

Relapsing Polychondritis in a Child with Autism: Rare within Rare 1st Case Described

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Abstract A relationship between autism and autoimmunity is well known and various autoimmune diseases were associated with the autistic spectrum. Relapsing polychondritis is a rare autoimmune disease manifested mainly in adults. Following is the first case presentation of a girl presented with relapsing polychondritis who was on the autistic spectrum. Several mechanisms can be envisioned to connect those two diseases.

Keywords: relapsing polychondritis, vasculitis, autism, Autism spectrum disorder, ASD

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1. Introduction

Relapsing polychondritis (RP) is a rare autoimmune disease with a wide individual heterogeneity, involving various human body organs. It is characterized by inflammation of cartilage tissues, mainly in the ears, nose, tracheobronchial tree, but also the inner ear, eyes, joints, cardiovascular system presentations were described [1] [2] [3] [4]. Very seldomly central nervous system and psychiatric behavioral manifestations were reported [5] [6] [7]. Despite the fact that autoimmunity, autoantibodies and autism spectrum disorder (ASD) relationship were reported [8], to our knowledge, no ASD were ever described in RP. A subset of patients bears some somatic mutations [9], however, no specific environmental factor was yet discovered [10]. Unfortunately, no efficient diagnostic and prognostic molecular biomarkers are available and the current ones lack specificity and sensitivity [11]. Clarifying the disease pathophysiology, definitive diagnosis, evaluation of activity, prognosis, and the most efficient therapeutic options remains a challenge [12] [13]. The present report is unique for the rarity of RP, the early age affected girl and never described association between RP and ASD. Some potential pathophysiological cross talks between RP and ASD will be suggested.

2. Case Presentation

A 7-year-old girl with a history of late neurodevelopment, in February 2020, started polyarthritides of her knees and elbows, episcleritis, associated with redness and pain in her ears (Figure 1). The girl went to the emergency department, and prednisone 0.5mg/kg/day was prescribed, and a marked improvement was observed after four doses of glucocorticoid. Her laboratory tests revealed white blood cells of 12,490, C-reactive protein of 6mg/L, and erythrocyte sedimentation rate (ESR) of 21 mm/1st hour (nr: < 10 mm/1st hour). She came to our consultation, no more arthritis was detected, and the ears and cartilages were normal. We ordered more laboratory tests that showed normal cell blood count, CRP, and ESR. All autoantibodies (antinuclear antibodies, rheumatoid factor, anti-CCP, anti-U1RNP, anti-Ro/SS-A, anti-SS-B, anti-Sm, anti-ribosomal P, anticardiolipin and lupus anticoagulant) were negative. All infectious serologies were negative. Having bilateral auricular scleritis, episcleritis and non-erosive polyarthritides, she fulfilled McAdam's criteria for the diagnosis of RP [14], hence, hydroxychloroquine 200mg/day and vitamin D 50,000IU/week were then initiated. The child continued to recover, and the glucocorticoid was tapered off. During a

2 year-follow-up, no flare of RP was detected, and all laboratory tests continued within the normal range. In parallel, during the investigation, the parents and the medical team noticed some behavioral changes. She exhibited minimal eye contact, smiled and laughed without reason, had solitary social activities, poor interaction with strangers, and stereotyped gestures. Those characteristics raised the suspicion of autistic spectrum disorder. A thorough neuropsychiatric test's evaluations confirmed the diagnosis of ASD, and the girl was sent for physical, psychologic and phono audiologist therapies and to an appropriate educational framework.

3. Discussion

The present case, to our knowledge, is the first descriptive association between a triple rarity. RP is a rare condition; childhood presentation of RP is rare, where less than 10% of reported patients occur in children and adolescents [15] [16] [17], and finally, ASD was never reported with this autoimmune entity.

Recent studies suggest immune dysregulation in ASD patients and brain-targeted autoimmune antibodies are increasingly described [8] [18] [19] [20] [21]. Interestingly, rheumatoid and psoriatic arthritis were related to ASD [22] [23], however, the association between RP and ASD was never reported.

An autoimmune background, including brain directed autoantibodies were reported in ASD [8] [24] [25] [26]. The autistic spectrum is the fastest-growing neurodevelopmental disability worldwide affecting one in 68 births in the United States, but, the causes and the pathophysiology of ASD are largely yet unknown. genetic abnormalities are increasingly identified but recent emerging studies documented various immune dysfunctions, presenting an additional risk factor for the neurobehavioral deficits observed in ASD [8] [18] [19] [20] [21] [24] [25] [26]. Taken together, the cross-talks between RP and ASD can involve immune dysbalance or autoimmune phenomena, joining together in the girl discribed.

Several potential mechanisms can be envisioned to connect the two diseases.

1. Loss of tolerance to a yet unidentified environmental factor.
2. Dysbiosis is a common feature in autoimmune diseases [27] [28] [29] [30] [31] and exist in RP. Propionate- producing microbes with suppressed IL-10 induced regulatory T cells was described in RP patients [32]. Parallely, altered composition and decrease variability of the gut microbiome is widely reported in ASD [33] [34] [35]. Intriguingly, co-morbid gastrointestinal symptoms were described in ASD and in joint affected patients [30] [31] [36] [37] [38].
3. Increased intestinal permeability is described in ASD [33] and in various rheumatological conditions [39]. All the three hypothetical pathways might be a part of the gut-brain axes [31] where luminal and mucosal eco events can irradiate to peripheral organs [38], including all those affected in RP.

4. Conclusions

The present manuscript described the first case of a triple rare conditions. RP is a rare autoimmune inflammatory entity where childhood presentation is rare and its association with ASD was never described. Several mechanisms that might connect RP targeted organs with autism that might bring new therapeutic strategy to both conditions are suggested.



Figure 1. redness and pain in the girl's left ear

Author's Contribution

AL- screened the literature, wrote the manuscript, JFdC- screened the literature, designed, wrote, edited and revised the manuscript, TFS- wrote the case presentation, MFLSR, MH, CB-revised and edited the manuscript. The six authors agreed to the published version of the manuscript.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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None

Abbreviations

RP-Relapsing polychondritis, ASD-autism spectrum disorder.

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