Rapid Article

Neurological involvement of relapsing polychondritis in Japan: An epidemiological study

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We conducted a large scale epidemiological study in Japan and revealed a high mortality rate in RP patients with neurological involvement. Japanese RP patients developed encephalitis/meningitis (12 out of 239 cases, 5.0%), cerebral infarct/bleeding (5 cases, 2.1%) and cerebral vasculitis (4 cases, 1.7%). The mortality rate was 18%, in contrast to 8.1% of RP patients without neurological involvement. We suggested that neurological involvement appeared to be a major determinant of disease severity in patients with RP.

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Relapsing polychondritis (RP) is a relatively rare disease, exhibiting swelling of the ear, destruction of the nose, fever, and arthritis. Tracheobroncheal involvement was potentially lethal through the occlusion[1]. Neurologic complications of RP have begun to attract increasing attention. There are some reports presenting neurological symptoms of RP[2]. In a multi-center study which enrolled 62 patients, CNS involvement was reported to be 10%[3].

We conducted a large scale epidemiological study in Japan[4] and revealed a high mortality rate in RP patients with neurological involvement. We reanalyzed the data in view of neurological involvement in patients with RP. A Multi-institutional surveillance study of Japanese major medical facilities was conducted from July to December, 2009. All subjects to whom the questionnaire was sent were informed of the purpose of the study and the responses would be kept confidential. All authors reviewed the questionnaire.

We obtained responses from 121 facilities with clinical information of 239 RP patients. The average age of onset was to be 52.7 years (range, 3-97) and the male-to-female ratio was 1.1:1 (127 males to 112 females)[4]. Biopsies were performed in 228 patients (95.4%) and histological confirmation of RP was obtained in 138 patients (57.7%).

Among 239 RP patients, 28 cases (12%) developed neurological involvement, excluding cochlear-vestibular symptoms (Table 1). The mean age of onset of RP with neurological involvement was 60 years. The ratio of men

Table 1 Characteristics of RP patients with neurological involvement in Japan

	Patients without neurological involvement (n=211)		Patients with neurological involvement (n=28)	
Profile				
Male-female ratio	106:105		21:7	
Mean age	57 (range 6-104)		64 (range 45-80)	
Mean age of disease onset	53 (range 3-97)		60 (range 38-78)	
Disease duration (yr)	5.3 (range 1-33)		4.2 (range 1-26)	
Mortality rate (%)	8.1		17.9	
Clinical features,	Number of patients (% in each group)			
	Onset	Follow-up	Onset	Follow-up
Neurological	0 (0)	0 (0)	6 (21)	28 (100)
External ear	124 (59)	159 (75)	12 (44)	27 (96)
Internal ear	7 (3.3)	53 (25)	2 (7.4)	12 (43)
Nasal cartilage	5 (2.4)	88 (42)	0 (0)	5 (18)
Airway	40 (19)	114 (54)	1 (3.6)	6 (21)
Eye	15 (7.1)	92 (44)	7 (25)	18 (64)
Arthritis	15 (7.0)	84 (40)	0 (0)	9 (32)
Cardiovascular	0 (0)	12 (5.7)	0 (0)	5 (18)

Table 2 Frequencies of central nervous system manifestations in relapsing polychondritis in Japan

Central nervous system manifestations	No. (%) of patients	No. of death
Encephalitis/meningitis	12 (43%)	2[a]
Cerebral vascular disease	5 (18%)	3[b]
Cerebral vasculitis	4 (14%)	
Brain abscess	2 (7.1%)	
Cerebral aneurysm	1 (3.6%)	
Hypertrophic pachymeningitis	1 (3.6%)	
The depression	5 (18%)	
Schizophrenia	3 (11%)	
Dementia	1 (3.6%)	
Insomnia	1 (3.6%)	
Parkinsonism	1 (3.6%)	
Tonic spasm and loss of consciousness	1 (3.6%)	

[a] Two deaths caused by encephalitis (76 year-old female) and myocardial infarction (54 year-old male)

[b] Three deaths caused by cerebral bleeding (77 year-old male), cerebral embolism (60 year-old male) and cerebral infarction (67 year-old female)

to women was 2.7 to 1 and thus men predominantly developed neurological symptoms.

RP patients with neurological involvement were diagnosed with the diagnostic criterion[4]. In addition, histological confirmation of RP was obtained 17 patients (64% of the 28 patients).

Based on the results of our study, we described incidence of the neurological symptoms and their outcome observed in patients with RP in Japan. Differential diagnosis of cerebrovascular disease and/or cerebral vasculitis, from encephalopathy, encephalitis, and meningitis, was not completely clear from this type of epidemiological studies.

Percentages of the RP patients who developed encephalitis/meningitis (12 out of 239 cases), cerebral infarct/bleeding and cerebral vasculitis were 5.0, 2.1 and 1.7%, respectively (Table 2). Our survey revealed that the RP death rate in Japan was 9%[4]. When we focused on RP with neurological involvement, 5 cases have died out of 28

cases; accordingly the death rate was 18%. Four deaths were caused by encephalitis, cerebral bleeding, cerebral embolism, and cerebral infarction. The remaining 54-year-old male patient had ten years of history of RP, during which he developed meningoencephalitis and died of acute myocardial infarction (Table 2). With regard to the atherosclerotic cardiovascular disease, two RP patients with neurological involvement (aseptic meningitis and cerebral infarction) had old myocardial infarction.

In our survey, 96% RP patients with neurological involvement accompanied inflammation in the head, such as auricular chondritis (Table 1)[1, 5]. Four RP patients (14% of 28 patients with neurological involvement) suffered from cerebral vasculitis and one of them had noninfectious aortitis. Systemic lupus erythematosus, Behcet's disease, Wegener's granulomatosis and infectious diseases were included in the differential diagnosis of the inflammatory disorders in the head and neck[6]. Further studies are needed to disclose the entire clinical pictures of RP patients with neurological involvements.

In conclusion, 12% of Japanese patients with RP developed relatively severe neurological involvement. Conventional treatment, such as administration of steroids and immunosuppressants, was not fully satisfactory and establishment of a new therapeutic strategy for neurological symptoms in patients with RP is awaited.

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Conflict of interests

None

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