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Relapsing polychondritis associated with heart block

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Abstract. – OBJECTIVE: The present article aims at describing a rare case of an RP patient who evolved with heart block and was successfully treated with corticoid pulse therapy, without the need for pacemaker insertion.

PATIENTS AND METHODS: A systematic research on relapsing polychondritis (RP) and heart block (HB) published in PubMed/MEDLINE, Web of Sciences, LILACS, and Scielo from 1966 to August 2020 was performed.

RESULTS: It was found 10 studies on RP associated with HB, and we added a case. Most were male (7/10) with ages 30 to 66 years old. RP disease duration was 1 week-6 years. In most cases (7/10), the RP was active when the HB occurred. A complete HB was observed in 4/7, followed by type II degree block in 3/7, and one patient had a sinus node dysfunction. Most patients received glucocorticoids. A pacemaker was inserted in 4/9 cases. Good outcome was observed in 3/9 patients and mortality in 2/10.

CONCLUSIONS: We report the first case of an RP patient who had a heart block and was successfully treated with methylprednisolone pulse therapy. The authors suggest that in these RP cases, an attempt with a glucocorticoid pulse therapy may be offered to treat the heart block and prevent the insertion of a pacemaker.

Key Words:
Relapsing polychondritis, Heart Block, Vasculitis, Autoimmunity, Autoantibodies.

Introduction

Relapsing polychondritis (RP) is an uncommon autoimmune condition characterized by inflammation of the nose, ears, and trachea's cartilaginous tissues. The diagnosis is determined on the presence of three of the following: bilateral auricular chondritis, nasal cartilage inflammation, chondritis of the trachea or bronchi, non-erosive polyarthritis, eyes inflammation, or audiovestibular involvement. The presence of these three of the above manifestations precludes the need for biopsy[1].

RP may lead to a local complication described above and may involve other organs such as kidneys and the cardiovascular system. The heart's involvement varies from 24 to 52% of the patients, and the most common anomaly is valvular heart disease[1]. The minority of the patients (4 to 6%) may develop a first to third-degree atrioventricular block, and it may be a consequence of a fibrotic involvement[2]. Therapy with glucocorticoids with or without immunosuppressive drugs is mandatory; however, many patients will need a permanent pacemaker. Therefore, the conduction system disease is a rare manifestation of RP.

The present study aims to describe a rare case of an RP patient who evolved to a heart block and was successfully treated with corticoid pulse therapy without pacemaker insertion.

Patients and Methods

Literature Review

We have systematically studied articles published in Pubmed/MEDLINE, Web of Sciences, LILACS, and Scielo from 1966 to August 2020 using the following MeSH entry terms: "relapsing polychondritis", "polychondritis cardiac involvement", and "conduction disturbances". We used equivalent strategies in the other databases. All the related articles are based on relapsing polychondritis and heart block in the English and French language. Besides, we describe a patient with RP who was diagnosed with heart block.

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The reference lists of the selected articles were analyzed to identify other publications. Initially, two authors (JFC and AFC) performed the literature search and independently selected the study abstracts. In the second stage, the same reviewers read the full-text articles selected by abstracts, also independently. Disagreements arising in the consensus meetings were also resolved with the same third reviewer. The authors followed the PRISMA guidelines. We designed a standardized form to extract the following information from relevant articles regarding the authors and year of publication, the number of patients studied, demographic data, type of heart block, treatments, pacemaker insertion, and outcomes. As this study was not quantitative or epidemiological, but a descriptive study, we do not assess the selected studies' quality and do not perform a meta-analysis. An informed consent was obtained from the patient.

Case Report

A 37-year old female with a previous history of relapsing polychondritis characterized by polyarthritis, nose, and bilateral auricular chondritis, improved with systemic glucocorticoids. Her laboratory tests were negative for antinuclear antibodies, rheumatoid factor, and anti antineutrophil cytoplasmic antibody. She also had a history of inflammatory bowel disease and was under therapy with mesalazine. She underwent the emergency department with dyspnea and chest discomfort. Her physical examination was unmarketable. An electrocardiogram was performed, and a sinus rhythm and a type I atrioventricular (AV) block (PR interval of 360 ms) was detected. An infusion of isoproterenol was administered and was observed an increase of sinus automatism; however, the AV block and PR interval did not change. An ergometric test was done, and the patient developed a type 2 AV heart block 2:1 (Figure 1A) at the peak of the effort and the recuperation phase. Transthoracic echocardiography was interpreted as normal, and the patient was submitted to coronary arteriography, which was normal. A methylprednisolone pulse therapy 1g per day for 5 days was initiated. Complete remission of the heart block was observed on the third day of the treatment (Figure 1B). She remained asymptomatic, and prednisone 40 mg *per ors* was started. After 30 days, a new ergometric test was done, and a complete PR interval normalization and absence of heart blocks were demonstrated.

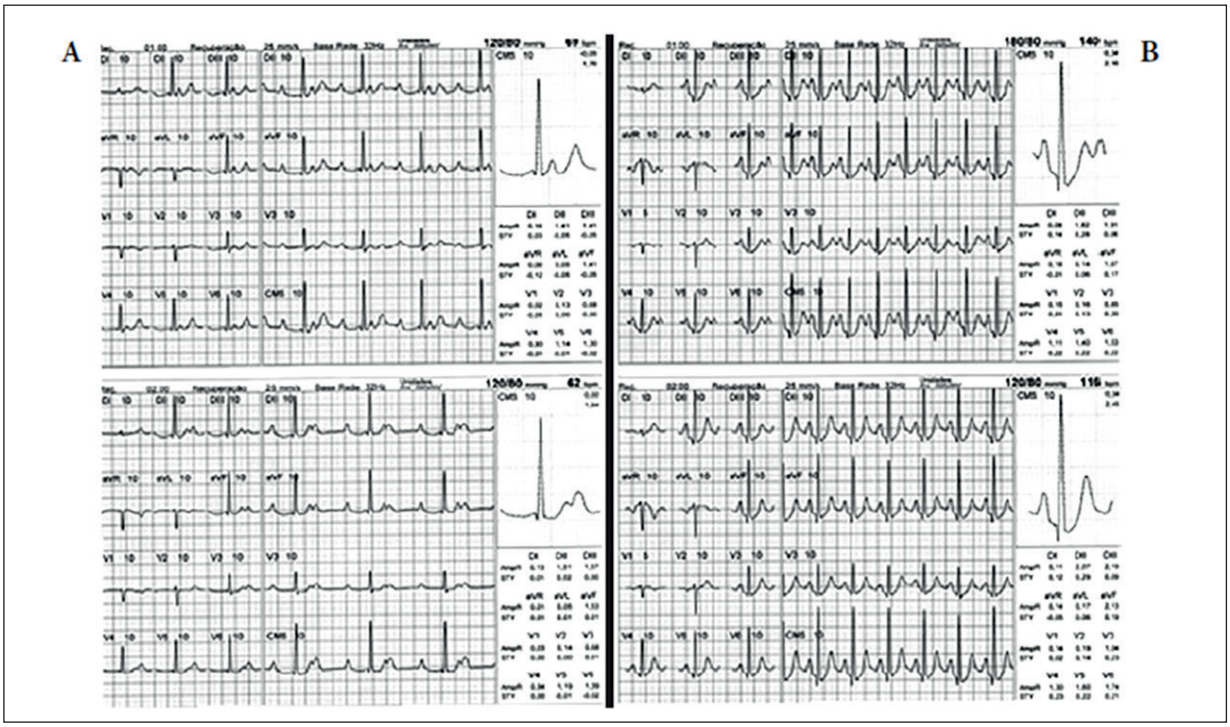

Figure 1. Electrocardiogram (ECG) from the ergometric test showing a type 2 AV heart block 2:1 at the recuperation phase **(A)** and normal ECG after methylprednisolone pulse therapy **(B)**.

Results

The initial search identified 19 publications. After reviewing titles and abstracts, 10 articles were selected for reading the full texts, of which 9 were selected for this review (Figure 2). The demographic, clinic, and laboratory characteristics of our patient with RP and heart block, as well as the other cases described in the literature reviews, are summarized in Table I.

According to the literature from 1966 to 2020, only 10 cases of RP associated with heart block were reported[1,3-9]. We have associated our case report with a total of 11 cases for the analysis. Routy et al[8] have described two patients.

The majority of the patients are male (7/9), ranging from 30 to 66 years old. RP disease duration varied from 1 week to 6 years.

For most of the patients (9/11), the RP was active when the HB was reported. Complete heart block was observed in 6/9, followed by type II second degree block in 3/9, and one patient had a suspected sinus node dysfunction.

Echocardiography was normal in half of the cases in which this procedure was performed (n=8). In the other half of the patients (4/8), aortic regurgitation in 2/5 and aortic dilatation in 2/4 were observed.

The majority of the patients received glucocorticoid (7/11), usual prednisone *per ors*; one received a pulse therapy with methylprednisolone and one intravenous methylprednisolone. Two patients did not receive corticoids and were treated with angiotensin converter enzyme inhibitor (n=2) and beta-blockers (n=1). Pacemakers were inserted in 6/11 cases. Good outcome was observed in 5/11 patients and death in 2/11.

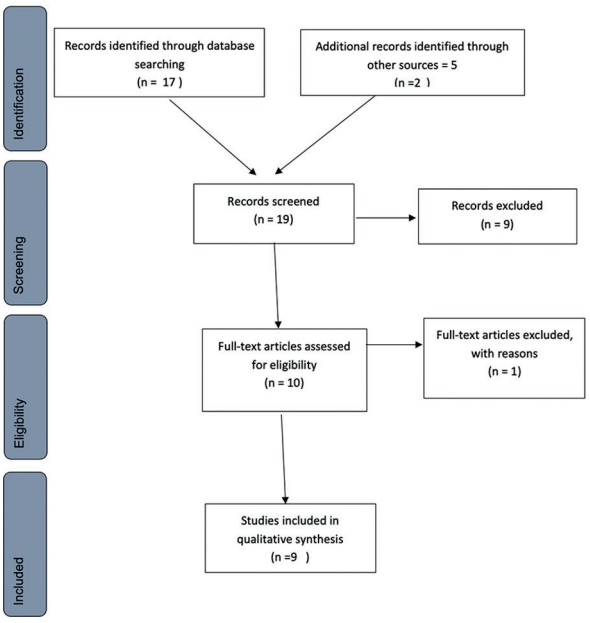

Figure 2. Flowchart of the included studies.

Discussion

This paper brings for the first time the description of an RP patient who evolved with heart blocked and was treated entirely with glucocorticoid pulse therapy. This study has some strengths, and we reviewed all cases published in the English and French medical literature on RP and HB, including those on the grey literature.

It is the first description of a patient with RP, who had a heart block, and the aggressive clinical approach with methylprednisolone pulse therapy had an excellent outcome. The patient did not need pacemaker insertion and evolved with complete restoration of her conduction system.

Cardiovascular complications reported in RP include vasculitis, arterial thrombosis, aneurysm formation, atrioventricular conduction disturbances, valvular regurgitation, and pericarditis[1].

The heart involvement in RP is relatively frequent; it may reach one quarter to a half of patients[1]. However, conduction disturbances are rare (4-6%)[2]. An electrophysiologic study on two patients with RP revealed that the conduction system's involvement is present in more than one level[8]. A histopathological study demonstrated the fibrosis of the atrioventricular node and the His-Purkinje conduction system[2].

Atrioventricular conduction disturbances ranging from first- to third-degree heart block have been observed in about 5% of patients[1,2]. The third-degree atrioventricular block has been associated with aortic valve disease, and it is associated with the contiguity of fibrosis from the aortic valve into the conducting system[1,2]. Another possibility for aortic root dilatation leading to aortic valve insufficiency may lead to impairment of the atrioventricular node function. In our case herein described, no evidence of an aortic impairment was detected.

HLA-DR4 was found in 50% to 60% of RP patients compared to 25% of the healthy controls[10]. Patients with RP may have both humoral responses with autoantibodies production and cellular response with T cells' participation, both directed to cartilage collagens, such as types II,

Table I. Summary of all published cases of relapsing polychondritis patients who had to block heart in their evolution.

Author, year	N, sex, age	Disease duration	RP was active during heart block	Type of heart block	Echocardiography	Treatment before heart block	Treatment after heart block	Pacemaker insertion	Outcome
De Carvalho et al (present study), 2021	1, female, 37 years old	7 years	No	Type I on rest, and type 2 AV heart block 2:1 on effort	Normal	Glucocorticoid year before	Methylprednisolone pulse therapy 1 g/d for 5 days	No	Complete ecovery of heart conduction
Butterton et al[3] 2006	1, male, 59 years old	6 weeks	Yes	Type II, second-degree heart block	Normal	Lisinopril, atenolol, isosorbide mononitrate, ranitidine, and monthly vitamin B12 injections	IV methylprednisolone (30 mg twice a day) and mycophenolate mofetil (750 mg twice daily)	Permanent dual-chamber pacemaker	Permanent pacemaker was needed.
Hojaili et al[4] 2008	1, female, 40 years old	1 week	Yes	Complete heart block	N/A	None	Prednisone 20 mg/day	No	Improvement
van Laarhoven et al[5] 2006	1, male, 30 years old	1 year	No	Complete heart block	N/A	Non-steroidal anti-inflammatory drugs	N/A	N/A	N/A
Saliba et al[6] 2003	1, female, 43 years old	6 years	Yes	Suspected sinus node dysfunction	Normal	Prednisone, azathioprine,	Increasing in prednisone and azathioprine dose	No	5 days later the heart rate gradually increased
Barretto et al[7] 2002	1, male, 42 years old	6 years	Yes, ESR 50 mm/1st hour	Complete heart block	Moderate/ severe aortic valve regurgitation, aortic root was dilated (43 mm at the sinuses of Valsalva) and thickened	Warfarin, prednisone 60 mg/d, and intravenous cyclophosphamide	Permanent dual-chamber pacemaker, β-blocker and ACE inhibitor	Temporary transvenous pacemaker followed by permanent dual-chamber pacemaker	Asymptomatic cardiovascular despite mild left ventricular enlargement on repeated echocardiography

Continued

Table I *(Continued)*. Summary of all published cases of relapsing polychondritis patients who had to block heart in their evolution.

Author, year	N, sex, age	Disease duration	RP was active during heart block	Type of heart block	Echocardiography	Treatment before heart block	Treatment after heart block	Pacemaker insertion	Outcome
Del Rosso et al[1] 1997	1, male, 66 years old	11 years	Yes, ESR of 36 mm/hr and CRP of 10 mg/dL	Transient II-degree type II and complete atrioventricular heart block (with pause > 3 seconds),	Augmented left ventricular end-diastolic diameter (80 mm), increased left atrial dimension (60 ram), reduced systolic shortening and ejection fraction (24% and 35%, respectively), and retraction of the aortic cusps	Corticosteroids and azathioprine	ACE inhibitors, digitalis and furosemide, pacemaker	Permanent dual-chamber pacemaker	Heart failure and death
Bowness et al[2] 1991	1, male, 33 years old	3 months	Yes	Complete heart block	Normal	Prednisolone 10 mg/day	Prednisolone (60 mg/day), and oral cyclophosphamide (2 mg/kg/day)	Permanent ventricular pacemaker	Acute aortic incompetence after 4 weeks RP disease activity Died
Routy JP et al[8] 1988	2, N/A	N/A	Yes	Complete heart block		N/A	Steroids	Transient pacemaker	Improvement
Manna et al[9] 1985	1, male, 30 years old	5 years	Yes	First degree heart block	Left ventricular enlargement, retraction of left coronary and posterior aortic cusps, and moderate postvalvular dilatation of ascending aorta, severe aortic regurgitation	N/A	Prednisone 75 mg/d, ampicillin 3 g/d, and diclofenac 200 mg/d, azathioprine 100 mg/d	No	Good

ACE: angiotensin-converting enzyme; CRP: c-reactive protein; ESR: erythrocyte sedimentation rate.

IX, and XI to cartilage matrix proteins, in special matrilin-1. An experimental study, using immunization of rats with matrilin-1, which is present in high amounts in the trachea but not in the adult human ear, was able to induce inflammation of the trachea and larynx, but not the outer ear or joints, suggesting that a cartilage component may be involved in the pathogenesis of RP[11]. Autoantibodies directed to type II collagen are described in 30% to 60% of the patients with RP, and these autoantibodies are more detected in the early phase of the RP[11].

Conclusions

We report the first case of an RP patient who had a heart block and was successfully treated with methylprednisolone pulse therapy. The authors suggest that in these RP cases, an attempt with a glucocorticoid pulse therapy may be offered to treat the heart block and prevent the insertion of a pacemaker.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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