Relapsing Polychondritis – An Oriental Case Series

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ABSTRACT

Introduction: Relapsing polychondritis (RPC) has been described mainly in Caucasian populations. Reports from other ethnic groups are few.

Objectives: To describe the clinical characteristics, management and outcome of RPC patients seen in an Oriental population in Singapore.

Methods: The case records of RPC patients treated in our department from 1989 to 2001 were reviewed. Only 12 fulfilled the McAdam-Michet-Damiani-Levine diagnostic criteria and these were studied.

Results: The female-to-male ratio in our series was 3:1. There were 10 ethnic Chinese and two Malay patients. The age of onset of symptoms ranges from three to 65 years, with a mean of 34 years. A diagnosis was made from two weeks to three years after onset, with a median of 4.5 months. There were 10 patients with pinna, nine articular, eight ocular, six laryngotracheal, five inner ear, four nasal and one cardiac involvement. Five presented with fever. None of them had cutaneous, renal or central nervous system involvement. Ten had raised ESR at presentation. One patient developed discoid lupus erythematosus two years later. All 12 patients received prednisolone with eight of them requiring additional immunosuppressants. Two patients had resistant disease failing to respond adequately to various immunosuppressants together with prednisolone. There was no mortality amongst the nine patients who had remained on follow-up at the time of this report. Five of the six patients with laryngotracheal involvement had tracheostomy and one of them had airway stenting as well.

Conclusion: Our series suggests that although the clinical manifestations of RPC are similar in the Oriental and the Caucasian populations, Oriental patients may have less cutaneous, renal or nervous system involvement and more serious airway complications.

Keywords: polychondritis, oriental, obstruction, airway, stent

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INTRODUCTION

Relapsing polychondritis (RPC) is a rare systemic inflammatory disorder, characterised by widespread, progressive and recurrent inflammation of cartilaginous tissues that may potentially be debilitating and life threatening. All types of cartilage, fibrocartilage, elastic, hyaline cartilage and cartilage in the tracheobronchial tree and other proteoglycan-rich structures, such as the eye, heart, blood vessels and inner ear, may be involved. Constitutional symptoms are common and vasculitis affecting skin or internal organs (heart, kidneys, nervous system) may occur.

Patients can present with a wide array of symptoms that often pose major diagnostic dilemmas. The diagnosis of RPC must be made on clinical grounds, as there is no specific test available. Various clinical criteria, including McAdam/Michet[1,2] with Damiani-Levine modification[3], had been proposed.

RPC was originally described in 1923 by Jaksch-Wartenhorst[4]. Since then, it has been described mainly in Caucasian populations. Most are as case reports, which may describe only those with severe disease course or extra-ordinary features. A few large Caucasian series had been published[1,2,5,6]. However, a Medline search of the published English literature did not yield any reported series from other ethnic groups. We describe the clinical characteristics, management and outcome of Oriental RPC patients seen in our department.

METHODS

All the patients with RPC treated in our department, the largest rheumatology department in Singapore, which provides both secondary and tertiary rheumatologic services nation-wide, between 1989 and 2001, were identified. Their case notes were reviewed retrospectively. Among 15 patients treated as RPC only 12 fulfilled the diagnostic criteria, as suggested by McAdam/Michet[1,2] and modified by

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Table I. Criteria for diagnosis of relapsing polychondritis as suggested by McAdam/Michet[1,2] with Damiani-Levine[3] modification.

- Bilateral auricular chondritis
- Nonerosive seronegative inflammatory polyarthritis
- Nasal chondritis
- Ocular inflammation – conjunctivitis, keratitis, scleritis/episcleritis, uveitis
- Respiratory tract chondritis – laryngeal and/or tracheal cartilages
- Cochlear and/or vestibular dysfunction – neurosensory hearing loss, tinnitus and/or vertigo

To establish the diagnosis, all patients were required to have one of the following:
- At least three of the above clinical criteria
- One or more of the above clinical criteria with positive histologic confirmation
- Chondritis at two or more separate anatomic locations with response to steroids and/or dapsone

Table II. Cumulative characteristics of patients with relapsing polychondritis: comparing the oriental patients seen in Singapore with four large series.

Variables	Current series (n=12)	Zeuner et al[6] (n=62)	Trentham et al[5] (n=66)	McAdam et al[1] (n=159)	Michet et al[2] (n=112)
Demographic characteristics					
Female: male ratio	3:1	13:18	49:17	76:83	55:57
Mean age at diagnosis	34	46.6#	46	44	51
(range), year	(3-65)	(17-86)	(16-68)	(NR)	(13-84)
Mean duration of follow-up, year	8	NR	8	NR	6
Clinical features, %					
Auricular chondritis	83	94	95	89	85
Arthritis	75	53	85	81	52
Laryngotracheal involvement	50	30	67	56	48
Ocular involvement	67	50	57	65	51
Nasal chondritis	33	56	48	72	54
Reduced hearing	17	19	42	46	30
Vestibular involvement	42	23	53	NR	13
Skin involvement	0	24	83	17	28
Saddle nose	17	23	20	NR	29
Cardiac involvement	8	23	8	9	6
Vasculitis	0	0	12	18	10
Nervous system involvement	0	10	NR	NR	NR
Renal involvement	0	6	NR	NR	NR
Complications and survival, %					
Death	0	3	6	NR	NR
Tracheostomy	42	5	6	NR	NR
Tracheal collapse	42	NR	14	NR	NR

NR = not reported
# = This is reported as median, instead of mean[6]

Damiani and Levine[3] (Table I) and these were studied. The three patients who were excluded from the series had bilateral auricular chondritis only. Two of them did not undergo cartilage biopsy while the other had biopsy that was inconclusive. All three of them responded well to prednisolone alone and no secondary aetiologies were found.

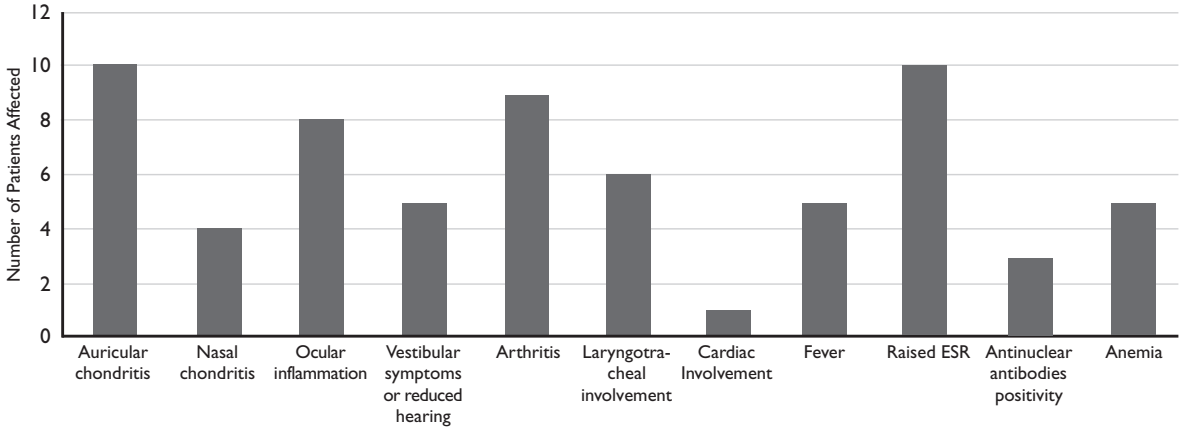
Clinical data, cumulative disease manifestations, laboratory investigations, associated diseases, therapy, disease course, complications of disease and outcome were obtained from the case notes.

The extent of organ involvement caused by RPC was classified into two categories: restricted and extensive according to the classification suggested by *Zeuner et al*[6]. If the patient fulfilled four or more of the following eight criteria, RPC is classified as extensive: involvement of nasal, auricular, laryngotracheal cartilages, disturbance of the vestibular organ, arthritis, ocular involvement, general/constitutional symptoms (fever, weight loss, malaise, anorexia), organ involvement (heart, kidney, nervous system). Each involved organ was given one point to give a sum of the index of organ involvement (range: 0-8)[6].

RESULTS

Over a period of 13 years, 15 patients were treated for RPC, with three of them not fulfilling the above diagnostic criteria (Table I). The mean duration of follow-up is eight years. Among the 12 patients who fulfilled diagnostic criteria, three were lost to follow-

Fig. 1 Clinical manifestations in 12 patients with relapsing polychondritis.



* Raised ESR = ESR >20 mm in first hour
* Anaemia = haemoglobin <13 g/dL for male and <11.8 g/dL for female

up eventually after 10, 12 and 17 years of follow-up respectively. They were well during their last follow-up review. One patient was transferred to the care of a paediatric rheumatologist after six years of follow-up.

The female-to-male ratio in our series was 3:1. There were 10 Chinese and two Malay patients. The age of onset of symptoms range from three to 65 years, with a mean of 34 years. The peak age of onset is the fifth decade of life. A diagnosis was made between two weeks to three years after onset of the first symptom, with a median of 4.5 months.

Fig. 1 shows the number of patients with various clinical manifestations of RPC in our series. None of the patients in the series had cutaneous, renal or central nervous system involvement. One of those with positive anti-nuclear antibodies developed discoid lupus erthematosus two years later. The rest of the patients in our series did not have other associated diseases.

Three of the patients had chronically active disease while the other nine had intermittent inflammatory episodes. Half of our patients[6] had extensive disease (five of them had laryngotracheal) and the other half had restricted disease. Five of the six patients with laryngotracheal involvement had tracheostomy with one of them being eventually able to have it closed off successfully. One of them had tracheostomy only after airway stenting failed to maintain patent airway a year after insertion. There was no mortality among the nine patients still on follow-up at the time of this report.

All 12 patients received prednisolone and eight required at least a second line agent: methotrexate (five patients), dapsone (four patients), and azathioprine (three patients). Two patients, both with extensive disease (index of organ of involvement of seven), had resistant disease failing to respond adequately to azathioprine, methotrexate, cyclophosphamide (oral or IV), cyclosporin, mycophenolate mofetil, chlorambucil and intravenous immunoglobulin in various combinations together with prednisolone. Both of them had laryngotracheal involvement. They required high dose prednisolone to control the disease. One of them was recently started on leflunomide but this had to be discontinued due to severe drug-induced transaminitis. The period of therapy with leflunomide was insufficient for evaluation of its efficacy.

DISCUSSION

RPC is a rare disorder, presumably of autoimmune origin as evidenced by the presence of auto-antibodies against native collagens (II, IX and XI)[7,8], cell mediated immune response toward cartilage components[9] and collagen II immunisation induced chondritis and arthritis in animal models[10,11]. Its clinical features and disease course showed marked inter-patient variability. Outcome is often difficult to predict.

We made an attempt to compare our series with four large Caucasian series. Table II compares the demographic and clinical features as well as outcome of our patients with four of the large Caucasian series[1,2,5,6]. In our series, the mean duration of delay in diagnosis was 4.5 months, which is shorter than that reported in the series of *Trentham et al*[5]. This is probably due to easy access to specialist care in our country. The clinical manifestations of our patients were fairly similar to the four large published Caucasian series, with the exception that none of our patients had cutaneous, nervous system or renal involvement. Our series showed a female preponderance as reported by *Trentham et al*[5], although it is generally believe that there is no sex predilection. However, our patients may have more severe disease than those reported: about a third of our patients had tracheostomy compared to 6% in the series of

Trentham et al[5], despite the earlier diagnosis in our patients. Based on the *Zeuner et al* index of organ involvement[6], 50% of our patients had extensive disease. Whether this implies a more severe manifestation among Oriental patients or is a result of referral bias will need to be confirmed.

Our retrospective study of RPC among Oriental patients has a few limitations: the retrospective design, the small number of subjects available and patient recruitment in a national referral centre. A larger series is needed to provide more insight into this condition among the Oriental population. However, due to its rarity, a multi-centre study in the Asia-Pacific region would be necessary.

CONCLUSION

Our series demonstrates that the clinical manifestations and disease course of RPC showed significant variability. Although the disease is probably similar in Oriental and Caucasian populations, we have shown that our patients do not have cutaneous, renal or central nervous system involvement and may have more serious disease despite earlier diagnosis. A larger series of Oriental RPC patients is needed to confirm these findings.

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