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CASE REPORT

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Obsessive-compulsive disorder and acquired toxoplasmosis in two children

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Abstract Two children presenting symptoms of obsessive-compulsive disorder (OCD) and with acquired toxoplasmosis are described and the possibility of a previously rarely reported association between OCD and acquired toxoplasmosis is discussed. Case 1 is a 14-year-old boy with Tourette syndrome (TS), attention deficit hyperactivity disorder (ADHD) in partial remission and a three-year history of OCD referred to our department due to an acute deterioration of obsessive-compulsive (OC) symptoms. Case 2 is an 11-year-old boy referred to our department because of a two-year history of OCD. The OC symptoms were observed immediately following an infection. In both cases laboratory tests confirmed the diagnosis of acquired toxoplasmosis. The pharmacological therapy of *T.gondi* infection without any psychopharmacological treatment caused remission or significant improvement regarding OC symptoms.

Key words Obsessive-compulsive disorder – Acquired toxoplasmosis – Case report – Therapy

Introduction

Toxoplasmosis, an anthropo-zoonosis caused by the protozoa *Toxoplasma gondi* is a worldwide health problem. Primary toxoplasmic infection is acquired usually by ingestion of *T. gondi* oocysts from soil contaminated by cat faeces or by ingestion of tissue cysts present in undercooked or raw red meats. Toxoplasmosis can also appear in a congenital form. In immunocompetent hosts the infection is usually asymptomatic or benign, but symptoms can also take a differentiated clinical course sometimes difficult to interpret. In cases of severe manifestations such as encephalitis, pneumonia or myocarditis, the patients should be checked for immunocompetence deficiencies. Autopsy findings suggest that the brain, heart and lungs are the most susceptible organs in both congenital and acquired forms. The special adherence of protozoan to CNS is probably due to the difficult access of antibodies to the neurones of the brain (17).

Toxoplasms primarily lodge in the CNS. Infections in early childhood may indirectly result in a degenerative disease causing an impairment of CNS function. This hypothesis is partially supported by studies noting that educationally subnormal children and adolescents exhibit a far greater proportion of antibodies to *T. gondi* than normally developing children of the same age (32). On the other hand, a latent *T. gondi* infection does appear to have some effects on behaviour and learning capacity. Piekarski emphasises that learning performance in rats and learning performance, memory, response to novel stimuli and overall activity in mice were reduced by infection. These studies indicate that *T. gondi* infection probably affects the animal's response to the environment and environmental stimuli and can even affect endogenous regulatory processes in the brain. There are similar observations in humans with an acquired asymptomatic infection (21).

Acquired toxoplasmosis can cause neurological symptoms or syndromes imitating various neurological

or mental disorders, a finding which is relatively rarely taken into account in the differential diagnosis of mental disorders. We have reviewed the literature on psychiatric manifestations of acute acquired toxoplasmosis in immunocompetent patients. The data available to us provide some examples of such clinical presentations and suggest certain conclusions. Many authors have proved that positive antibodies anti-*T. gondi* were considerably more frequent among patients with mental disorders than among healthy controls (3, 6, 7). On the other hand, the results of other studies have not confirmed such differences (8). The probable causal relationship between acquired toxoplasmosis and mental disorders has been reported in several papers (9, 10, 16, 18, 22, 24, 25, 31). It should be underscored that in Kramer's analysis of 114 cases of neurotoxoplasmosis, 24 presented different psychopathological symptoms (15). In the above-mentioned studies the most frequently described disorders were: various psychotic states (including catatonia), as well as dementia, depression, sleep disorders, i. e. insomnia or recurring somnolence such as in Kleine-Levin syndrome,"hysterical, psychasthenic, neurasthenic" disorders, undefined anxiety and also non-specific symptoms such as headache, vertigo, loss of appetite and energy, suspicion, irritation, emotional instability.

The purpose of our work is to describe the cases of two children presenting symptoms of obsessive-compulsive disorder (OCD) and diagnosed as having acquired toxoplasmosis and to discuss the possibility of a previously rarely reported (24, 31) association between OCD and acquired toxoplasmosis. In both cases the pharmacological treatment of *T. gondi* infection without any psychopharmacological treatment caused remission or significant improvement regarding OC symptoms.

Case 1

A 14-year-old boy with Tourette syndrome (TS), attention-deficit hyperactivity disorder (ADHD) in partial remission and a three-year history of OCD referred to our department due to an acute worsening of obsessive-compulsive (OC) symptoms lasting for three months. He was born from a normal pregnancy. The family history was negative for ADHD, tic disorders and OCD.

He demonstrated compulsive checking, repeating, counting, compulsive hand movements and intrusive vocalisations, symptoms of primary obsessional slowness, but the most important clinical problem was extensive "protective" ritualisation to keep the family safe. Particularly at bedtime the boy felt compelled to repeat certain actions or to check repetitively. Moreover, he developed new obsessions and fears concerning his family coming to harm, and he had intrusive thoughts about counting days of separation from his mother. Admission induced complete separation anxiety disorder (SAD) with persistent worries about losing his family. During weekends at home he refused to go out without his mother and reported physical complaints before coming back to hospital. The diagnosis of TS, OCD with moderate severity of symptoms and SAD were made according to DSM-IV criteria. He received no psychopharmacological treatment before or during his stay in the ward.

After admission, physical examination did not show any abnormalities. Laboratory tests were normal except for the result of the indirect immunofluorescence test (IF), which showed titter 1:160 of anti-*T. gondi* antibodies. After one month the titter of antibodies was checked, which peaked at 1:1280. The level of ISAGA (immunosorbent agglutination assay) IgM was positive and estimated at 11 points (the norm is up to 5 points). We decided there were no indications for performing such an invasive test as a lumbar puncture. The boy was given treatment with cotrimoxazole and left hospital for a two-week winter holiday with his parents. After this period the patient and his family reported a significant reduction of OC symptoms to a level similar to that before deterioration. The control serological analysis after the treatment showed in IIF a titter of 1:320, and after two months, 1:160.

The boy was discharged and underwent intensive behavioural therapy for OCD at home. Ambulatory family therapy was continued for several months supporting the patient's emancipation and solving the family separation problems. Now he experiences only sporadic compulsions pertaining to the need for symmetry or exactitude and occasional vocal tics.

Case 2

An 11-year-old boy was referred to our department because of a two-year history of OCD with symptoms in the form of compulsive stroking of various surfaces, spitting and rubbing spit on his sleeves, repeating certain words, e. g. "no, never in my life", obsessions and fears about harm coming to his mother and to his older brother. He also reported persistent worry about losing his mother, fear of darkness and sporadic visual illusions. In the parent's own opinion, for the last two years he had been anxious, irritable and had demonstrated sporadic aggressive behaviour.

In the family there were no cases of psychiatric or neurologic disorders. The boy was born from a normal pregnancy; the developmental milestones were normal. His performance at school was good and he had normal peer relations. At the age of eight he contracted right-sided pneumonia, urinary tract infection and angina, although at that time the serological investigation for toxoplasmosis was negative. After one year, at the age of

nine he suffered a febrile infection of unknown origin, lasting up to 10 weeks, with generalised tonic-clonic seizures and left-sided hemiclonias. After a short-term prophylactic treatment with anticonvulsants he was seizure-free. The described OC symptoms and behavioural changes were observed immediately after the infection. He also reported frequent headaches in the frontal region at this time.

After admission to our department physical examination did not show any abnormalities except for paleness and very slight anisocoria. The boy was depressed, inhibited, anxious, reported various somatic complaints and worries concerning losing his mother. The above-described OC symptoms were also observed. He was ashamed because of his compulsions and recognised that these behaviours were distressful, excessive and unreasonable and he tried to resist them.

Ophthalmologic examination and CT were normal. EEG: normal background activity, in the somnolence series of generalised high-voltage sharp waves and delta waves. Laboratory tests were normal except for the result of IIF, which showed titter 1:1280 of anti-*T. gondi* antibodies. Detection of specific IgM and IgG antibodies (IgM 1:40, IgG 1:320) confirmed the diagnosis of acquired toxoplasmosis. The lumbar puncture was not performed due to the lack of parental consent. The standard treatment with cotrimoxazole combined with rovamycine was initiated. He had never been treated with any psychopharmacological agents previously. During anti-protozoal therapy gradual improvement was observed: the OC symptoms disappeared completely, the boy was less anxious, he became more active and started to take part in lessons and play. The control serological investigation for anti-toxoplasma antibodies showed titter 1:160. The boy was discharged and in a follow-up arranged by our out-patient clinic he declared he felt well, without any OC symptoms.

Discussion

Although the aetiology of OCD is still unknown, a growing body of evidence demonstrates that it is a neuropsychiatric disorder, aetiologically heterogeneous. The family-genetic data show that familial forms of OCD may be associated with a specific genetic susceptibility (20). The effectiveness of clomipramine and other serotonin re-uptake inhibitors supports serotoninergic dysfunction as a basis of aetiology of OCD (4), but some studies provide further evidence that multiple neurotransmitters might also be involved in this disorder (11). On the other hand, case reports and anecdotal experience suggest that hormonal dysfunction may be aetiologically related to OCD as well (26). Data from adult studies suggest that OCD may be related to abnormalities in circuits connecting frontal cortex, basal ganglia and limbic structures (5, 28). Recent investigations have associated development of OCD with infectious illness, i. e. symptoms can arise or exacerbate in the context of group A beta-haemolytic streptococcal infection (2, 27). There is a single case report of reduction of OC symptoms during specific antiprotozoal treatment in 34-year-old women with AIDS and neurotoxoplasmosis in form of bilateral toxoplasmic lesions involving basal ganglia (24).

In our study we describe the unusual appearance of acquired toxoplasmosis in two children and take into consideration a relationship between OCD and acquired toxoplasmosis. Both OCD cases were diagnosed according to DSM criteria (case 1 according to DSM-IV and case 2 to DSM-III-R) (1). In both cases the diagnosis of *T. gondi* infection was made on the basis of the clinical methods and on specific serologic tests. Analyses of both IgM and IgG classes of anti-toxoplasma antibodies combined with immunofluorescent tests at first showed high titters in the blood with subsequent tendencies to normalise due to the standard antiprotozoal treatment. The presence of anti-toxoplasma IgM antibodies suggested recent infection. In both cases there was no evidence for paediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS) (27).

Diagnosing CNS toxoplasmosis is complex. The serological testing in the CSF may determine the diagnosis. However, the titters of antibodies anti-*T. gondi* in the CSF may be also negative in some cases (12, 14). Results of CT scans, particularly in the presence of hypodensive lesions, may be highly suggestive and helpful, but the absence of changes is not synonymous with a negative diagnosis of neurotoxoplasmosis. In a chronic phase of neurotoxoplasmosis the cysts are not encapsulated by inflammatory infiltration and cannot be seen in CT scans (30). In case 2 CT was performed two years after the hypothetical onset of the infection, which indicates that the patient could have been in the chronic phase of the disease. The definitive diagnosis of neurotoxoplasmosis can be made only by demonstrating the presence of *T.gondi* in brain tissue (13), so on the mere basis of serological and neuroimaging changes or clinical picture the CNS toxoplasmosis (diagnosis) can neither be confirmed nor excluded with certainty.

The clinical presentation of OC symptoms in case 1 was congruent to other descriptions of OCD in childhood TS. We did not find any trigger incident resulting in exacerbation of OC symptoms, so it is possible that the described severe worsening of OCD followed the T. *gondi* infection. The growing titters of antibodies anti-*T. gondi* associated with increasing severity of symptoms and significant improvement parallel to antiprotozoal treatment and decreasing of titters seem to suggest the presence of neurotoxoplasmosis (23). Behavioural therapy helped to stabilise the disorder and to reduce the OC symptoms to being less pronounced than those experi-

enced prior to the deterioration of the patient's condition.

In case 2 the OC symptoms were atypical and appeared suddenly. The febrile infection in connection with tonic-clonic seizures may be interpreted as symptoms of the acute encephalitis caused by *T. gondi*. The OC, anxiety symptoms and the subsequently observed chronic frontal headache may also be interpreted as manifestations of a chronic phase of neurotoxoplasmosis. Apparently, the period between the acute and chronic phase of the disease can range from days to years (23). Therapy including antiprotozoal drugs only caused complete remission of OC symptoms coupled with a decrease of serum titters of anti-toxoplasma antibodies: a clinical picture which in this case suggests an aetiologic link between OCD and acquired toxoplasmosis.

Although a certain causal relationship is not established, we suggest that patients with sudden onset or exacerbation of OC symptoms should be studied serologically for *T. gondi* infection, which should be considered as a sporadic but possible triggering agent associated with the development (case 2) or exacerbation of symptoms (case 1) of childhood OCD. The prime reason for such an examination is of course the possibility of an appropriate antiprotozoal therapy producing remission of symptoms or a significant improvement in the patient's condition. Secondly, it is hard to foresee how an acute non-treated recent toxoplasmosis could influence the course and prognosis of the disorder and if the exacerbation of OC symptoms could be a consequence of the infection alone. It should be emphasised that Korowickij (cited by 29), who, for over five years, observed 4997 patients with acquired toxoplasmosis, concluded that an important factor causing mental symptoms in the course of a *T. gondi* infection could be its chronicity.

Toxoplasmic infection is very common in the human population. Hence, it is very risky to casually connect the abnormalities in the laboratory tests with symptoms. Kramer wrote: "…by taking only very high titters into consideration, toxoplasmosis is without doubt a very rare disease, … when giving too much diagnostic significance to very low titters, it seems as if toxoplasmosis plays a role in every disease" (15). However, in our cases the corresponding changes in the serological testing and severity of symptoms without any pharmacological or antiobsessional treatment, led us to hypothesise about the aetiological relationship. In our opinion, there are no data supporting the hypothesis that the pathomechanism of the OC symptoms in these cases is close to that of PANDAS. Symptoms of the CNS toxoplasmosis are associated with the presence of parasites in the brain tissue and with releasing them from the cysts (30), which seems to indicate that the mechanism is associated with the direct inflammatory reaction. The hypothesis that the OC symptoms in our cases may be associated aetiologically with *T.gondi* infection may be supported by results of CT scans, neuropathological findings and neurological evaluations in some cases of neurotoxoplasmosis, which showed lesions in basal ganglia (12, 19, 24).

Despite the limitations of such reasoning, the proposed conclusion is that some (perhaps very rare) cases of the chronic severe manifestations of OCD may be related to toxoplasmosis acquired during childhood or adolescence. This suggestion could be important in the context that among adults with OCD one third to one half develop the disorder during childhood and given that *T. gondi* infection is so frequent in the human population.

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