

CASE REPORT

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Coexistence of PFAPA syndrome with separation anxiety

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Abstract

PFAPA syndrome is an auto inflammatory disease. Researchers have stated that auto inflammatory mechanisms can play a role in etiology of several psychiatric diseases and for this reason auto inflammatory diseases are frequently associated with psychiatric disorders. The purpose of this paper, it is aimed to report two cases diagnosed with PFAPA syndrome and having psychiatric symptoms and to discuss them accompanied by literature data. As authors, in the light of cases we report and literature knowledge, we think that children with PFAPA syndrome could be under risk in terms of psychiatric problems due to common inflammatory etiology.

Keywords: Auto inflammation, PFAPA syndrome, separation anxiety

Introduction

Periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis syndrome (PFAPA syndrome) is an autoinflammatory disease characterized by existence of fever attacks with at least one of the three major symptoms as aphthous stomatitis, pharyngitis, and cervical adenitis [1,2]. Researchers have stated that autoinflammatory mechanisms can play a role in etiology of several psychiatric diseases and for this reason autoinflammatory diseases are frequently associated with psychiatric disorders [3]. The purpose of this paper is to report two cases diagnosed with PFAPA syndrome and having separation anxiety disorder.

Case Report

Case 1

A student in the 1st class of primary school, 6-year-old male, was admitted to child psychiatric clinic with complaints of difficulty in leaving his mother and father, and all the time staying with his teacher at school. According to information received from parents, these were learned that he had difficulties in staying at school after he started to school, he left his parents after his parents waited at

school a few months, but at this time, he did not leave his teacher at school, and he did not leave the classroom without his teacher in the breaks. In addition, these were learned that the patient did not leave his parents after school, he wanted his parents even when he was playing with his peers, he experienced intense anxiety about it, he had fear of harm to his parents or himself, the difficulty of leaving from his parents remained since infancy. Family of the patient had no psychiatric disease history.

In the psychiatric assessment by authors, these were observed that the patient dressed in consistent with his age and socio-economic status, verbal and non-verbal communication were normal, his mood was euthymic, his affection was anxious, he had not perceptual disorder, his cognitive functions were consistent with his age. At the result of administered psychiatric examination and psychometric assessments considering for DSM-5 diagnostic criteria, the patient was diagnosed with separation anxiety disorder. Cognitive behavioral therapy and psychopharmacological treatment were planned for the patient. As a psychopharmacologic treatment, 5 mg/day fluoxetine was administered to the patient. After four weeks, dose of fluoxetine was increased to 10 mg/day. In three months, 12 cognitive behavioral therapy sessions implemented by authors.

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In the second month of psychiatric treatment, the patient referred to our pediatric rheumatology and otolaryngology clinic for recurrent

and resistant fever attacks and cervical adenitis. Laboratory tests for infectious diseases, familial mediterranean fever, immunological and hematological diseases and pandas were negative. Pediatric rheumatology clinic was diagnosed with “Ppapa Syndrome” due to cervical adenitis and recurrent-resistant fever attacks.

Patient who did not benefit enough from cognitive behavior therapy for three months continued to be followed only by psychopharmacologic treatment (Fluoxetine 10mg / day). At six months of psychopharmacologic treatment, the patient had no significant improvement in symptoms of separation anxiety. During the sixth month of psychiatric treatment, the patient underwent surgery for tonsillectomy because of PFAPA syndrome. Symptoms of separation anxiety of the patient who continued psychopharmacologic treatment after tonsillectomy operation decreased significantly within six months. The patient doesn't have any problem in the school now, and he can join the activities of peers without family members and teachers.

Case 2: A kindergarten student, four years old male, was admitted to our clinic in with complaints of difficulty in leaving his parents. According to information received from his family, these were learned that the patient did not want to leave his parents, he was reluctant to go to school, so that he cried often and he presented aggressive behavior, he did not allow his parents to leave the school, and he experienced intense anxiety when he went to school, but he was compatible when his parents were next to himself, he has fear of harm to his parents or himself. The complaints of the patient started seven months ago and family of the patient had no psychiatric disease history. Additionally, it was learned that the patient had recurrent attacks of fever refractory to medical treatment and cervical adenitis, therefore, he was evaluated by pediatric rheumatology clinic in our hospital and he was followed with the diagnosis of PFAPA syndrome. The patient's laboratory tests for infectious diseases, familial mediterranean fever, immunological and hematological diseases and pandas were negative.

In the psychiatric assessment by authors, these were observed that the patient dressed in consistent with his age and socio-economic status, verbal and non-verbal communication were normal, his mood was euthymic, his affection was anxious, he had not perceptual disorder, his cognitive functions were consistent with his age. At the result of administered psychiatric examination considering for DSM-5 diagnostic criteria, the patient was diagnosed with separation anxiety disorder. Cognitive behavioral therapy was planned for the treatment.

The patient, whose psychiatric symptoms partially regressed as a result of weekly intensive psychiatric interview and cognitive behavioral therapy lasting approximately two months, failed to complete the follow-up and treatment process because of the change of address. This case has not undergone tonsillectomy operation yet and has not received a regular treatment for PFAPA syndrome, and was undergoing symptomatic treatments for bringing the fever down when fever attacks occurred.

Discussion

PFAPA syndrome was first described by Marshall in 1987 [4]. The syndrome usually begins before the age of 5 years and ends in adolescence. The diagnosis is based on the basic clinical

criteria (existence of fever attacks with at least one of the three major symptoms as aphthous stomatitis, pharyngitis, and cervical adenitis) and exclusion of other reasons (infectious diseases, familial mediterranean fever, immunological, hematological diseases, etc.) that may cause recurrent fever [1,4]. Both of our cases were diagnosed by our pediatric rheumatology clinic within this scope and other causes that may result in recurrent fever were eliminated. In the first case, symptoms of separation anxiety occurred before the symptoms of PFAPA syndrome. In the second case, symptoms of separation anxiety occurred after the symptoms of PFAPA syndrome.

Autoinflammatory mechanisms are studied by emphasizing a possible irregularity in natural immune system for etiology of PFAPA syndrome. Treatment is symptomatic and applied when fever attacks occur [5]. The fact that patients benefit from steroids and tonsillectomy used in symptomatic therapy is another finding which indicates that this disease might be resulted from autoinflammatory mechanisms. In immunological studies, CRP, TNF-alpha, IL-1, IL-6, IFN-gamma levels were determined to be higher in these patients [5]. Likewise, CRP, TNF-alpha, and IL-6 levels were shown to be higher in children with anxiety disorder [3,6]. However, it is not clear that whether these immunological factors elevated due to increasing stress observed in anxiety disorder or whether immunological mechanisms caused anxiety disorder.

Some researchers speculate that inflammatory mechanisms may play role in etiology of psychiatric disorders and proinflammatory markers may have biomarker potential in terms of diagnosis and course of psychiatric diseases and therapeutic interventions. In addition, it was emphasized in some studies that antiinflammatory treatments such as aspirin, nonsteroidal antiinflammatory drugs, tumor necrosis factor (TNF)—a antagonists and omega-3 fatty acids could be potential psychiatric interventions [3].

Conclusion

The immunologic markers are not continuous high in the PFAPA syndrome. In some patients, periodic elevations can be seen, and in some cases immunologic markers can be always normal. Immunologic markers were normal in our both cases. However, the decline of PFAPA syndrome and separation anxiety symptoms after tonsillectomy in the first case suggests that autoinflammatory mechanisms may play a role in the etiology of both diseases.

As authors, in the light of cases we report and literature data, we think that children with PFAPA syndrome could be under risk in terms of psychiatric problems due to common inflammatory etiology and further controlled studies are needed to guide to assess the risk of psychiatric disorders in PFAPA syndrome.

Competing interests

The authors declare that they have no competing interest.

Financial Disclosure

The financial support for this study was provided by the investigators themselves.

Ethics committee approval

While this study is a case report, there isn't any ethics committee approval. There is the case's informed consent form.

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