CLINICAL OBSERVATIONS

Relapsing polychondritis that developed after piercing (clinical case)

Movsesyan A.A.[1], Krasnenko S.O.[1], Urumova M.M.[1], Godzenko A.A.[1,2]

[1]V.A. Nasonova Research Institute of Rheumatology, Moscow; [2]Department of Rheumatology Russian Medical Academy of Continuing Professional Education, Ministry of Health of Russia, Moscow

[1]34A, Kashirskoe Shosse, Moscow 115522, Russia; [2]2/1, Barrikadnaya Street, Build. 1, Moscow 125993, Russia

Relapsing polychondritis (RPC) belongs to a group of rare rheumatic diseases with poorly understood etiology and pathogenesis. It is based on progressive systemic inflammatory damage to the cartilage tissue, primarily affecting ears, nose, trachea and bronchi. A standardized approach for the treatment of RPC has not yet been developed, so the treatment tactics are individualized for each patient.

We describe a clinical case of a 39-year-old patient, who developed RPC after piercing the cartilaginous part of the ear. The components of the alloy used for the piercing could presumably serve as adjuvants and cause the development of a disease similar to ASIA syndrome (Autoimmune/Inflammatory Syndrome Induced by Adjuvants) with inflammation of the cartilage of the nose and ears. Possible pathogenetic mechanisms are presented, as well as diagnostic criteria for ASIA syndrome.

Keywords: *relapsing polychondritis; adjuvants; ASIA syndrome.*

Contact: *Anastasia Armenovna Movsesyan;* ***an.ar.mov@mail.ru***

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Relapsing polychondritis (RPC) is an immune-mediated systemic disease characterized by recurrent episodes of inflammation of cartilaginous and proteoglycan-rich tissues, leading to progressive anatomical deformation and dysfunction of the affected structures [1]. The origin of the disease, provoking factors, pathogenetic mechanisms remain unspecified and continue to be discussed, although 100 years have passed since the first case was described by R. Jaksch-Wartenhorst in 1923 [2].

Data from genetic studies have demonstrated the association of the histocompatibility antigen HLA-DR4 with the risk of developing RPC [1, 3, 4].

However, no convincing evidence of inheritance of the disease has been obtained. Components of both humoral and cellular immunity are involved in the development of the pathological process. In patients with RPC, circulating autoantibodies to collagen types II, IX and XI were detected, which suggested a leading role of autoimmunity to one's own cartilage tissue in the pathogenesis of the disease [5].

Other autoantigen targets include cartilage oligomeric matrix proteins (COMP), contained in the extracellular matrix of cartilage, ligaments and tendons, and matrilin 1 - an extracellular matrix protein highly expressed in the cartilage tissue of the trachea, nose, ears and sternocostal joint [6].

Histopathological examination of the affected tissues has shown that the inflammatory infiltrate, represented by T lymphocytes (mainly CD4+ T-cells), macrophages, and plasma cells, covers the perichondral zone and then spreads deep into the cartilage. As the disease progresses, high expression of proteolytic enzymes – cathepsins, elastases, matrix metalloproteinases – is detected in perichondral cells and chondrocytes, which, along with perichondral inflammation, contribute to the destruction of cartilage [7, 8].

The initiating phase of the pathological process leading to the destruction of cartilage tissue is described mainly in the form of hypotheses. According to some authors, various triggers (infectious agents, mechanical or chemical influences) can cause protein degradation with subsequent release of cartilage tissue antigens, which in genetically predisposed individuals leads to immunization against these autoantigens [9].

The most common and early clinical manifestation of RPC is bilateral auricular chondritis, which is observed in 90% of patients [10]. The course of the disease is undulating, with alternating exacerbations and remissions, as a result of which the cartilaginous matrix is gradually replaced by fibrous connective tissue, the ear becomes nodular and flabby due to the loss of cartilaginous support and can take on the appearance of a "cauliflower". Destruction of the cartilage, as well as swelling of the external auditory canal, contribute to the development of otitis media and hearing loss. Vestibular disorders and sensorineural hearing loss occur in approximately 6–13% of patients and may be caused by vasculitis of the branches of the internal auditory artery [11, 12].

The second most common symptom is nasal chondritis, which develops in more than a half of patients [8]. The inflammatory process, manifested by pain and redness, affects the bridge of the nose, which leads to its flattening and ultimately to a saddle-shaped deformation of the nose.

Damage to the laryngo-tracheobronchial region is a harbinger of a poor prognosis and the main cause of mortality. Chondritis of the larynx can manifest as pain in the area of the thyroid cartilage and trachea, with subsequent laryngomalacia or persistent laryngeal stenosis accompanied by hoarseness, unproductive cough, shortness of breath, stridorous breathing. Inflammation of the trachea is characterized by thickening of the walls with destruction of cartilaginous rings, tracheomalacia with subsequent collapse of the airways, as well as the development of fibrosis and strictures [13, 14].

In addition to chondritis, common clinical manifestations of RPC include arthritis, usually non-erosive, and eye damage in the

form of conjunctivitis, episcleritis, scleritis, and uveitis. Cardiovascular disorders (valvulitis, aortic dilatation with aortic regurgitation, aortic aneurysms), polymorphic skin changes, and neurological disorders are less commonly observed [15–17].

An important feature of RPC is its frequent combination with other diseases, including various immunoinflammatory rheumatic diseases, myelodysplastic syndrome, and solid tumors. Such a variety of clinical overlaps, as well as the polymorphic clinical picture and rarity of the disease, make the diagnosis difficult. Several variants of diagnostic criteria for RPC have been proposed, among which the McAdam criteria of 1976 [18] prioritizing characteristic clinical signs are most often used.

According to these criteria, the diagnosis is considered reliable if 3 of the following 6 signs are present:

- bilateral auricular chondritis;
- nonerosive seronegative inflammatory arthritis;
- nasal chondritis;
- eye inflammation (conjunctivitis, keratitis, scleritis, episcleritis, uveitis);
- chondritis of the respiratory tract (cartilages of the larynx and/or trachea);
- cochlear and/or vestibular disorders (sensorineural hearing loss, tinnitus, dizziness).

If the number of clinical criteria is insufficient, histological confirmation is required. It reveals lymphoid and plasma cell infiltration of the cartilage matrix with areas of metachromasia, degeneration of chondrocytes, penetration of active fibroblasts inside the cartilage, fiber disintegration, lysis and sequestration of the cartilage matrix [18, 19].

RPC must be distinguished from infectious perichondritis, which can develop in all structures that have cartilage: bilateral damage to the auricles, involvement of cartilages of different localizations with the development of systemic inflammation, and an undulatory progressive course should be taken into account [8].

Due to the rarity and variety of variants of the course of the disease, there is no unified approach to treatment; treatment tactics for each patient are individual and determined by the severity of clinical manifestations and the involvement of vital organs. In most cases, glucocorticoids are prescribed as monotherapy or in combination with synthetic basic anti-inflammatory drugs. Data on the effectiveness of genetically engineered biological drugs are contradictory [20–22].

Publications devoted to RPC, in most cases, represent clinical observations, the number of which has been growing in recent years. Thus, the Pubmed database for 2022 contains 44, and for the first half of 2023 – 38 articles describing similar clinical cases. However, many questions still remain regarding the etiology of the disease; cases that developed after injury, infection, medical and cosmetic interventions were presented.

We present a medical history of a patient whose disease began 2 weeks after ear piercing (the patient consented to the publication of her data).

Clinical case

Patient K., *female, 39 years old, was admitted to the Federal State Budgetary Institution "Research Institute of Rheumatology named after. V.A. Nasonova" (NIIR named after V.A. Nasonova) with complaints of pain and redness of her ears, slight deformation of the back of her nose, increased fatigue, periodic increases in temperature up to 37.2 °C.*

There is a history of rheumatic diseases in the patient's family: her father has familial Mediterranean fever, her mother has psoriatic arthritis.

Over the past 5 years, the patient has repeatedly undergone invasive cosmetic procedures, including mesotherapy, biorevitalization, botulinum therapy, tattooing of eyebrows, eyelids, and lips. In August 2019, the cartilaginous part of the right auricle was pierced with the implantation of a steel earring, the exact composition of the alloy of which is unknown.

Two weeks after the piercing, pain, hyperemia and swelling of the right auricle appeared. Until March 2020, attempts had been made to independently reduce the inflammatory process with antiseptic solutions and ointments. Then the earring was removed, but the symptoms continued to increase. An otorhinolaryngologist diagnosed chondroperichondritis and prescribed therapy with penicillin antibiotics, which had no effect. Over the next 2 years, she was consulted by several otorhinolaryngologists, and repeated courses of treatment with antibacterial drugs of different groups were carried out. Topical betamethasone was administered by an oral and maxillofacial surgeon in February 2022 with short-term positive results.

In September 2022, the left auricle became involved in the pathological process: hyperemia, swelling, pain. During the examination in October 2022, an increase in ESR to 22 mm/h and CRP level to 9.3 mg/L was noted. The analysis of other indicators, including antinuclear factor (ANF), rheumatoid factor, antineutrophil cytoplasmic antibodies, immunoblot of antinuclear antibodies, did not reveal any deviations. A rheumatologist diagnosed RPC and recommended colchicine at a dose of 1 mg/day and non-steroidal anti-inflammatory drugs, which the patient received with short-term minor improvement. In December 2022, the patient noted a mild deformation ("sink") of the nasal dorsum.

In January 2023 the patient was hospitalized to the Research Institute named after. V.A. Nasonova. Hyperemia, swelling, deformation, pain on palpation of both ears were noted (Fig. 1, a, Fig. 2, a), as well as a moderate saddle-shaped deformation of the nose. No other abnormalities were detected during physical examination, including pathologies of the respiratory, cardiovascular, digestive, and nervous systems.

Complete blood count, biochemical and immunological blood tests, general urine test were without significant abnormalities: ESR according to Westergren - 20 mm/h, CRP – 2.3 mg/L, antibodies to myeloperoxidase – 0.5 U/ml, antibodies to proteinase 3 – 2.2 U/ml, ANF – 1/160 (granular, cytoplasmic types of luminescence); antibodies to cyclic citrullinated peptide, to Ro/SSA and La/SSB were not detected.

Computed tomography (CT) visualized parietal thickening of the mucous membrane of both maxillary sinuses and signs of rhinitis; calcification in the cavity of the left maxillary sinus; deviated nasal septum, a bulla of the left middle turbinate. A CT scan of the chest did not reveal any pathological changes. The endoscopic examination of the larynx revealed no pathology. An ophthalmologist diagnosed dry keratoconjunctivitis, grade 3 epithelial corneal dystrophy on the right. At the same time, the patient had no eye complaints, and there was no dryness of the mouth.

Diagnosis: RPC with damage to the ears (bilateral chondritis), nose (chondritis of the nasal dorsum, rhinosinusitis), eyes (keratoconjunctivitis sicca). The patient was administered an intravenous drip of methylprednisolone at a dose of 500 mg, and also prescribed oral methylprednisolone 8 mg/day and methotrexate 15 mg/week. As a result of treatment, an improvement in the condition was achieved: swelling, hyperemia and soreness of the ears decreased

(Fig. 1, b, Fig. 2, b), the body temperature did not increase.

Discussion. A peculiarity of the described case is the development of RPC after a trivial cosmetic procedure. The components of the alloy used for piercing could serve as adjuvants and provoke the disease. Of course, there is no clear evidence of a cause-and-effect relationship between earring implantation and the appearance of clinical symptoms of chondritis, nor is there data on the presence of specific antibodies to the putative adjuvants. However, the existence of a connection between the events is supported by the short period of time between them (2 weeks), as well as the primary localization of inflammation at the piercing site. Predisposing factors can be the family history of the patient, whose parents suffer from rheumatic diseases, and the previous use of cosmetic techniques with the implantation of various materials.

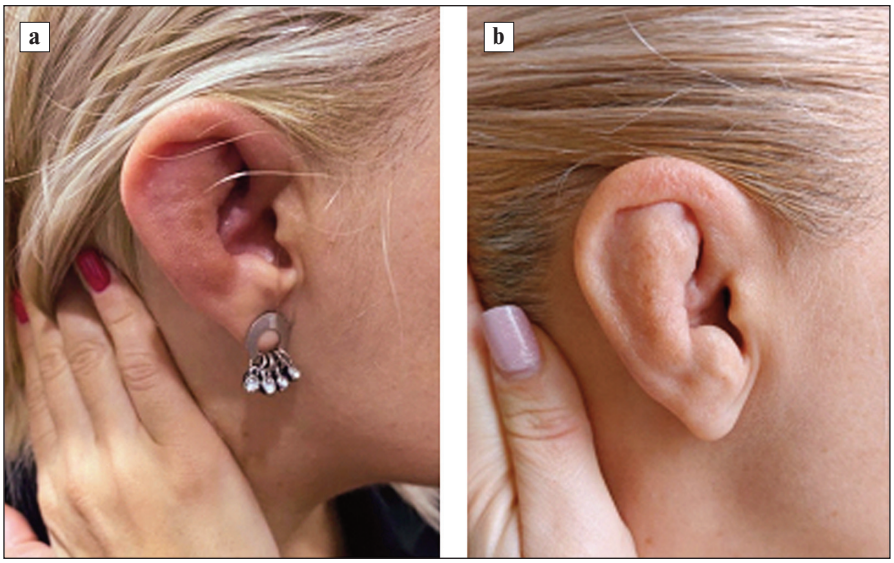

Fig. 1. *Right auricle of patient K. before hospitalization (a) and on discharge (b)*

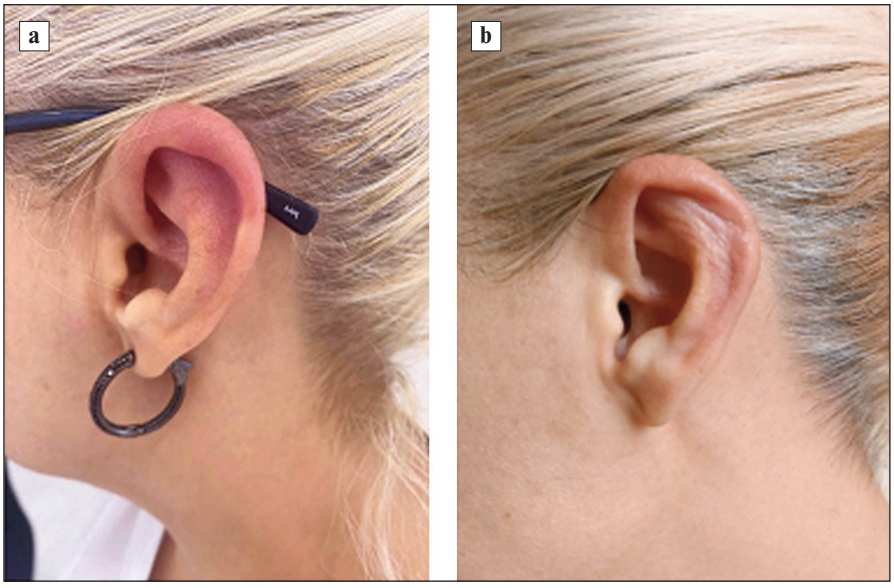

Fig. 2. *Left auricle of patient K. on admission (a) and on discharge (b)*

Publications devoted to pathological conditions provoked by adjuvants began to appear in the medical literature quite a long time ago. In 1914, induced scleroderma in miners due to exposure to silicon was first described [23]. Subsequently, cases of induced scleroderma were reported after exposure to certain organic solvents, drugs, foods and other substances that are immunological adjuvants that can nonspecifically alter the human immune response [23, 24].

Later, the term "adjuvant human disease" was proposed, most often used in plastic surgery in connection with the development of scleroderma-like syndromes after the introduction of silicone breast implants [25].

The development of plastic surgery and cosmetic techniques has led to another rise in interest in such diseases. Evidence of the importance of the problem of adjuvant autoimmune diseases was their integration under the term "ASIA syndrome" (Autoimmune/Inflammatory Syndrome Induced by Adjuvants –autoimmune/inflammatory syndrome induced by adjuvants). This syndrome was first described in 2011 by Y. Shoenfeld and N. Agmon-Levin [26] due to the need to bring together a number of pathological conditions with a common development mechanism caused by various adjuvants. Diagnosis of ASIA syndrome is based on major and minor criteria formulated by these authors [26] (see Table). To confirm the diagnosis, 2 major or 1 major and 2 minor criteria are required.

Currently, ASIA syndrome is defined as a prenosological condition, which, with continued stimulation of the immune system, can transform into an autoimmune disease, depending on the individual characteristics of the patient [27].

The pathogenesis of this syndrome has not been sufficiently studied. It is believed that the adjuvant effect is achieved through several mechanisms that affect both the innate and adaptive immune systems [28–30]. Firstly, adjuvants promote the deposition of the antigens with which they are associated at the site of implantation, translocation of the antigens into local and distant lymphoid tissue and the prolonged synthesis of antibodies. Long-term exposure to antigens and adjuvants leads to activation of B- and T-cell immune responses [31]. Some adjuvants directly stimulate the production of proinflammatory factors: cytokines and chemokines, which support the chronic inflammatory response, and also induce a humoral immune response by stimulating Th2 lymphocytes. Adjuvants enhance the innate immune response by mimicking evolutionarily conserved molecules (eg, bacterial cell walls, lipopolysaccharides) and binding to Toll-like receptors. In addition, they enhance the activity of dendritic cells, lymphocytes, macrophages and activate intracellular inflammasome complexes; they can directly activate the major histocompatibility complex [13]. Thus, in addition to the local immune response, adjuvants

Table. ASIA syndrome criteria [26]

Major Criteria	Minor Criteria:
External factors (infection, vaccination, silicone) preceding clinical symptoms	The appearance of autoantibodies or antibodies to a presumptive adjuvant
Typical clinical manifestations (myalgia, myositis and muscle weakness, arthralgia or arthritis, chronic fatigue syndrome, neurological disorders, mainly associated with demyelination of nerve fibers, impaired intelligence and memory, fever, dry mouth, dry eyes)	Other clinical manifestations (irritable bowel syndrome, Raynaud's phenomenon)
Elimination of the damaging factor leads to remission	Presence of HLA-DRB1, HLA-DQB1
Typical histological changes in organs	Signs of an autoimmune disease (SLE, RA, SSc, vasculitis, etc.)

Note. SLE – systemic lupus erythematosus; RA – rheumatoid arthritis; SSc – systemic scleroderma.

promote the generalization of the immune response to the development of systemic disease [28, 32–34].

Along with plastic surgery, ASIA syndrome is also described in cosmetology (contour plastic surgery with fillers), dentistry (installation of dental implants), and immunology (vaccination). Often cases of ASIA syndrome mimic various rheumatic diseases: RA, Sjogren's disease, SLE, systemic vasculitis.

In recent years, there have been a number of reports of ASIA cases provoked by previously unknown adjuvants, in particular the Essure hysteroscopic intrauterine sterilization system [35]. The Essure device is a small flexible insert with an internal stainless steel coil wrapped in polyethylene terephthalate fibers and an outer nickel- titanium alloy coil to secure the device. It turned out that all components of Essure have adjuvant activity, and surgical removal of the device leads to a noticeable regression of ASIA symptoms [36].

Also interesting are reports of the development of adjuvant syndromes after vaccination against the new coronavirus infection COVID-19. The first such case of immunothrombosis with thrombocytopenia after use of the AstraZeneka vaccine was described in 2021 [37]. By 2022, there had been more than 270 reports of various autoimmune diseases that developed within 28 days after vaccination against COVID-19, including cutaneous and systemic vasculitis, lupus-like syndrome, RA, IgA nephropathy, etc. [38].

Adjuvant syndromes after piercing have not been previously described, although these technologies have been known since antiquity. The so-called medical steel commonly used for piercing contains nickel, which is not an inert metal. Prolonged contact of such an alloy with the tissues of the human body leads to nickel oxidation, which can cause various inflammatory and allergic reactions.

In the presented case, there was a clear chronological connection with the introduction of an external substance into the cartilage tissue and a number of clinical manifestations of an immunoinflammatory disease, which presumably suggests the impact of the alloy components. It should be noted that our patient's symptoms continued to progress after the removal of the piercing. Literature data indicate that the course of the disease after removal of the adjuvant depends on various factors: its properties, duration of the exposure, and the patient's condition [36].

Conclusion. This observation is of interest as the first described case of RPC that developed after piercing. The use of invasive cosmetic techniques, including routine ones, can provoke the development of a systemic inflammatory disease in predisposed individuals.

REFERENCES

1. Borgia F, Giuffrida R, Guarneri F, Cannavo SP. Relapsing Polychondritis: An Updated Review. *Biomedicines*. 2018 Aug 2; 6(3):84. doi: 10.3390/biomedicines6030084.
2. Jaksch-Wartenhorst R. Polychondropathia. *WienArch F Inn Med*. 1923;(6):93-100.
3. Balsa A, Expinosa A, Cuesta M, et al. Joint symptoms in relapsingpolychondritis. *Clin Exp Rheumatol*. 1995 Jul-Aug;13(4):425-30.
4. Zeuner M, Straub RH, Rauh G, et al. Relapsing polychondritis: clinical and immunogenetic analysis of 62 patients. *J Rheumatol*. 1997 Jan;24(1):96-101.
5. Yang CL, Brinckmann J, Rui HF, et al. Autoantibodies to cartilage collagens in relapsing polychondritis. *Arch Dermatol Res*. 1993; 285(5):245-9. doi: 10.1007/BF00371591.
6. Kempta Lekpa F, Piette JC, Bastuji-Garin S, et al. Serum cartilage oligomeric matrix protein (COMP) level is a marker of disease activity in relapsing polychondritis. *Clin Exp Rheumatol*. 2010 Jul-Aug;28(4):553-5. Epub 2010 Aug 30.
7. Ouchi N, Uzuki M, Kamataki A, et al. Cartilage destruction is partly induced by the internal proteolytic enzymes and apoptotic phenomenon of chondrocytes in relapsing polychondritis. *J Rheumatol*. 2011 Apr;38(4):730-7. doi: 10.3899/jrheum.101044. Epub 2011 Jan 15.
8. Arnaud L, Mathian A, Haroche J, et al. Pathogenesis of relapsing polychondritis: A 2013 update. *Autoimmun Rev*. 2014 Feb; 13(2):90-5. doi: 10.1016/j.autrev.2013.07.005. Epub 2013 Sep 17.
9. Son SB, Han WH, Park JH, et al. Aggravation of relapsing polychondritis due to the infection and its manifestation on a nasal tip graft. *Clin Exp Otorhinolaryngol*. 2014 Mar;7(1): 63-5. doi: 10.3342/ceo.2014.7.1.63. Epub 2014 Feb 5.
10. Michet CJ, McKenna CH, Luthra HS, O'Fallon WM. Relapsing polychondritis: Survival and predictive role of early disease manifestations. *Ann Intern Med*. 1986 Jan;104(1): 74-8. doi: 10.7326/0003-4819-104-1-74.
11. Kashihara K, Kawada S, Takahashi Y. Autoantibodies to glutamate receptor GluRepsilon2 in a patient with limbic encephalitis associated with relapsing polychondritis. *J Neurol Sci*. 2009 Dec 15;287(1-2):275-7. doi: 10.1016/j.jns.2009.08.004. Epub 2009 Aug 28.
12. Kent PD, Mitchet CJ Jr, Luthra HS. Relapsing polychondritis. *Curr Opin Rheumatol*. 2004 Jan;16(1):56-61. doi: 10.1097/00002281-200401000-00011.
13. Chang SJ, Lu CC, Chung YM, et al. Laryngotracheal involvement as the initial manifestation of relapsing polychondritis. *J Chin Med Assoc*. 2005 Jun;68(6):279-82. doi: 10.1016/S1726-4901(09)70151-0.
14. Ernst A, Rafeq S, Boiselle P, et al.

Relapsing polychondritis and airway involvement. *Chest*. 2009 Apr;135(4):1024-1030. doi: 10.1378/chest.08-1180. Epub 2008 Nov 18.
15. Baretto SN, Oliveira GN, Michet CJ, et al. Multiple cardiovascular complications in a patient with relapsing polychondritis. *Mayo Clin Proc*. 2002 Sep;77(9):971-4. doi: 10.4065/77.9.971.
16. Савельев АИ, Черняк ВИ, Вороненкова ЕА, Шаркова ЮВ. Десять случаев рецидивирующего полихондрита. В кн.: Ольбинская ЛИ, редактор. Актуальные вопросы внутренней медицины: Сборник научных трудов. Москва; 2000. С. 244-56.
[Savel'ev AI, Chernyak VI, Voronenkova EA, Sharkova YuV. Ten cases of recurrent polychondritis. In: Ol'binskaya LI, editor. *Aktual'nye voprosy vnutrennei meditsiny: Sbornik nauchnykh trudov* [Topical issues of internal medicine: Collection of scientific papers]. Moscow; 2000: P. 244-56].
17. Hsu KC, Wu YR, Lyu RK, et al. Aseptic meningitis and ischemic stroke in relapsing polychondritis. *Clin Rheumatol*. 2006 Mar; 25(2):265-7. doi: 10.1007/s10067-005-1152-3. Epub 2005 Jul 26.
18. McAdam LP, O'Hanlan MA, Bluestone R, Pearson CM. Relapsing polychondritis: Prospective study of 23 patientsand a review of the literature. *Medicine (Baltimore)*. 1976 May; 55(3):193-215.
19. Asadi AK. Relapsing polychondritis. *Dermatol Online J*. 2003 Oct;9(4):3.
20. Тюрин ВП, Мезенова ТВ. Успешная диагностика и лечение рецидивирующего полихондрита. Вестник Национального медико-хирургического центра им. Н.И. Пирогова. 2006;3(2):37-43.
[TyurinVP, Mezenova TV. Successful diagnosis and treatment of recurrent polychondritis. *Vestnik Natsional'nogo Mediko-Khirurgicheskogo Tsentra im. N.I. Pirogova*. 2006;3(2): 37-43. (In Russ.)].
21. Черняк ВИ, Савельев АИ, Погромов АП. Рецидивирующий полихондрит. Клиническая медицина. 2014;92(11):22-8.
[ChernyakVI, Savel'evAI, PogromovAP. Recurrent polychondritis. *Klinicheskaya Meditsina*. 2014;92(11):22-8. (In Russ.)].
22. Сайковский РС, Бабак ВВ, Григорьева МА. Рецидивирующий полихондрит. Случай из практики.Клиническая практика. 2011;(4):44-9.
[Saykovskiy RS, Babak VV, Grigor'eva MA. Recurrent polychondritis. Case study. *Klinicheskaya Praktika*. 2011;(4):44-9. (In Russ.)].
23. Black CM, Pereira S, McWrirter A, et al. Genetic susceptibility to scleroderma-like syndrome in symptomatic and asymptomatic workers exposed to vinyl chloride. *J Rheumatol*. 1986 Dec;13(6):1059-62.
24. Кряжева СС, Хамаганова ИВ, Макушина ЗВ. Бляшечная склеродермия, развившаяся после инъекций пенициллина. Вестник дерматологии.1992;(1):43-45.
[Kryazheva SS, Hamaganova IV, Makushina ZV. Plaque scleroderma developed after penicillin injections. *Vestnik dermatologii*. 1992;(1):43–45. (In Russ.)].
25. Куницкая НА. Индуцированная склеродермия – необычный случай развития. Sciences of Europe. 2020;(55):15-18.
[Kunickaya NA. Induced scleroderma – an unusual case of development. *Sciences of Europe*. 2020;(55):15-18. (InRuss.)].
26. Shoenfeld Y, Agmon-Levin N. 'ASIA' – autoimmune/inflammatory syndrome induced by adjuvants. *J Autoimmun*. 2011 Feb; 36(1):4-8. doi: 10.1016/j.jaut.2010.07.003.
27. Золотых ВГ. «После» не значит – «вследствие»? ASIA-синдром в течение годового наблюдения пациенток с операциями на молочных железах. От Иегуды Шенфельда – к Роману Баевскому. Russian Biomedical Research. 2021;6(2):3-14.
[Zolotykh VG. "After" does not mean – "due to"? ASIA-syndrome during the annual follow-up of patients with breast surgery. From Yehuda Shenfeld to Roman Baevsky. *Russian Biomedical Research*. 2021;6(2):3-14. (In Russ.)].
28. Burek CL, Talor MV. Environmental triggers of autoimmune thyroiditis. *J Autoimmun*. 2009 Nov-Dec;33(3-4):183-9.
29. Vermeulen RC, Scholte HR. Rupture of siliconegel breastimplants and symptoms of pain and fatigue. *J Rheumatol*. 2003 Oct; 30(10):2263-7.
30. Brown SL, Pennello G, Berg WA, et al. Siliconegel breastimplant rupture, extracapsular silicone, and health status in a population of women. *J Rheumatol*. 2001 May;28(5): 996-1003.
31. Marrack P, McKee AS, Munks MW. Towards an understanding of the adjuvant action of aluminium. *Nat Rev Immunol*. 2009 Apr;9(4):287-93. doi: 10.1038/nri2510.
32. Fryzek JP, Signorello LB, Hakelius L, et al. Self-reported symptoms among women after cosmetic breastimplantand breastreduction surgery. *Plast Reconstr Surg*. 2001 Jan; 107(1):206-13. doi: 10.1097/00006534-200101000-00034.
33.Vasey FB, Zarabadi SA, Seleznick M, Ricca L. Where there's smoke there's fire: the silicone breastimplant controversy continue stoflicker: a new disease that needs to be defined. *J Rheumatol*. 2003 Oct;30(10):2092-4.
34. Janowsky EC, Kupper LL, Hulka BS. Meta-analyses of the relation between silicone breastimplants and the risk of connective-tissue diseases. *N Engl J Med*. 2000 Mar 16; 342(11):781-90. doi: 10.1056/NEJM 200003163421105
35. Chauhan U, Cassidy B, Cohen Tervaert JW. ASIA (Shoenfeld's syndrome) due to hysteroscopic Essure sterilization. *Autoimmun Rev*. 2021 Dec;20(12):102979. doi: 10.1016/j.autrev.2021.102979. Epub 2021 Nov 6.
36. Tervaert JWC, Martinez-Lavin M, Jara LJ, et al. Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) in 2023. *Autoimmun Rev*. 2023 May;22(5):103287. doi: 10.1016/j.autrev.2023.103287. Epub 2023 Feb 3.
37. Parums DV. Editorial: SARS-CoV-2 mRNA Vaccines and the Possible Mechanism of Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT). *Med Sci Monit*. 2021 Apr 26:27:e932899. doi: 10.12659/MSM.932899.
38. Chen Y, Xu Z, Wang P, et al. New-onset autoimmune phenomena post-COVID-19 vaccination. *Immunology*. 2022 Apr;165(4): 386-401. doi: 10.1111/imm.13443. Epub 2022 Jan 7.

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Conflict of Interest Statement

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Movsesyan A.A. https://orcid.org/0009-0002-3473-2480
Krasnenko S.O. https://orcid.org/0000-0002-4505-0162
Urumova M.M. https://orcid.org/0000-0002-9755-5760
Godzenko A.A. https://orcid.org/0000-0002-5493-6045