Clostridium in Autism, causal or casual?

Autism or autistic disorder was first described by Kanner in 1943. It is associated with abnormalities of communication, of social development and a restriction of behavioUr and interests.

The prevalence of autism is put at 30- 40 per 100,000 children and is four times as common in boys as in girls. Onset is usually before age of three (3) years

The etiology of autism has been a matter of speculation. Genetic abnormalities have been suggested because of higher concordance in monozygotic than dizygotic twins and higher prevalence among siblings of autistic patients. Organic brain disorder has been suspected as a cause because of increased frequency of obstetric complications (in pregnancy and birth) of autistic patients and increased association with epilepsy.

Autistic disorder is pervasive with no specific treatment but family support, behavioural modification and pharmacological treatment to reduce hyperactivity, aggression and self-injurious behaviours.

In recent times an association between autism and clostridium was noted. Bolte[1] outlined the possibility of a sub acute, chronic tetanus infection of the intestinal tract as the underlying cause for symptoms of autism observed in some individuals. He based his evidence on the fact that a significant percentage of individuals with autism have a history of extensive antibiotic use. The oral antibiotics significantly disrupt protective intestinal microbiota, creating a favorable environment for colonization by opportunistic pathogens such as clostridium tetani, a ubiquitous anaerobic bacillus, which produces neurotoxin. He explained that the neurotoxin travels along the vagus nerve to the central nervous system (by passing the normal preferential binding sites in the spinal cord and therefore the symptoms of a typical tetanus infection are not evident). He further explained that once in the brain, tetanus neurotoxin (TeNT) disrupts the release of neurotransmitters by the proteolytic cleavage of synaptobrevin, a synaptic vesicle membrane protein. This inhibition of neurotransmitter release was explained as the cause of a wide variety of behavioral deficits apparent in autism because laboratory animals injected with TeNT have exhibited many of these behaviours. Bolte concluded his evidence with the fact that some children with autism showed a significant reduction in stereotyped behaviours when treated with antimicrobials effective against clostridia.

Sandler and colleagues[2] recruited 11 children with regressive-onset autism into a study to demonstrate the usefulness of antibiotic in reducing symptoms of autism. Inclusion criteria included antecedent broad-spectrum antimicrobial exposure followed by chronic persistent diarrhea, deterioration of previously acquired skills, and then autistic features. Minimally absorbed oral antibiotic, vancomycin was then administered to the patients. Short-term improvement was noted using multiple pre- and post-therapy evaluations in 8 of the children studied suggesting a possible gut flora-brain connection.

To further support the evidence of a relationship between regressive autism and clostridia, Finegold and colleagues[3] compared the fecal flora count of children with regressive autism with that of control children. They demonstrated that children with autism had nine species of clostridia not found in controls, whereas controls yielded only 3 species not found in children with autism. In all, there were 25 different clostridia species found. In gastric and duodenal specimens, the most striking finding was total absence of non-spore-forming anaerobes and microaerophilic bacteria from control children and significant numbers of such bacteria from children with autism. These studies demonstrate significant alterations in the upper and lower intestinal flora of children with late-onset autism and may provide insights into the nature of this disorder. This has also supported by Martirosian's study of anaerobic intestinal microflora in pathogenesis of autism.[4]

The findings of association between clostridium and autism is mind bugling and quite challenging because it might provide the leading solution to the disabling disorder (autism) especially the regressive autism. The probable pathophysiology has also been reasonably explained by the various authors. However, the studies have not examined other reasons why there may be colonization of the gastro intestinal tract by clostridium other than antecedent broad spectrum antibiotic use and have also not explained why other children who were equally exposed to broad spectrum antibiotics have not developed autism. A possible genetic predisposition or some yet other factors may be responsible for this.

In a study by Horvath and colleagues[5] histological examination of 36 children with autistic disorder showed that significant percentage of the children had oesophagitis, chronic gastritis, and chronic duodenitis. They also had low intestinal carbohydrate digestive enzyme activities, increase pancreatico-biliary fluid out put after intravenous secretin administration. The authors suggested that these disorders especially reflux oesophagitis and disaccharide malabsorption may contribute to the behavioral problems of the non-verbal autistic patients. In my own opinion carbohydrate malabsorption could on its own have contributed to the growth of clostridia through fermentation and subsequent provision of an enabling anaerobic environment for these bacteria to thrive.

In the light of these findings further studies are necessary to explore the relationship between these gastrointestinal disorders in autism and clostridium colonization. Again, if TeNT is to be held responsible for the behavioral problems in autism, the proponents have not explained why local gastrointestinal symptoms, similar to local tetanus, are not reported in autistic disorder. It is also expected that reported cases of autistic disorder would be higher in developing countries of Africa where hygiene is still a problem. This has not been the case. Though there is dearth of literature on the prevalence of autistic disorder in

developing countries, clinical practice has not shown that autism is so prevalent.

The challenge to researchers is how to marry these issues together and provide more convincing evidence supporting or refuting the association between autism and microbes and clarifying whether it is causal or casual. A definite link may bring succor to autistic children just as penicillin did to once thought irredeemable conditions like paralytic disease of the insane.

The motive for this write up is actually borne out of curiosity; as a psychiatrist who has interest in sub specializing in child psychiatry, and also concern that a solution has not been found for a disorder as serious as autism. So, when I came across Sandler et al's[2] article in a journal of child neurology I was prompted to look for related works on the subject. I have also reached an agreement with microbiologists at our center here to investigate the relationships between autism and clostridium, if any. This is therefore a call to other people to join those who are already in the process.

References

1. *Bolte ER. Autism and Clostridium tetani. Med Hypothesis 1998; 51(2):133-144.*
2. *Sandler RH, Finegold SM, Bolte ER, Buchanan CP, Maxwell AP, Vaisanen ML, et al. Short-term benefit from oral vancomycin treatment of regressive-onset autism. J Child Neurol 2000;15(7):429-435.*
3. *Finegold SM, Molitoris D, Song Y, Liu C, Vaisanen ML, Bolte E, et al. Gastrointestinal microflora studies in late-onset autism. Clin Infect Dis 2002; 35(Suppl 1):S6-S16*
4. *Martirosian G. Anaerobic intestinal microflora in pathogenesis of autism? Postepy Hig Med Dosw (Online) 2004; 20(58):349-351.*
5. *Horvath P, Papadimitriou JC, Rabztyn A, Drachenberg C, Tildon JT. Gastrointestinal abnormalities in children with autistic disorder. J Pediatr 1999; 135(5):559-563.*

Dr BA Issa
Department of Psychiatry, College of Health Sciences, Ladoke Akintola University of Technology, Osogbo, Osun State, Nigeria
email:issababa2002@yahoo.com