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A BOY WITH ASPERGER'S DISORDER, CROHN'S DISEASE AND EPILEPSY

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Asperger's disorder (AD) is a pervasive developmental disorder that is part of autism spectrum disorders. It is characterized by daydreaming, hallucinations and disregard of external reality. The feeding habits of these patients are often peculiar and inadequate, and therefore frequently ascribed to the clinical features of pervasive developmental spectrum. Besides neurological disorders, these children often complain of gastrointestinal (GI) discomfort such as constipation, diarrhoea, abdominal pain and abdominal distension. Most of these signs are also present in chronic inflammatory bowel disease. Apart from neurological disorders, pathohistological changes in the GI tract of autistic children have also been described. On the basis of these findings the term "autistic enterocolitis" has been suggested as an independent diagnosis. However, recent studies question the reliability of this tenet.

Here we describe a patient with AD, Crohn's disease and epilepsy. This finding stresses the need for the completion of basic algorithm examinations in autistic children.

Descriptors: CHILD; CROHN DISEASE; ASPERGER SYNDROME; EPILEPSY

INTRODUCTION

Pervasive developmental disorder is a syndrome of early childhood characterized by abnormal social relationships and communication. This group of disorders includes classical autism, Rett syndrome, childhood disintegrative disorder, Asperger sy, atypical autism (1). The aetiology of pervasive developmental disorders remains unknown. There are studies suggesting possible genetic involvement, developmental abnormality of the brainstem, the influence of various postnatal factors including environmental dietary factors and toxins, as well as infectious agents (2). Intolerance to gluten and casein has also been reported, as well as measles and MMR vaccination that have caused much interest (3, 4).

The individual features of pervasive developmental disorders differ in their neurological symptomatology. Nevertheless, children with pervasive developmental disorder frequently present symptoms in other organs and systems. When investigating and describing these disorders scientists have not distinguished various forms of pervasive developmental disturbance and examine them as the homogenous group of "autistic children".

Gastrointestinal disorders and associated symptoms are commonly reported in individuals with pervasive developmental disorder. A central difficulty in recognizing and characterizing gastrointestinal dysfunction with pervasive developmental disorder is the communication impairment experienced by many affected individuals (5).

CASE REPORT

A boy was born by caesarean section, two weeks before term, after a normal pregnancy. There was no family history of autoimmune diseases. He was the first born. At the age of 12 months he was able to sit and at 16 months he started to walk. He articulated his first coherent words at the age of 18 months, but his speaking ability did not develop until the age of 4 when he started to construct whole sentences. Vaccination procedures (including MPR) proceeded by the regular protocol and at the age of 3 the boy started attending a day care centre. At the age of 4 yrs the parents noticed his augmented aggressiveness and refusal of food he used to consume, and while eating with anxiety he faced the wall. In the day care he showed abnormal social behaviour: a lack of attention, increased motor restlessness and impulsive reactions. In parallel he expressed special interest in numbers and time categories but with no harmonic cognitive function. His global intellectual reasoning was at the average level, while his ability for nonverbal analytic and synthetic thinking was well developed. His graphemics were immature and the possibility of synthetic and space planning was inadequate for the age. Stereotyped hand movements were noticed. Communicative function was maintained but his speech was occasionally out of context. Neurological assessment, including electroencephalography (EEG), was within normal ranges. Asperger's disorder was diagnosed. At the age of 6 years the boy was admitted to a school specialized for autistic children. At the age of 10 years he

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was hospitalized due to repeated episodes of abdominal pain, diarrhoea, vomiting and gaseousness. Gastritis due to *H. pylori* was diagnosed by esophagogastroduodenoscopy (EGDS). The symptoms were resolved upon eradication treatment with antibiotics and proton pump inhibitors.

Two years later he again experienced an episode of abdominal pain with bloody diarrhoea. His body weight and physical development were adequate for his age. Laboratory analyses revealed altered sedimentation rate (21mm/h), levels of fibrinogen (4.8 g/L), haemoglobin (110 g/L), iron (3.1 μmol/L), UIBC (71,7μmol/L), ferritin (11.0 (μg/L) and reticulocyte count (0.014 x 10^{-10}). Red blood cell and white blood cell counts including differential, C-reactive protein (CRP), and proteinogram were all within normal ranges for the age. Tests for endomyseal antibodies were negative. Stool cultures were positive for *Enterobius vermicularis*. Abdominal ultrasonography was normal. EGDS exploration revealed hyperemia of the antrum mucosa. Pathohistological findings showed *H.pylori* infiltration of the antral mucosa, and hyperemic, edematous duodenal mucosa infiltrated with mononuclears. Colonoscopy showed follicular hyperplasia and hyperemia of the distal ileum. Pathohistologically, the ileum was infiltrated with mononuclear cells forming large follicles and granulomas. Similar changes were found in coecum and colon. These findings suggested Crohn's disease. The Paediatric Crohn's Disease Activity Index was 23, indicating mild disease activity.

H. pylory eradication therapy was instituted followed by mesalazine treatment. Stools normalized but occasional episodes of abdominal pain and nausea were observed. Regular laboratory analyses were all within normal ranges.

At the age of 14 years the boy was hospitalized because of seizures. Laboratory and diagnostic tests gave normal results but the EEG displayed short-lived high voltage bursts of slow and sharp activity (waves). Brain magnetic resonance imaging was normal. Primary generalized epilepsy was diagnosed. The patient responded well to antiepileptic therapy.

DISCUSSION

Children with Asperger's disorder have behavioural disturbances characterized by impairment of social contact. Behavioural disturbances are similar to autism but without delayed of cognitive development. Their usual behaviour is stereotyped, repetitive and ritual. It may include feeding specificities such as favouring certain food (i.e. drinking only red coloured liquid, eating from a distinct dish and at a determined place). Some show particular skills in determined areas (5).

The disorder appears in about 1-5 per 10 000 children; boys are affected 3 to 4 times more than girls (3, 4, 6, 7). Patients may have other psychiatric and neurological disturbances, including epilepsy. According to recent reports, both autistic disorder and epilepsy occur in up to 30% of patients (8). There is a number of reports concerning the association of autism with GI disorders. Nevertheless, there are many factors which complicate the collection and interpretation of the pertinent information. The main obstacles are the non-uniform diagnostic criteria and difficulties in communication with autistic children. These patients are not able to describe their abdominal disturbances, and are not cooperative during diagnostic procedures (5). Thus, it is difficult to distinguish whether changes in behaviour are result of GI or neurological disorders (9).

Constipation, diarrhoea, abdominal pain, gastroesophageal refluxes, gaseousness and distension as well as functional disorders are frequently described in autistic children (3, 9, 10, 11). Data regarding alimentation and nutritive status are important in understanding changes that occur in the GI tract of autistic children. The feeding habits of these children are frequently strange and insufficient, and ascribed to the clinical features of pervasive developmental disorder (5). However, these children may also suffer from inflammatory bowel disease (IBD), food allergy and casein intolerance that require an adequate alimentary regimen. Erickson et al. differentiate gross pathologic, histological and microbiologic gut abnormalities in autistic children. The main pathologic changes revealed by EGDS include reflux esophagitis, chronic gastritis and chronic duodenitis (9, 10, 11). The finding of chronic gastroduodenitis in our patient suggested the presence of *H pylori*, which was confirmed on two occasions. However, in 36 cases reported by Horvath et al. (9) using the same bioptic procedure, *H. pylory* was not found in any of them.

Over the past decade, the possible association of autism and ileocecal diseases has attracted much attention. Wakefield et al. and other authors describe the existence of chronic inflammatory process in the GI tract of these children, i.e. lymphoid nodular hyperplasia of ileum and colon (12, 13). Active ileocolitis, characterized by an increase in intraepitelial lymphocytes and eosinophil infiltation of the *lamina propria* was found in 10% of autistic children. Since the patients did not manifest other signs of chronic IBD, the described disorder was named "autistic enterocolitis". Its fundamental cause remains unknown. Bearing in mind that Crohn's disease and ulcerative colitis appear rarely in children younger than 14, it is difficult to predict whether the disturbance would progress into *IBD phenotype*. At present there is no firm evidence of the existence of autistic enterocolitis as a separate clinical entity (14).

In our report the diagnosis of Crohn's disease was established on the basis of clinical signs and diagnostic procedures, including endoscopy and histology of bioptic material.

Based on our findings we may conclude that feeding disorders in children with pervasive developmental disorders should not *eo ipso* be considered as one of the presenting features of autistic behaviour. Clinical practice guidelines for the evaluation and management of pervasive developmental disorders do not include a routine consideration of potential gastrointestinal and other medical problems (5).

We therefore suggest that a thorough examination algorithm, including GI examination, is needed in these children in order to exclude the possible GI disease.

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S a ž e t a k

DJEČAK S ASPERGEROVIM POREMEĆAJEM, CROHNOVOM BOLEŠĆU I EPILEPSIJOM

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Aspergerov poremećaj pripada pervazivnim razvojnim poremećajima poznatijim kao autizam. Karakterizirani su poremećajima u socijalnoj interakciji, komunikaciji i ponašanju. Prehrambene navike tih bolesnika nerijetko su neobične i nedostatne, pa se često pripisuju kliničkoj slici pervazivnog razvojnog poremećaja. Uz neurološke autistična djeca često imaju i gastrointestinalne smetnje (opstipaciju, dijareju, abdominalnu bol, meteorizam i distenziju). Većina tih smetnji prisutna je i u kroničnim upalnim bolestima crijeva. Osim kliničkih, u djece s autističnim poremećajima opisane su i patohistološke promjene gastrointestinalnog sustava. Temeljem tih nalaza predlagalo se etablirati „autistični enterokolitis" kao samostalnu dijagnozu. Noviji radovi ipak preispituju utemeljenost tog nastojanja.

U članku smo opisali bolesnika s Aspergerovim poremećajem, jasno diferenciranom Crohnovom bolešću i epilepsijom, uz preporuku nadopune osnovnog algoritma pretraga autistične djece.

Deskriptori: DIJETE; CROHNOVA BOLEST; ASPERGEROV SINDROM; EPILEPSIJA

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