

## Short Communication

# Gluten hyper sensitivity: an unseen storm of neurological spectrum disorders

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### ABSTRACT

Gluten sensitivity, an autoimmune systemic disease with its protean manifestation occur in genetically susceptible individuals with gluten in their diet. Coeliac disease is the intestinal form of disease mostly seen in children with predominant gastrointestinal manifestations. The neurological presentation of gluten sensitivity mostly without enteropathy are also frequent and affect adult population in contrast. The most common presentation includes cerebellar ataxia, peripheral neuropathy and seizure followed by encephalopathy, schizoaffective and movement related manifestations. These varied clinical presentations are attributed to an immune related attack on central and peripheral nervous system involving both adaptive and innate immunity. Early suspicion, prompt diagnosis and institution of gluten free diet provides remarkable benefits to these patients with amelioration of troublesome symptoms. A better understanding of disease etiopathogenesis is likely to add more therapeutic options.

**Keywords:** Ataxia, Coeliac disease, Gluten-free, Gluten sensitivity, Neuropathy

## INTRODUCTION

Being considered as a disease of paediatric age group as coeliac disease (CD), now the gluten sensitivity disorder is a well-recognised entity in adult population with varied symptoms ranging from mild gastrointestinal symptoms to debilitating neurological involvement.<sup>1</sup>

Coeliac disease causes the body immune system to respond by attacking the intestinal mucosal epithelium with resultant malabsorption of vital nutrients. Non coeliac gluten sensitivity on the other hand does not affect the gastrointestinal tract lining and is otherwise also more common than CD.

Gluten related disorder represents a spectrum of manifestations sharing a common trigger i.e. ingestion of gluten. As with other autoimmune disorders it is more prevalent in women.

## *Etiopathogenesis*

Gluten (a protein present in wheat, rice or barley) induces an immune reaction in host leading to coeliac disease in 1% population of children worldwide. The clinical presentations are generally characterised by gastrointestinal symptoms in form of bloating, steatorrhea and weight loss. The diagnosis rests upon triad of duodenal villous atrophy, cryptal hyperplasia and increased intraepithelial lymphocytic response with or without auto antibodies against gluten i.e. transglutaminase (TG) or endomysial antibodies (EMA).<sup>2</sup>

In recent years another gluten related disease entity 'Non Coeliac Gluten Sensitivity' (NCGS) is emerging in adult population with as much as six times greater in frequency than CD. Predominantly it manifests with extra intestinal features in form of neuropsychiatric presentation and lacks enteropathy on duodenal biopsy but with presence of auto

antibodies against gliadin (present in gluten) i.e. antigliadin IgG and/or IgA.<sup>3</sup>

Improvement of systems on a gluten free diet (GFD) in presence of normal duodenal biopsy with sero positivity defines NCGS. In other words NCGS is the term used to describe patients with primary extra gastrointestinal symptoms (related with ingestion of gluten in diet) without any associated gastropathy and could be benefitted by a gluten free diet.

### ***Neurological spectrum of gluten sensitivity***

Although neurological manifestation occur in almost equal frequency in CD and NCGS involving both central and peripheral nervous system. Due to lack of gut involvement and related symptoms, the primary presentation of NCGS is related with neurological and psychiatric manifestations.<sup>4</sup> The various neurological presentation in NCGS are as follows:

#### ***Cerebellar ataxia***

It is a sporadic, insidious onset, progressive ataxia responsible for almost 40% of all cases of idiopathic ataxias. Amongst the protean neurological manifestation, the one best characterised in NCGS is ataxia now termed as 'Gluten Ataxia'. It manifests either as limb ataxia (both upper and lower limbs), gait ataxia or dysarthria. This is related with loss of purkinje cells with atrophy and gliosis of cerebellum especially vermis.<sup>5</sup>

Loss of purkinje fibres is irreversible so embarkment on a strict gluten free diet early in the disease process results in improvement or stabilisation of ataxia. The elimination of anti-gliadin antibodies in serum further correlates with improvement in ataxia test scores.

#### ***Peripheral neuropathy***

The second most common manifestation of gluten sensitivity is peripheral neuropathy which is usually chronic, gradually progressive large fibre neuropathy with serological gluten sensitivity. The most common type being symmetrical, sensory-motor, axonal, length dependant neuropathy affecting the limbs which is seen in around 70-75% cases. Involvement of small fibres i.e. A delta and C fibres presenting as painful burning sensations in distal parts especially in sole and figure tips is also seen. This small fibre neuropathy is often associated with the large fibre one.<sup>6</sup>

The role of IVIG in these subset of patients is still not well documented.

#### ***Epileptic seizures***

Epilepsy in gluten sensitivity encompasses full spectrum of semiology with or without overt radiological features on neuroimaging in the form of cerebral calcification,

hippocampal sclerosis or temporal lobe etiology.<sup>7</sup> These patients may or may not respond to conventional anti-epileptic drugs (AED) but those patients who fall in category of medically refractory epilepsy being unresponsive to AED alone can be benefitted further with gluten free diet.<sup>8</sup>

#### ***Gluten encephalopathy***

The presentation of severe headache, brain fog, slow thinking along with cognitive and memory impairment is also considered to be a part of neurological gluten syndrome. These symptoms correlates well with white matter abnormalities on MRI which generally gets arrested with gluten free diet along with clinical improvement.

The less common neurological manifestation includes vertigo, insomnia, anxiety, depression, schizophrenia and bipolar disorder. It has been postulated that gluten related intestinal damage may cause deficit in nutrients (especially Vitamin B) which responsible for anxiety and depression in these patients but the occurrence of these symptoms in patients who are well nourished further complicates the issue. The spectrum of gluten syndrome extend to involve headache, developmental and learning delay and dysautonomia as its clinical presentation.<sup>9</sup>

#### ***Clinical suspicion***

As a natural course people with gluten related neurological disorders i.e. NCGS are diagnosed as much as 8-10 years later in comparison to those who have gut symptoms because typical gastrointestinal symptoms of coeliac disease makes the suspicion more stronger.

The clinical suspicion of coeliac disease or NCGS rests upon unexplained neurological symptoms especially headache, peripheral neuropathy and ataxia. In the laboratory antigliadin antibodies may be a useful marker. Recently estimation of tTG6 antibody titres are closely related to gluten related neurological disorders.<sup>10</sup>

#### ***Treatment***

Strict 'Gluten free diet' remains the corner stone of treatment for those individuals having manifestations in the form of gluten related ataxia or peripheral neuropathy as sole neurological involvement. Only limited patients may require additional mycophenolate or immunosuppressive agents to control their neurological issues.

## **DISCUSSION**

Sharing the common etiological agent 'the gluten', coeliac disease of childhood is represented more commonly as non coeliac gluten sensitivity (NCGS) in adults. Lacking the gastrointestinal symptoms and associated histopathological trial, the NCGS characterises with predominantly neuropsychiatric manifestations.<sup>11</sup> The

unexplained neurological symptoms in form of ataxia, peripheral neuropathy, epilepsy and encephalopathy along with psychiatric illness like anxiety, depression and bipolar disorder should raise a strong suspicion to gluten related disorders. This etiological consideration in most of the cases is delayed by many years due to prevalence of other common diseases which bears the similar semiology as NCGS. Abstinence from gluten as a therapeutic measure leads to marked improvement in symptoms. The institution of 'gluten free diet' is probably the cheapest way to treat these patients, but an early suspicion and diagnosis by exclusion is warranted.<sup>12</sup> More insight in down regulation of immune system and resultant clinopathological features is required to understand the gluten related diseases and their better therapeutic options in future.

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## REFERENCES

1. Marsh MN. The natural history of gluten sensitivity: defining, refining and re-defining. *QJM: Int J Med.* 1995 Jan 1;88(1):9-13.
2. Dicke WK, Weijers HA, KAMER JV. Coeliac Disease The Presence in Wheat of a Factor Having a Deleterious Effect in Cases of Coeliac Disease. *Acta Paediat.* 1953 Jan;42(1):34-42.
3. Grodzinsky E, Franzen L, Hed J, Ström M. High prevalence of celiac disease in healthy adults revealed by antigliadin antibodies. *Ann Aller.* 1992 Jul;69(1):66-70.
4. Cooke WT, Smith WT. Neurological disorders associated with adult celiac disease. *Brain.* 1966 Dec 1;89(4):683-722.
5. Hadjivassiliou M, Grünewald RA, Chattopadhyay AK, Davies-Jones GA, Gibson A, Jarratt JA, et al. Clinical, radiological, neurophysiological, and neuropathological characteristics of gluten ataxia. *Lancet.* 1998 Nov 14;352(9140):1582-5.
6. Hadjivassiliou M, Chattopadhyay AK, Davies-Jones GA, Gibson A, Grünewald RA, Lobo AJ. Neuromuscular disorder as a presenting feature of coeliac disease. *J Neurol, Neurosurg Psych.* 1997 Dec 1;63(6):770-5.
7. Bouquet F, Ventura A, Gobbi G, Greco L, Lambertini A, Zaniboni MG, Tassinari CA. Coeliac disease, epilepsy, and cerebral calcifications. *Lancet.* 1992 Aug 22;340(8817):439-43.
8. Julian T, Hadjivassiliou M, Zis P. Gluten sensitivity and epilepsy: a systematic review. *J Neurol* 2018;16(8):1014-38.
9. Catassi C, Rättsch IM, Fabiani E, Rossini M, Coppa GV, Giorgi PL, et al. Coeliac disease in the year 2000: exploring the iceberg. *Lancet.* 1994 Jan 22;343(8891):200-3.
10. Zis P, Rao DG, Sarrigiannis PG, Aeschlimann P, Aeschlimann DP, Sanders D, et al. Transglutaminase 6 antibodies in gluten neuropathy. *Digest Liver Dis.* 2017 Nov 1;49(11):1196-200.
11. Holmes GK. Neurological and psychiatric complications in coeliac disease. Epilepsy and other neurological disorders in coeliac disease. London: John Libbey. 1997;251:64.
12. Hadjivassiliou M, Davis Jones GAB, Sanders DS, Grünewald RAG. Dietary treatment of gluten ataxia. *J Neurol Neurosurg Psych.* 2003;74(9):1221-4.

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