Characteristics and Clinical Outcome of 295 Patients with Relapsing Polychondritis

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Key Indexing Terms: relapsing polychondritis, cartilage, airway obstruction, prognosis

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Running head: Relapsing polychondritis in China

ABSTRACT

Objectives: This study analyzes the clinical features of Chinese patients with relapsing polychondritis (RP).

Methods: The clinical data of 295 patients with RP of Beijing Tongren Hospital were retrospectively analyzed.

Results: The mean age of onset was 41.0 ± 15.0 years. The sex ratio was 1:1. Up to 70.5% of the patients had airway involvement during the disease course; among them, the larynx was most commonly affected (82.2%). Exactly 25.7% of the patients with laryngeal involvement underwent tracheotomy due to progressive dyspnea or acute laryngeal obstruction. Younger onset age and initially presenting with respiratory symptoms were independent risk factors for tracheotomy in patients with RP with laryngeal involvement. The risk of tracheotomy in patients who presented with respiratory symptoms was 2.354 times higher than that in patients who presented with other symptoms (hazard ratio [HR], 2.354; 95% confidence interval [CI], 1.230–4.503; p =0.010). The risk of tracheotomy increased by 4.8% for every 1 year decrease in the onset age (HR, 0.952; 95% CI, 0.931–0.973; $p < 0.001$). The incidence of lower respiratory tract infection was much higher in patients with airway involvement than that in those without airway involvement. The main cause of death was respiratory failure due to airway obstruction.

Conclusions: There is a high prevalence of airway involvement in Chinese patients with RP. Laryngeal involvement is associated with a high risk of death. More attention should be paid to RP patients with laryngeal involvement who are young at disease onset and present with respiratory symptoms.

INTRODUCTION

Relapsing polychondritis (RP) is a rare autoimmune disease, which can be disabling and life threatening. RP mainly involves the cartilaginous components of the ear, nose, larynx, and tracheobronchial tree. Recurrent inflammation causes cartilage degeneration and destruction. Moreover, other proteoglycan-rich structures may be involved, such as the eyes, cardiovascular system, and inner ear. RP may be isolated or associated with other diseases(1,2). Due to the rarity of this disease, its etiopathogenesis is unknown, clinical manifestations are diverse, its evolution is unpredictable, the standard treatment strategy is lacking, and its diagnosis and treatment remain a challenge for rheumatologists(3,4).

RP is a rare autoimmune disorder, and its annual incidence is estimated to be 0.71–3.5 per million person-years(5,6). The calculated prevalence of RP is 4.5 per million(7). To date, only approximately 1,000 cases of RP have been reported in English, and most cases are Caucasians(3). Recently, with more cases being reported, the polymorphism of clinical features and prognoses among different races and countries has been emphasized(8-11). A preliminary study has shown that Chinese patients with RP are distinct from patients from Western and other Asian countries in terms of clinical characteristics and prognosis(11).

To better describe the clinical features of Chinese patients' RP, especially respiratory involvement patterns and prognosis, we have conducted this study involving the largest cohort of patients with RP. In addition, factors predicting a high risk of undergoing tracheotomy were explored to provide more information for this rare disease.

MATERIALS AND METHODS

The study protocol has been approved by the Institutional Review Board (IRB) of Beijing Tongren Hospital, Capital Medical University (No. TRECKY2020-166). Due to the retrospective nature of the study, our local IRB approved a waiver of informed consent.

Patient selection

Patients with RP who were followed up in our department at Beijing Tongren Hospital affiliated to Capital Medical University between July 2006 and June 2020 were included in this study. RP was defined according to the criteria proposed by Michet(12) and Damiani et al.(13). Patients with ANCA-associated vasculitis (AAV) were excluded.

Data collection

RP cases were identified by searching the electrical medical record system of our hospital. Recorded information included demographic data, time from disease onset to diagnosis, initial and constitutional symptoms, and multisystem involvement during the disease course, including the external ear, nose, larynx, tracheobronchial tree, costochondral cartilage, eye, joints, inner ear, central nervous system (CNS), heart, blood vessels, kidney, and skin. The presence of airway chondritis was determined using the computed tomography (CT) images of the larynx and chest. The CT findings of laryngeal involvement included thickening of the aryepiglottic folds, ventricular folds, or vocal cords, and posterior wall of the larynx; marked thickening or irregular enlargement of the laryngeal cartilages; and laryngeal stenosis. Some of the laryngeal cartilages may be totally destroyed and replaced by soft tissue. Obvious calcification or ossification of the laryngeal cartilages in patients younger than 18 years is a sign of abnormality (14,15). The patterns of tracheobronchial involvement include the following: (1) thickening of the tracheal or bronchial wall (the segmental bronchus and the areas above it), defined by a wall

thickness > 2 mm, with or without calcifications, and (2) tracheal or main bronchial narrowing as assessed by comparing the diameter of the involved segment with that of the corresponding uninvolved segment. The narrowing was considered present when the luminal diameter was narrowed by >25% of its original diameter. Tracheobronchial wall thickening and luminal narrowing were defined on the basis of the definitions provided by references 16 and 17. The site of airway chondritis was recorded. All the CT images were interpreted independently by two radiologists who were interested in RP, each with >10 years of experience in laryngeal and chest imaging. When disagreement occurred, the final diagnosis was made in consensus. Moreover, the time from the onset of respiratory symptoms to tracheotomy was recorded. Provided that there was no other medical explanation, laryngeal cartilage lesions or tracheobronchial wall thickening or stenosis without subjective respiratory symptoms was defined as asymptomatic airway chondritis. Inner ear damage was evaluated using pure tone audiometry (PTA), acoustic immittance, and vestibular function examination. The proportions of deafness(18) and blindness(19) were calculated. Furthermore, comorbidities, the presence of lower respiratory tract infection, and laboratory results were recorded. The diagnosis of lower respiratory infection was based on the presence of cough, purulent sputum, plaques, or consolidation shadows seen on chest CT with or without fever, leukocytosis, and sputum culture, confirming the presence of pathogenic bacteria from the lower respiratory tract. Follow-up data were obtained via telephone calls. Moreover, the causes of death were recorded.

Statistical analysis

Statistical Package for the Social Sciences (version 23.0; IBM Corporation, Armonk, NY, USA) was used for all statistical analyses. Data are presented as the mean ± standard deviation for continuous variables with a normal distribution and as the median and interquartile range (IQR) for continuous

variables with a skewed distribution. Categorical variables are presented as percentages (%). Continuous variables were compared using independent Student's t-test or the Mann–Whitney U test. Categorical variables were compared using Fisher's exact test or the chi-square test, as appropriate. Cox proportional hazards regression model was used to explore independent risk predictors of tracheotomy in patients with RP with larynx involvement. The variables with statistical significance in univariate analysis were included in multivariate analysis. All reported *P* values were 2-sided, and *P* values of <0.05 were used to denote statistical significance.

RESULTS

This study included 295 patients. Among them, 286 met Michet et al.'s criteria, the remaining 9 patients who only had isolated auricular or airway chondritis were diagnosed using cartilage biopsy according to Damiani and Levine's criteria. The female–male ratio was 1:1. The mean age at onset of symptoms was 41.0 ± 15.0 years. The distribution of age at onset is shown in Figure 1. The age at onset of males and females was similar (40.8 ± 15.5 years vs. 41.3 ± 14.4 years; $p = 0.792$). The median time from the onset to diagnosis was 9.5 months (IQR, 4–24 months). The common presenting symptoms and multi-organ involvement during the course of the disease are shown in Figure 2 and Table 1.

Among all patients, 70.5% (208/295) had airway involvement, 32.7% (68/208) had extensive involvement of the larynx, trachea, and bronchus (Figure 3a); among them, the larynx was the most commonly affected (82.2%; 171/208) (Figure 3b). Patients with laryngeal involvement usually complained of hoarseness, throat pain, or foreign body sensation. However, 8.2% (14/171) were asymptomatic. With the deterioration of the disease, stridor and dyspnea occurred. In our series, 31 of the 171 patients (18.1%) with laryngeal involvement underwent tracheotomy due to progressive dyspnea. Furthermore, acute laryngeal obstruction leading to loss of consciousness and acute cardiopulmonary arrest was seen in 13 of the 171 patients (7.6%). Although emergency tracheotomy was performed, four patients died. The calculated incidence of tracheotomy was 25.7% (44/171). Among all tracheotomies, 40.9% (18/44) were performed within half a year since the onset of respiratory symptoms. The median time from the onset of respiratory symptoms to tracheotomy was 7.5 months (IQR, 3.25–21.5 months). Patients with RP with laryngeal involvement were divided into two groups according to whether they had undergone a tracheotomy. The median age at onset in the tracheotomy group (25 years [IQR, 16–45.25 years]) was significantly lower than that in the non-tracheotomy group (42 years [IQR, 34–50

years]) ($p < 0.001$). Besides, the proportion of patients who presented with respiratory symptoms ($p = 0.006$), and the incidence of nasal chondritis during the course of the disease ($p = 0.021$) was higher in the tracheotomy group. However, the incidence of auricular chondritis ($p = 0.332$), costal chondritis ($p = 0.534$), arthritis ($p = 0.284$), eye disease ($p = 0532$), hearing impairment ($p = 0.191$), vestibular dysfunction ($p = 0.953$), fever ($p = 0.986$), and rash ($p = 0.751$) during the course of the disease, the sex ratio ($p = 0.822$), and diagnostic time ($p = 0.903$) were similar between the two groups. The independent risk factor for tracheotomy in patients with RP was evaluated using the Cox proportional hazard model. It was shown that younger age at onset and initially presenting with respiratory symptoms were independent risk factors for tracheotomy in patients with RP. The risk of tracheotomy in patients who presented with respiratory symptoms was 2.354 times higher than that in patients who presented with other symptoms (hazard ratio [HR], 2.354; 95% confidence interval [CI], 1.230–4.503; p =0.010). The risk of tracheotomy increased by 4.8% for every 1 year decrease in the age at onset (HR, 0.952; 95% CI, 0.931–0.973; $p < 0.001$).

Furthermore, tracheal and bronchial involvement accounted for a great proportion in this series (Fig. 3b). Patients with tracheobronchial involvement often complained of cough, sputum, and progressive dyspnea. The incidence of lower respiratory tract infection was 24.4% (72/295). Lower respiratory tract infection occurred more frequently in patients with airway involvement (32.2%, 66/208) than that in patients without airway involvement (6.9%, 6/87), and the difference was statistically significant ($p < 0.001$).

In total, 46.1% (136/295) patients suffered from different forms of ocular lesions during the course of the disease, among whom 77.2% (105/136) were bilateral ocular lesions. The most common ocular lesions were scleritis, conjunctivitis and keratitis. One patient had RP-related binocular low vision, three patients had monocular low vision, five patients had monocular blindness, and one patient had binocular

blindness.

In addition, 36.9% (109/295) of the patients had tinnitus, ear tightness, or hearing loss. The incidence of hearing impairment found using PTA was 61.7 % (177/287). Bilateral sensorineural deafness was the most common hearing impairment (65.0%, 115/177), followed by unilateral sensorineural deafness (15.3%, 27/177) and unilateral conduction deafness (8.5%, 15/177). Among the 295 patients, 7.1% (n = 21) met the criteria of hearing disability and 10.8% (n = 32) experienced dizziness, among whom 75% had abnormal results in vestibular examination. In total, vestibular dysfunction was found in 61.0% (163/267) of the patients.

Among the 295 patients, 40.0% (n = 118) complained of arthralgia. Swollen joints were found in 14.2% (42/295). Most arthropathies were symmetrical. Both the axial and peripheral joints were affected. The most commonly involved joints were the knees (21.0%, 62/295), interphalangeal joints (14.9%, 44/295), and ankles (8.5%, 25/295).

Cutaneous involvement was seen in 14.2% (42/295) of the patients; recurrent aphthosis was the most common (5.1%, 15/295). Other manifestations included urticaria, folliculitis, and nonspecific nodules.

Echocardiographic abnormalities in 72 of 201 revealed valvular regurgitation in 20.9 % (42/201), including mild aortic regurgitation (11.4 %, 23/201), mild mitral regurgitation (6.0%, 12/201), and mild tricuspid regurgitation (5.5%, 11/201). Aortic sinus or ascending aorta dilation was seen in 16.4% (33/201); however, 69.7% (23/33) of these patients were older than 50 years, and 36.4% (12/33) of them had hypertension. Two patients with aortic aneurysms and inflammatory changes in the aorta and its branches were detected using CT angiography. Thrombosis was seen in 2.0% (6/295), including deep vein thrombosis (1.4%, 4/295), intermuscular venous thrombosis of the lower extremity (0.7%, 2/295), and pulmonary embolism (0.3%, 1/295).

CNS involvement was observed in 4.7% (14/295), including optic neuropathy (five cases), facial neuropathy (four cases), and cerebral infarction (two cases), and three patients had distinct manifestations. The first patient presented with headache, diplopia, mental disorder, fecal incontinence, and weakness of the lower limbs. Magnetic resonance imaging (MRI) showed multiple abnormal signals in the bilateral frontal parietal lobes and the periventricular cortex. The second patient complained of short-term and long-term memory declines, accompanied by a sense of stepping on cotton. MRI showed bilateral lesions in the semiovale center, corona radiate, and periventricular white matter, along with brain atrophy and bilateral hippocampal volume reduction. The third patient suffered from memory loss and recurrent syncope. MRI showed multiple abnormal signals in bilateral subcortical and white matter areas.

Only one patient had persistent unexplained microscopic hematuria, with an erythrocyte count of 4–18/HP in the urine. Urine contrast microscopy showed mild deformation in 70% of the erythrocytes. Our nephrologist regarded this as not of renal origin. Urine protein (trace levels to 0.3g/L) was seen in 1.7% (5/288).

Among all patients, 6.1% (18/295) had other autoimmune diseases and 2.0% (6/295) had malignancies. One patient had congenital hypogammaglobulinemia. In addition, 1.0% (3/295) had concomitant hematologic disease (Table 2).

Laboratory results are shown in Table 3. In patients with positive antinuclear antibody (ANA), two had systemic lupus erythematosus, two had progressive systemic sclerosis, and one had primary biliary cirrhosis.

After a median follow-up period of 68 months (range, 2–530 months) since the first symptoms, 8.8% (26/295) of the patients had died. The rate of lost to follow-up was 8.8% (26/295). The main cause of death was respiratory failure due to airway obstruction (11 cases), followed by infection (seven cases),

including pulmonary infection in six patients and sepsis in one patient. Other causes of death included lung cancer in two patients, cerebral hemorrhage in one patient, gastrointestinal bleeding in one patient, intestinal obstruction in one patient, and unknown causes in three patients. Respiratory failure caused by airway obstruction or pulmonary infection accounted for 65.4% (17/26) of all patients who died.

DISCUSSION

RP is a rare autoimmune disease. Patients with RP from different ethnic groups have various clinical characteristics and prognoses(8-11). To date, most cases were Caucasians, with limited reports from Asia(3). As far as we know, this study included the largest cohort of patients with RP; the results of this study may provide more information for this rare disease.

It has been highlighted that oriental patients with RP are more likely to develop severe airway complications(23). Lin et al. have summarized the clinical characteristics of 158 patients with RP by searching Chinese databases and found that the incidence of airway involvement in Chinese patients with RP was higher than that of patients from other countries (69% vs. 31%–67%, respectively) (11). However, the definition of airway involvement is not uniform across previous studies. Some of the studies defined airway involvement by respiratory symptoms(11,12,22), while others did not clarify the definition of airway involvement(7-9,20,21). Thus, the differences in the prevalence of airway involvement observed across different studies should not be simply attributed to biological differences(7-9,11-12,20-22). In this study, airway involvement was based on CT imaging of the larynx and chest, providing a more objective assessment than patient-reported symptoms. Notably, 70.5% of the patients had airway involvement during the course of the disease, which indicates a high prevalence of airway involvement in Chinese patients with RP. The main causes of death were different between Chinese and Western patients with RP. Michet et al. have reported that the most frequent causes of death were infection, systemic vasculitis, and malignancy(12). In a French cohort by Dion et al., none of their patients died of airway collapse or obstruction due to RP(8). In contrast, respiratory failure and pulmonary infection due to airway obstruction accounted for 65.4% (17/26) of the deaths in this study, suggesting that airway involvement is an important prognostic factor for RP in Chinese patients.

In patients with airway involvement, laryngeal involvement is more common than tracheobronchial involvement. The larynx is a cone-shaped organ mainly composed of cartilaginous tissue(24). The laryngeal cartilages include thyroid, cricoid, arytenoid, and epiglottic cartilages. The cricoid cartilage is the only complete structure of the larynx, whose integrity is of great importance for the patency of the respiratory tract. In this study, up to 25.7% of the patients with laryngeal involvement had to undergo tracheotomy due to progressive dyspnea or acute laryngeal obstruction. Four patients died even urgent tracheotomy had been performed, suggesting that laryngeal involvement is associated with a high risk of death. In addition, 40.9% of the tracheotomies were performed within half a year after the onset of respiratory symptoms, indicating the rapid progression of laryngeal involvement. Further analysis revealed that the younger age at onset and initially presenting with respiratory symptoms were independent risk factors for tracheotomy in patients with RP with laryngeal involvement. The risk of tracheotomy in patients who presented with respiratory symptoms was 2.354 times higher than that in those who presented with other symptoms. Furthermore, the risk of tracheotomy increases by 4.8% for every 1-year decrease in the age at onset. Notably, special attention should be paid to patients with RP with laryngeal involvement who are young at disease onset and present with respiratory symptoms, since the laryngeal lesions of such patients may progress in a short time and cause acute laryngeal obstruction and even death. Aggressive treatment and intensive airway evaluation are crucial for their outcomes.

In addition, tracheal and bronchial involvement accounts for a great proportion in this series. Approximately one-third of the patients had combined laryngotracheobronchial lesions. The trachea and bronchus are rich in cartilaginous components. With the grading of the bronchus, the number of cartilage rings decreases, and the shape of the cartilage rings becomes incomplete. The cartilage pieces begin to disappear in the bronchioles and disappear in the bronchioli terminales(24). Recurrent inflammation

destroys the cartilage rings, which are an essential scaffold for maintaining airway patency, resulting in tracheobronchial malacia, thus affecting the drainage of secretions and making patients prone to repeated infections(25). Meanwhile, infection will aggravate tracheobronchial malacia, in turn leading to a vicious circle(16,26). In this study, lower respiratory tract infection was more common in patients with airway involvement. Given that pneumonia is the second leading cause of death, excessive immunosuppressive treatment should be avoided.

The mean age at onset was 41.0 years, which is lower than those in previous reports, which may be due to the high proportion of adolescent patients in our series (Fig. 1) (7-9, 11-12, 20-22). Inner ear impairment may be asymptomatic. Due to the routine examination of inner ear function, the percentages of hearing impairment and vestibular dysfunction in this study were much higher than those in previous reports (Table 1). Some patients had severe visual impairment, and hearing disability was observed in 7.1% of the patients, suggesting the disabling potential of RP. The incidence of articular and skin involvement in China was slightly higher than that in Japan, but lower than that in other countries(7-9, 11-12, 20-22). Likewise, the rate of CNS involvement in this study was slightly higher than that reported by McAdam (3.1%) but lower than other studies (8%–12%) (8-9,11,20-21). Asymptomatic valve regurgitation detected using echocardiography was present in 20.9% of the patients. Interestingly, instead of primary valve degeneration, valvular regurgitation is secondary to dilation of the aortic root or mitral annulus(2). Aortic sinus or ascending aorta widening was seen in 16.4% (33/201) of the patients. However, several patients with cardiovascular lesions were older than 50 years or had hypertension. Thus, distinguishing the cause of the aforementioned cardiovascular abnormalities is difficult. Notably, cardiovascular involvement in RP is insidious and often occurs in the late stage of the disease. Baseline evaluation and regular screening are crucial for the early detection of cardiovascular involvement in RP.

Myelodysplastic syndrome (MDS) was barely seen in Chinese patients with RP. In our series, only one patient had MDS. Moreover, severe renal impairment was not seen.

This study reports the clinical characteristics of the largest RP cohort in the world. We highlighted the rapid progression and fatal potential of laryngeal involvement. Our study has several limitations. First, this is a single-center study. Second, a few patients were lost to follow-up; therefore, the mortality rate might be underestimated. Third, the reliability metrics between the different readers was not available; thus, the difference in the subjective interpretations of the CT scans between the two readers could not be clarified. Further studies are being conceived to explore the phenotypes of respiratory involvement and to investigate whether the pulmonary parenchyma may be involved in RP. Further follow-up is needed to explore the long-term prognosis of RP in China.

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FIGURE LEGENDS

Figure 1. Age distribution of patients with RP.

Figure 2. Initial symptoms of patients with RP.

Figure 3. Patterns of airway involvement in patients with RP (Figure 3a). The incidence of laryngeal, tracheal, and bronchial involvement in patients with RP (Figure 3b).

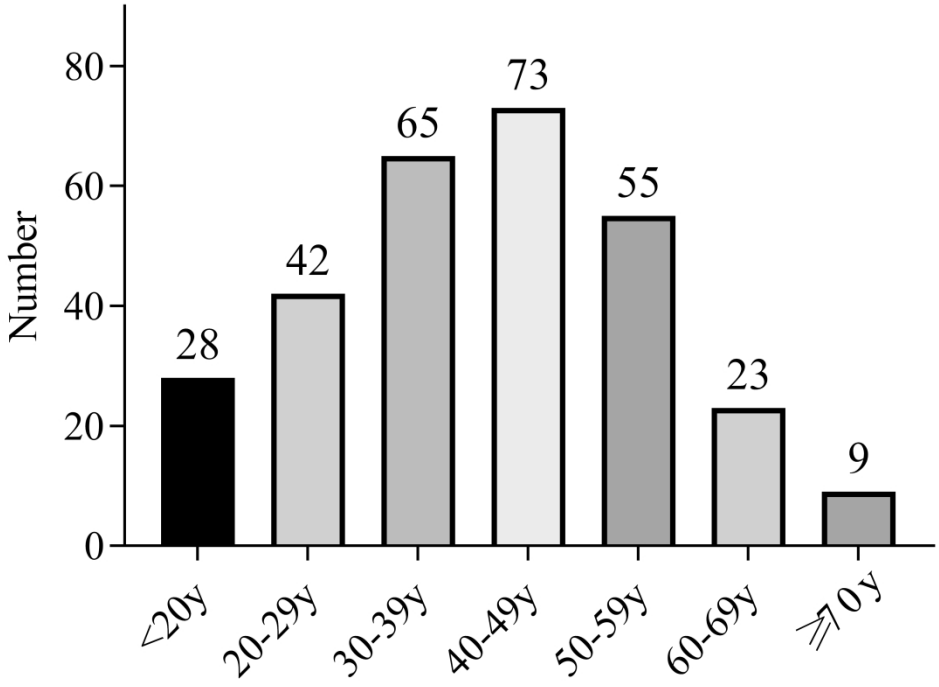

Figure 1. Age distribution of patients with RP.

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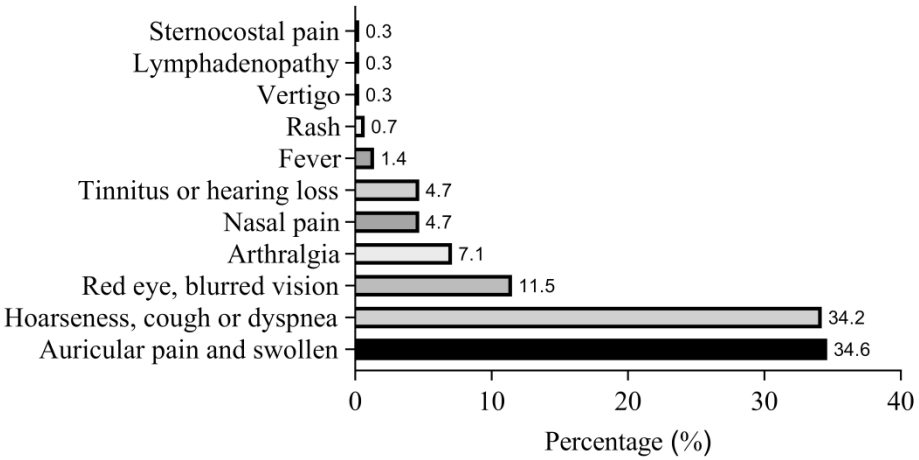

Figure 2. Initial symptoms of patients with RP.

139x73mm (1200 x 1200 DPI)

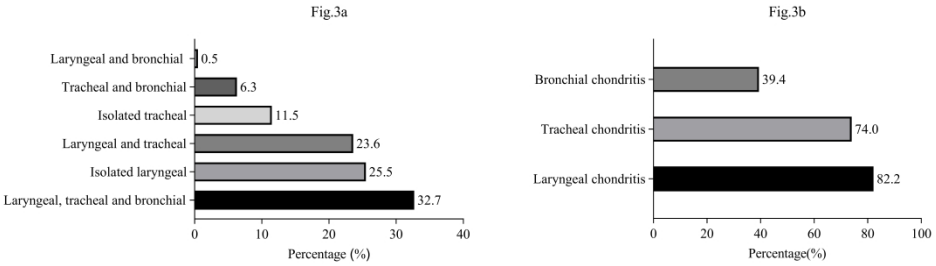

Figure 3. Patterns of airway involvement of patients with RP (Figure 3a). The incidence of laryngeal, tracheal and bronchial involvement in patients with RP (Figure 3b).

241x75mm (1200 x 1200 DPI)

Table 1 Demographics and clinical features of RP in Chinese and international cohorts

	Current	McAdam et al(20)	Michet et al(12)	Zeuner et al(21)	Trentham and Le(22)	Mathew et al(7)	Shimizu et al(9)	Lin et al(11)	Dion et al(8)
Number of patients	295	159	112	62	66	43	239	158	142
Mean age at onset, years	41	44	53	47	46	43	53	45	43
Female, n (%)	146 (49.5)	76 (47.8)	55 (49.1)	26 (41.9)	49 (74.2)	23 (53.5)	112 (46.9)	65 (41.1)	86 (60.6)
Auricular chondritis, n (%)	206 (69.8)	141(88.7)	95 (85.0)	58 (93.5)	63 (95.0)	38 (88.4)	187 (78.2)	107 (67.7)	127 (89.4)
Airway involvement, n (%)	208 (70.5)	89 (56.0)	54 (48.0)	19 (30.6)	44 (67.0)	16 (37.2)	120 (50.2)	109 (69.0)	71 (50.0)
Nasal chondritis, n (%)	119 (40.3)	115 (72.3)	60 (54.0)	35 (56.5)	32 (48.0)	15 (34.9)	94 (39.3)	85 (53.8)	89 (62.7)
Arthralgia, n (%)	118 (40.0)	129 (81.1)	58 (52.0)	33 (53.2)	56 (85.0)	26 (60.5)	92 (38.5)	88 (55.7)	98 (69.0)
Ocular involvement, n (%)	136 (46.1)	104 (65.4)	57 (51.0)	31 (50.0)	38 (57.0)	23 (53.5)	109 (45.6)	70 (44.3)	80 (56.3)
Hearing impairment, n (%)	177 (61.7) *	65 (40.9)	29 (26.0)	12 (19.4)	28 (42.0)	16 (37.2)	52 (21.8)	39 (24.7)	39 (27.5)
Vestibular dysfunction, n (%)	163 (61.0) *	41 (25.8)	15 (13.4)	14 (22.6)	35 (53.0)	NR	39 (16.3)	28 (17.7)	29 (20.4)
Skin involvement, n (%)	42 (14.2)	26 (16.4)	31 (28.0)	15 (24.2)	25 (38.0)	NR	32 (13.4)	17 (45.9) *	40 (28.2)
Valvular regurgitation, n (%)	42 (20.9) *	14 (8.8)	7 (6.0)	0	5 (8.0)	8 (32.0) *	5 (2.1)	5 (3.1)	31 (21.8)
CNS involvement, n (%)	14 (4.7)	5 (3.1%)	NR	6 (9.7)	NR	NR	23 (9.6)	8 (11.6) *	11 (7.7)

NR: not recorded; CNS: central nervous system

* The denominator is the number of patients who underwent the corresponding test or had relevant record in the medical records

Table 2 Associated diseases among 295 patients with RP

Associated disease	**Cases (n)**
Rheumatic disease	
Rheumatoid arthritis	3
Systemic lupus erythematosus	2
Sjogren Syndrome	2
Ankylosing spondylitis	3
Primary sclerosing cholangitis	1
Ulcerative colitis	1
IgG4 related disease	1
Hashimoto disease	5
Malignancy	
Rectal stromal tumor	1
Vocal cord carcinoma	1
Thyroid cancer	1
Lung cancer	1
Breast cancer	1
Glioma	1
Hematological Disease	
MDS	1
Myeloproliferative disease	1
Severe anemia with unknown cause	1

MDS: myelodysplastic syndrome

Table 3 Laboratory features in 295 patients with RP

Laboratory tests	n * (%)
Elevated ESR	148/286 (51.7)
Elevated CRP	102/285 (35.8)
TGAB（+）	29/173 (16.8)
TMAB（+）	20/174 (11.5)
ANA（+）	28/277 (10.1)
1:320	22/28 (78.6)
1:1000	4/28 (14.3)
1:3200	2/28 (7.1)

* The numerator is the number of patients who had positive test result, the denominator is the number of patients who underwent corresponding test

ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; TGAB: antithyroglobulin antibody; TMAB: Anti-thyroid microsomal antibody; ANA: antinuclear antibody