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Case Report

Polychondritis Recidivans – A Case Report with a Review of the Literature

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Abstract: Polychondritis recidivans is a rare immune-mediated autoimmune, multisystemic disease. It proceeds with recurrent inflammation of both cartilage tissue, mainly the ears, nose, larynx, tracheobronchial tree, ribs and joints, as well as the proteoglycan-rich tissues of the heart valves, blood vessels and eyes. The clinical picture is diverse. Symptoms often overlap with other diseases and diagnosis is delayed. Late diagnosis is the main cause of complications, and life-threatening damage to the affected structures. Polychondritis recidivans may be self-contained or associated with other autoimmune diseases, vasculitis, or hematological disorders. The diagnosis is clinical. The main manifestation of diagnostic value is chondritis with sequential or simultaneous involvement of several cartilage organs. There is no specific laboratory test for the disease. A cornerstone of therapy is glucocorticoids. With severe course, immunosuppressants are also used, and recently biological agents. We describe a case of a 51-year-old woman with repeated recurrences of moving inflammation of the ear cartilage, accompanied by arthritis, severely reduced hearing, hoarseness, conjunctivitis and episcleritis, and CNS symptoms. Blood tests showed leukocytosis and elevated C-reactive protein. Polychondritis recidivans is diagnosed based on the diagnostic criteria of L. P. McAdam et al., J. M. Damiani and H. L. Levine and C. J. Michet et al. Dramatic improvement from methylprednisolone treatment supported the diagnosis. An overview of the epidemiology, pathogenesis, clinical picture, complications, laboratory and imaging diagnostic methods, and treatment of polychondritis recidivans are presented.

Keywords: Polychondritis, Recidivans, Epidemiology, Pathogenesis, Clinical Picture, Paraclinical Studies, Treatment

1. Introduction

Polychondritis recidivans (PR) is a rare immune-mediated multisystem disease presented with recurrent inflammation of cartilage tissue of the ears, nose, respiratory tract/tracheobronchial tree and joints. Proteoglycan-rich tissues of heart valves, blood vessels and eyes are also affected [1, 2]. The disease was first described in 1923 by the Austrian internist Rudolf Ritter Jaksch von Wartenhorst [3]. The term relapsing polychondritis was coined by C. M. Pearson et al in 1960 and emphasizes the relapsing nature of the disease [4]. Clinical manifestations range from mild symptoms to anatomical damage and disturbances in the normal functioning of the affected structures, which can be life-threatening [5, 6]. PR is an extreme diagnostic and therapeutic challenge. Its verification is often delayed with years, ranging from 2 to 21 years (median 3.5 years) [1, 7-9]. Corticosteroids are the main choice of treatment [2, 5, 10, 11].

Herein, a very rare case of current polychondritis complicated with arthralgias and ocular complication is desscribed. A comprehensive analysis of the recent medical research is also presented.

2. Clinical Case

A 51-year-old woman was admitted to our ward with fever, edema, erythema and severe pain in her left auriculae with 3-day duration. Every few months in the last 3 years, she receives such symptoms, alternatively on both ears. She underwent antibiotic treatment with minor response. Knee and hip joints pains often deteriorate her general condition in the last 5 years. She has severely reduced hearing and wears a hearing aid since 2 years. She had a hoarse voice for a year. From 4 months, headaches, dizziness, insomnia and burning in the eyes appear.

On physical examination, her heart rate was 89bpm, blood pressure 120/75 mmHg and respiratory rate 18rpm. The body temperature was 37.4ºC. Dermatological changes were localized on the left auricle, where diffuse erythematous patches with edematous edge were seen (Figure 1). Her acute inflammatory parameters were elevated (ESR 40 mm/h and C-reactive protein 28 mg/l). Bilateral knee artritis and sacroiliitis were detected on computer tomography. Chronic rhinopharyngitis and otosclerosis with labyrinthization were objective by an otorhynolaryngologist. Ophthalmology consult verified bilateral conjunctivitis and episcleritis. Chronic vertebrobasilar insufficiency and paroxysmal activity on the left occipital were proven by encephalography.

Based on common relapses of recurrent inflammation of the ear cartilage, accompanying with arthritis, severely reduced hearing loss, voice hoarseness, conjunctivitis, episcleritis, and CNS symptoms the diagnosis of recurrent polychondritis was concluded. Methylprednisolone 60 mg/day therapy was initiated with a rapid dramatic improvement that further supported the diagnosis. The dose was tapered with a step of 10 mg per week to a maintenance rate of 8 mg daily. The patient had 2 relapses within 1 year due to voluntary interruption of therapy.

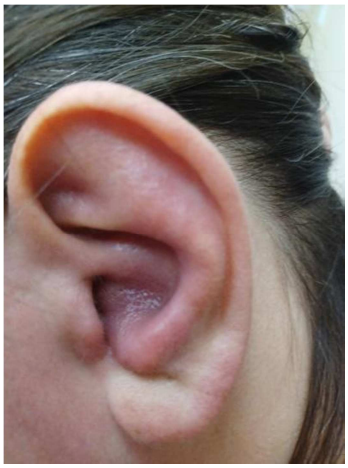

Figure 1. *Erythema and edema of the left auricle.*

3. Discussion

About 400 patients with polychondritis recidivans have been reported in the scientific literature. Epidemiological studies from the United Kingdom, Hungary and the United States show an annual incidence of 0.7–3.5 per million people, with the highest incidence reported in the United States. [12-14]. PR usually starts in the 4th decade of life, but can occur at any age [2, 5, 6]. Paediatric cases are up to 5% of all patients with an age range between 1.7 months and 17 years [15]. The disease was found even in a newborn whose mother had multiple relapses of PR during pregnancy [16]. PR indicates a high preference for female gender, as men cases are considered an exception [2, 6].

About 35% of patients with PR have associated diseases. The most common are autoimmune diseases, various systemic vasculitis, rheumatoid arthritis and myelodysplastic syndrome. [2, 5, 6, 9-11, 17, 18]. Solid tumors (bladder, breast, lung and pancreas) and lymphomas [19] are also described.

In recent years, the autoimmune hypothesis of the occurrence of the disease has been imposed. PR primarily affects cartilage structures, suggesting that immune mechanisms work against proteoglycan, the main constituent of cartilage. In patients with PR, circulating and tissue-specific antibodies were detected against collagen types II, IX and XI, matriline-1 and COMP (cartilage oligomeric matrix complex) [10, 19-21]. Cellular immune response is dysregulated, too [2, 10, 22]. Th1/Th2 imbalance is suggested to increase the expression of INF-γ, IL-2, IL-12, matrix metalloproteinase (MMP)-3, 8, 9, and cathepsins K and L. An absolute reduction in regulatory T cells enhances cartilage inflammation, while CD4+ cells secrete cytokines, such as interleukin-8 (IL-8), macrophage inflammatory protein-1β (MIP-1β) and monocyte chemoattractant protein-1 (MCP-1) to activate monocytes, macrophages and neutrophils. Macrophages release proteolytic enzymes, matrix metalloproteinase (MMP-3), and cathepsins K and L, which destroy cartilage.

Based on the detected deviations in autoantibodies against collagen type II, IX and XI, matriline-1 and COMP and the cell-mediated immunity with increased expression of INF-γ, IL2, IL12, MMP-3, 8, 9, cathepsins K and L as well as in the secretion of cytokines by CD4+ cells activating leukocytes, the most likely hypothesis for pathogenesis of the disease is that triggering factors, such as infectious agents, drugs, chemicals, toxins or direct trauma, provoke protein degranulation and cause the release of specific antigens against cartilage structures [5, 10, 18, 23-25].

It is assumed that the disease occurs in genetically predisposed individuals. HLA-DR4 antigen is more commonly seen in PR patients [26], supporting the autoimmune nature of the disease.

PR is characterized by multisystemic involvement, hence, the main manifestation with primary diagnostic value is chondritis with sequential or simultaneous involvement of several cartilage organs [1, 2, 5, 6-11, 18]. The cartilage of the outer ear and nose is most often affected, 80-90% and 50-70%

of cases, respectively [1, 2, 6-8]. In the acute stage, the auricle became tender, erythematous and edematous. The process can be bilateral, unilateral or moved from one auricle to the other. Relapses usually last 1-2 weeks. The manifestations of nasal cartilage involvement are similar, often accompanied by epistaxis or nasal clogging. After subsidence of acute manifestations, cauliflower ears and saddle nose can be formed [2, 6].

Joint involvement is the second most common manifestation. It affects 50% to 75% of patients [5, 9-11, 18, 27], usually presenting with non-erosive inflammatory arthritis. It is most often localized on the wrists, metacarpophalangeal and proximal interphalangeal joints. There are recurrent arthralgic. Sometimes joint injuries progress, lead to deformities and permanent disability of patients [27]. Joint syndrome is exacerbated simultaneously with chondritis, but in some anecdotal cases, it can precede it.

Cartilage of the larynx, tracheobronchial tree and ribs are affected in 30-50% of patients [2, 6, 9, 28]. They are not demonstrative for a long time. Main symptoms are cough, hoarse voice, wheezing, dyspnea, frequent lung infections and chest pain. The most common cause for death is restrictive respiratory failure and asphyxia due to cartilage tissue distruction in the larynx and tracheobronchial tree [28].

PR can also affect organs that do not contain cartilage tissue. Ocular changes occur in 20% to 60% of patients with PR [2, 7, 18, 29]. Usually conjunctivitis, episcleritis, scleritis, uveitis, iritis, chorioretinitis or dry keratoconjunctivitis and keratitis are seen. A severe, though rare, complication is the development of blindness, which is due to an acute and destructive form of keratitis or iritis [29].

The skin is affected in about 40% of patients [2, 7, 30]. They are nonspecific and sometimes resemble those observed in Behçet disease or inflammatory bowel diseases. Their presence in the elderly warrants repeated blood cell counts to detect a smouldering myelodysplasia. Oral and complex aphthosis, nodules on the limbs, purpura, papules, sterile pustules, superficial phlebitis, livedo reticularis, ulcerations on the limbs, and distal necrosis can also be detected.

The cardiovascular system is damaged in about 30% of patients [2, 7, 18, 31]. The heart valves with manifestations of both stenosis and insufficiency are affected. Damage to the elastic fibers of the aorta can lead to an aneurysm and a rare but fatal rupture [32].

Neurological manifestations occur in less than 3% of cases [33]. Dizziness, confusion, headache, cranial nerve involvement, seizures, cerebral dysfunction with ataxia, cerebral aneurysms, ischaemic encephalopathy, aseptic meningitis, stroke and rarely encephalitis have been described. Inner ear involvement can cause tinnitus, dizziness, and hearing problems [7, 34]. Irreversible nature and significant frequency indicates complete hearing loss, due to cochlear/vestibular destruction or neurosensory impairment [7]. Studies have found that dementia and mental changes associated with PR are reversible with treatment [35]. Rarely, renal arteries are affected or renal failure develops [36].

Usually, PR proceeds benignly, but frequent relapses worsen the quality of life [1, 2, 5, 9]. About one third of patients experience fatal outcome. Mortalityrate is twice higher than in the general population [1, 2, 6, 8-10, 12]. The main causes are respiratory failure and asphyxia, aneurysm rupor, systemic vasculitis, renal failure and infections [28, 32, 36]. A 2016 study of 256 Hungarian patients recorded higher 5- and 10-year survivals, 88% and 81%, respectively, compared with 74% and 55%, respectively, in 1986 [13]. R. Chopra et al. found an increase in survival from 70% at five years to 91% at ten years [14]. This is probably due to the greater awareness of doctors, better imaging capabilities and the application of immunosuppressive drugs and biological products.

The diagnosis is clinical. Anemia, leukocytosis, proteinuria and elevated acute proteins are commonly detected on routine laboratory tests [11]. Type II collagen antibodies are considered more specific [19-21]. They are found in 50% of patients. It is assumed that they play a role in the release of local lysosomal enzymes, executing highly destructive nature. ANA and LE cells are also detected.[20, 37, 38]. Higher urine excretion of mucopolysaccharides is found to be related to the degree of cartilage damage [39]. Increased circulating immune complexes [20, 38], serum cryoglobulins [40], positive rheumatoid factor [18, 40], Wasserman's false-positive reaction [18], and hypocomplementemia in serum or inflammatory fluid from the ear are also in positive correlation with the degree of inflammation [38]. The role of cellular immune response is suggested by the positivity of the blasttransformation test in response to cartilage antigen during relapses [41].

The histological findings show basophilia of the cartilage matrix, focal decay of cartilage tissue, and lymphocyte infiltrate in the perichondria in the acute stage of the disease, while the old lesions present with chondrocyte apoptosis, focal calcification and cartilage fibrosis [2, 10, 18, 19, 39]. The inflammatory infiltrate composes primarily of CD4+ T cells, macrophages and plasma cells are found [18]. A deposit of IgG and fibrinogen is found in the basal membrane area on immunofluorescent studies [39].

PR diagnosis is aided by imaging studies. Radiographically, non-erosive juxta-articular osteopenia and uniform narrowing of the joint space were observed [6, 27]. A dynamic computed tomography scan is recommended to assess airway involvement. Functional abnormalities, thickening of the airway wall and narrowing of the lumen are detected [2, 5, 28]. The study of lung function is carried out to further assess the state of the respiratory tract and to assess lung volumes [10, 11]. 18 F-fluorodeoxyglucose positron emission tomography (18F-FDG-PET/CT) supports early recognition of the disease and is particularly useful in patients without typical clinical manifestations [43].

The diagnosis of RP is based on a combination of clinical features, radiographic findings, and cartilage biopsy. The diagnostic criteria are mainly clinical. Histology is often confirming. The first diagnostic criteria were proposed by L. P. McAdam et al. based on the monitoring of 159 patients [7]. They are guided by a set of clinical criteria. The diagnosis is

made in the presence of three out of six criteria and includes:

1. Recurrent chondritis of both earlobes;
2. Non-erosive inflammatory arthritis;
3. Chondritis of nasal cartilage;
4. Inflammation of the eye structures, manifested as conjunctivitis, keratitis, scleritis or uveitis;
5. Chondritis of the respiratory tract with involvement of laryngeal or tracheal cartilage;
6. Cochlear or vestibular damage manifested by sensorineural hearing loss, tinnitus or dizziness.

Later J. M. Damiani and H. L. Leveni [42] and C. J. Michet et al. [8] modify these criteria (Table 1). Although similar, the criteria of J. M. Damiani and H. L. Leveni have the greatest sensitivity.

Table 1. *Diagnostic criteria for polychondritis recidivans.*

McAdams et al. criteria	Damiani and Leveni criteria	Michet et al. criteria
3 of 6 of the following: 1) Recurrent chondritis of both earlobes 2) Chondritis of the respiratory tract 3) Cochlear and/or vestibular damage 4) Chondritis of nasal cartilage 5) Inflammation of eye structures 6) Non-erosive inflammatory arthritis	3 of 6 McAdams et al. criteria OR 2 of 6 McAdams et al. criteria + response to corticosteroids or dapsone OR 1 of 6 McAdams criteria + histological characteristics	Inflammation in 2 of 3 following: 1) Ear 2) Nasal 3) Laryngotracheal OR 1 of the above and 2 of the following: 1) Ocular inflammation 2) Hearing loss 3) Vestibular dysfunction 4) Seronegative inflammatory arthritis

Various subsets of PR have also been proposed. M. A. Ferrada et al. [44] propose three groups of dependence on the localization of cartilage damage: cartilage damage to the ears, nose and respiratory tract (Type 1); predominant damage to the lower respiratory tract (Type 2) and absence of obvious cartilage damage (Type 3). J. Dion et al. [45] identified three other groups - haematological, respiratory and mild. J. Shimizu et al. [46] divided patients with PR into three subgroups: patients with respiratory involvement (R subgroup); patients with auricular involvement (A subgroup) and overlapping patients with both participations (O subgroup), each group having distinctive clinical features. The usefulness of these categorizations is considered to be limited in undiagnosed PR.

A relatively new indicator is the recurrent polychondritis activity index (RPDAI) [47]. It is intended to assess disease activity and to follow the outcome of treatment [37]. 27 clinical signs and laboratory parameters reported over a period of 28 days, each ranging from 1 to 24 are considered. Theoretically, the maximum RPDAI is 265.

PR has a complicted differential diagnosis. Recurrent erysipelas affects the same area without alternation and responds to antibiotic treatment [30]. Otitis, Meniere's syndrome, vasculitis, gout, granuloma annulare, and trauma or secondary chondritis after use of thiouracil can also mimick PR [2-8]. Damage to the nose can occur with drug abuse (cocaine), following infections (micotic, tuberculosis, syphilis) and granulomatous conditions (ANCA-associated vasculitis and limphomatoid granulomatosis) [9-11]. Joint and eye involvement in PR should also be differentiated from rheumatoid arthritis, ANCA-related vasculitis, nodosis polyarteritis, Kogan's syndrome (an autoimmune disease primarily with inflammation of the eyes and ears), Behche's syndrome or MAGIC syndrome [29, 48].

In patients with auricular, nasal or joint involvement, without systemic manifestations, treatment is carried out with nonsteroidal anti-inflammatory drugs, colchicine or dapsone [49, 50].

Glucocorticoids are the gold standard for the treatment of PR [1, 2, 5, 10, 11]. The initial dose is 40-60 mg daily, and the maintenance dose is 8-16 mg. In patients with more severe manifestations, such as involvement of the major airways, laryngeal or tracheobronchial chondritis, sudden onset of sensorineural hearing loss or eye involvement, intravenous methylprednisolone 1 g for three days is indicated, followed by oral prednisone 1 mg/kg, combined with immunosuppressors. The latter are also applied to patients refractory to glucocorticoid therapy or when a glucocorticoid-sparing effect is needed [2, 10, 51, 52]. Cyclophosphamide, methotrexate, azathioprine and ciclosporin are most often used.

Biological therapy is considered on refractory and severe cases [51-53]. TNFα inhibitors are most commonly used. Infliximab and adalimumab are preferred due to their rapid onset and higher retention rate. Abatacept and tocilizumab are second-line biological agents. The first is applied to refractory chondritis and joint symptoms, but there is a high risk of infections. The second is effective for almost all manifestations of PR, but especially in patients with refractory aortitis. Data on anakinra and rituximab are conflicting. The use of JAK inhibitors is still uncertain.

Surgical reconstructive treatment is applied in patients with nasal cartilage damage [2, 54]. Tracheobronchial and laryngeal chondritis, airway dilation, tracheostomy, tracheobronchial stenting and laryngotracheal reconstruction are need in all cases with severe respiratory obstruction [6, 8, 28, 55]. In an aortic aneurysm, a stent is implanted, and in case of damage to the heart valve, replacement is needed [31, 31, 56].

4. Conclusion

PR proceeds with recurrent inflammation of both cartilage tissue, mainly the ears, nose, larynx, tracheobronchial tree, ribs and joints, as well as the proteoglycan-rich tissues of the heart valves, blood vessels and eyes. There is multisystemic

involvement and risk of acute, life-threatening or permanent complications. The frequency and severity of relapses are unpredictable. PR diagnosis is challenging both due to the unspecific clinical symptoms and overlaps with associated autoimmune diseases. Good knowledge of the disease is needed by otorhinolaryngologists, rheumatologists, pulmonologist, cardiologists, ophthalmologists, infectionists, dermatologists and other specialists, both for diagnosis and adequate treatment/control, as well as for readiness to prevent complications.

Conflicts of Interest

Authors have no conflicts of interest to declare.

References

[1] Sharma A, Law AD, Bambery P, et al. Relapsing polychondritis: clinical presentations, disease activity and outcomes. Orphanet J Rare Dis. Dec 20, 2014; 9: 198.

[2] Chauhan K, Surmachevska N, Hanna A. Relapsing Polychondritis. [Update: July 4, 2023]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan. 2023 Jul 4.

[3] Jaksch-Wartenhorst R von. Polychondropathia. Wien Arch Inn Med. 1923; 6: 93-100.

[4] Pearson CM, Kline HM, Newcomer VD. Relapsing Polychondritis. N Engl J Med. 1960; 263: 51-58.

[5] Borgia F, Giuffrida R, Guarneri F, et al. Relapsing polychondritis: an updated review. Biomedicines. 2018; 6(3): 84. doi: 10.3390/biomedicines6030084.

[6] Chen N, Zheng Y. Characteristics and clinical outcomes of 295 patients with relapsing polychondritis. J Rheumatol. 2021; 48(12): 1876–1882.

[7] McAdam LP, O'Hanlan MA, BluestoI1e R, et al. Relapsing polychondritis: prospective study of 23 patients and a review of the literature Medicine (Baltimore). 1976; 55(3): 193-215.

[8] Michet CJ Jr, Mckenna CH, Luthra HS, et al. Relapsing polychondritis: survival and predictive role of early disease manifestations. Ann Intern Med. 1986; 104(1): 74–78.

[9] Longo L, Greco A, Rea A, et al. Relapsing polychondritis: A clinical update. Autoimmun Rev. 2016; 15(6): 539–543.

[10] Vitale A, Sota J, Rigante D, et al. Relapsing polychondritis: an update on pathogenesis, clinical features, diagnostic tools, and therapeutic perspectives. Curr Rheumatol Rep. 2016; 18(1): 3. doi: 10.1007/s11926-015-0549-5.

[11] Rednic S, Damian L, Talarico R, et al. Relapsing polychondritis: state of the art on clinical practice guidelines. RMD Open. 2018; 4 (Suppl 1): e000788. doi: 10.1136/rmdop.

[12] Hazra N, Dregan A, Charlton J, et al. Incidence and mortality of relapsing polychondritis in the UK: a population-based cohort study. Rheumatol. 2015; 54(12): 2181–2187.

[13] Horváth A, Páll N, Molnár K, et al. A nationwide study of the epidemiology of relapsing polychondritis. Clin. Epidemiol. 2016; 8: 211–230.

[14] Chopra R, Chaudhary N, Kay J. Relapsing polychondritis. Rheum Dis Clin North Am. 2013; 39(2): 263–276.

[15] Belot A, Duquesne A, Job-Deslandre C, et al. Pediatric-onset relapsing polychondritis: case series and systematic review. J Pediatr. 2010; 156(3): 484–489.

[16] Papo T, Wechsler B, Bletry O, et al. Pregnancy in relapsing polychondritis: Twenty-five pregnancies in eleven patients. Arthritis Rheum. 1997; 40(7): 1245–1249.

[17] Ludvigsson JF, van Vollenhoven R. Prevalence and comorbidity of relapsing polychondritis. Clin Epidemiol. 2016; 8: 361–362.

[18] Gange RW. Relapsing polychondritis. Report of two cases with an immunopathological review. Clin Exp Dermatol. 1976; 1(3): 261-268.

[19] Halber S, Kastor D, Saldeld K. Polychondritis chronica atrophicans. Z Hautkr. 1984; 59(17): 1147-1159.

[20] Foidart JM, Abe S, Martin GR, et al. Antibodies to type II collagen in relapsing polychondritis. N Engl J Med. 1978; 299(22): 1203–1207.

[21] Buckner JH, Wu JJ, Reife RA, et al. Autoreactivity against matrilin-1 in a patient with relapsing polychondritis. Arthritis Rheum. 2000; 43(4): 939–943.

[22] Hu FY, Wang J, Zhang SX, et al. Absolute reduction of peripheral regulatory T cell in patients with relapsing polychondritis, Clin Exper Rheumatol. 2021; 39(3): 487–493.

[23] Stabler T, Piette J-C, Chevalier X, et al. Serum cytokine profiles in relapsing polychondritis suggest monocyte/macrophage activation. Arthr Rheum. 2004; 50(11): 3663–3667.

[24] Arnaud L, Mathian A, Haroche J, et al. Pathogenesis of relapsing polychondritis: A 2013 update. Autoimmun Rev. 2014; 13(2): 90–95.

[25] Yoshida T, Yoshifuji H, Shirakashi M, et al. Risk factors for the recurrence of relapsing polychondritis. Arth Res Ther. 2022; 24(1): 127-130.

[26] Lang B, Rothenfusser A, Lanchbury JS, et al. Susceptibility to relapsing polychondritis is associated with HLA-DR4. Arthritis Rheum. 1993; 36(5): 660–664.

[27] Kingdon J, Roscamp J, Sangle S, et al. Relapsing polychondritis: a clinical review for rheumatologists. Rheumatology. 2017; 57(9): 1525–1532.

[28] Eng J, Sabanathan S. Airway complications in relapsing polychondritis. Ann Thor Surg. 1991; 51(4): 686–692.

[29] Fukuda K, Mizobuchi T, Nakajima I, et al. Ocular involvement in relapsing polychondritis. J Clin Med. 2021; 10(21): 4970.

[30] Francès C, El Rassi R, Laporte JL, et al. Dermatologic manifestations of relapsing polychondritis. A study of 200 cases at a single center. Med (Baltim). 2001; 80(3): 173–179. doi: 10.1097/00005792-200105000-00003.

[31] Lang-Lazdunski L, Hvass U, Paillole C, Pansard Y, Langlois J. Cardiac valve replacement in relapsing polychondritis. A review. J Heart Valve Dis. 1995; 4(3): 227–235.

[32] Selim AG, Fulford LG, Mohiaddin RH, Sheppard MN. Active aortitis in relapsing polychondritis. J Clin Pathol. 2001; 54(11): 890–892.

[33] Requena MA, Palma DA, Popescu BM. Neurologic involvement in relapsing polychondritis. Medicina (B Aires). 2007; 67(2): 156–158.

[34] Kumakiri K, Sakamoto T, Karahashi, T, et al. A case of relapsing polychondritis preceded by inner ear involvement, Auris Nasus Larynx. 2005; 32(1): 71–76.

[35] Swen SJ, Leonards DJ, Swen WA, et al. Reversible cognitive decline in a patient with relapsing polychondritis. Tijdschr Gerontol Geriatr. 2009; 40(5): 203–207.

[36] Chang-Miller A, Okamura M, Torres VE et al. Renal involvement in relapsing polychondritis. Med (Baltim). 1987; 66(3): 202–217.

[37] Piette J-C, El-Rassi R, Amoura Z. Antinuclear antibodies in relapsing polychondritis. Ann Rheum Dis. 1999; 58(10): 656–657.

[38] Smal P, Frankiel S. Relapsing polychondritis. A feature of systemic lupus erythematosus. Arthritis Rheum. 1980; 23(3): 361-363.

[39] Krishnan Y, Grodzinsky AJ. Cartilage diseases. Matrix Biol. 2018 Oct; 71-72: 51-69.

[40] Sidi Y, Weinberger A, Berliner Sh, et al. Relapsing polychondritis associated with mixed cryoglobulinemia. Dermatologica. 1982; 165(1): 66-70.

[41] Herman JH, Dennis MV. Relapsing polychondritis. J Clin Invest. 1973; 52(3): 549-558.

[42] Damiani JM, Levine HL. Relapsing polychondritis–report of ten cases. Laryngoscope. 1979; 89 (6 Pt 1): 929–946.

[43] Okuda S, Hirooka Y, Itami T, et al. FDG-PET/CT and auricular cartilage biopsy are useful for diagnosing with relapsing polychondritis in patients without auricular symptoms. Life. 2021; 11(9): 956.

[44] Ferrada M, Rimland CA, Quinn K, et al. Defining clinical subgroups in relapsing polychondritis: a prospective observational cohort study. Arthritis Rheumatol. 2020; 72(8): 1396–1402.

[45] Dion J, Costedoat-Chalumeau N, Sène D, et al. Relapsing polychondritis can be characterized by three different clinical phenotypes: analysis of a recent series of 142 patients. Arth Rheumatol. 2016; 68(12): 2992–3001.

[46] Shimizu J, Yamano Y, Kawahata K, et al. Relapsing polychondritis patients were divided into three subgroups: patients with respiratory involvement (R subgroup), patients with auricular involvement (A subgroup), and overlapping patients with both involvements (O subgroup), and each group had distinctive clinical characteristics. Medicine. 2018; 97(42): E12837. doi: 10.1097/md.0000000000012837.

[47] Arnaud L, Devilliers H, Peng SL, et al. The Relapsing Polychondritis Disease Activity Index: Development of a disease activity score for relapsing polychondritis. Autoimm Rev. 2012; 12(2): 204–209.

[48] Firestein GS, Gruber HE, Weisman MH et al. Mouth and genital ulcers with inflamed cartilage: MAGIC syndrome. Am J Med. 1985; 79: 69-72.

[49] Mark KA, Franks AG. Colchicine and indomethacin for the treatment of relapsing polychondritis. J Am Acad Dermatol. 2002; 46: S22-4.

[50] Barranco VP, Minor DB, Solonom H. Treatment of polychondritis with dapsone. Arch DermatoI. 1976; 112: 1286-1288.

[51] Petitdemange A, Sztejkowski C, Damian L, et al. Treatment of relapsing polychondritis: a systematic review. Clin Exp Rheumatol. 2022; 40 Suppl 134(5): 81-85.

[52] Lekpa FK, Chevalier X. Refractory relapsing polychondritis: challenges and solutions. Open Access Rheumatol. 2018; 10: 1–11.

[53] Padoan R, Campaniello D, Iorio L, et al. Biologic therapy in relapsing polychondritis: navigating between options. Expert Opin Biol Ther. 2022; 22(5): 661-671.

[54] Shah R, Alford EL. Reconstructive rhinoplasty using cadaver cartilage in relapsing polychondritis. Proc (Bayl Univ Med Cent). 2022; 36(1): 130-131.

[55] Handa H, Ooka S, Shimizu J, et al. Evaluation of airway involvement and treatment in patients with relapsing polychondritis. Sci Rep. 2023; 13(1): 8307. doi: 10.1038/s41598-023-35616-4.

[56] Dib C, Moustafa SE, Mookadam M, et al. Surgical treatment of the cardiac manifestations of relapsing polychondritis: overview of 33 patients identified through literature review and the Mayo Clinic records. Mayo Clinic Proc. 2006; 81: 772–776. doi: 10.4065/81.6.772.