CELIAC DISEASE, EPILEPSY, CEREBRAL CALCIFICATIONS: A MODEL OF IMMUNO-MEDIATED NEUROLOGICAL PATHOLOGY.

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Celiac disease, epilepsy and cerebral calcification syndrome (CEC) is a rare disorder characterized by the combination of auto-immune intestinal disease, epileptic seizures and cerebral calcifications.

CEC was first described in 1992 and less than 200 cases have been reported so far.

Celiac disease (CD) and epilepsy manifest at a variable age, and diagnosis of CD is frequently done in late childhood, when specific investigations are led secondary to observation of epileptic seizures and cerebral calcifications (CC). CD can present with a typical form characterized by chronic diarrhea, weight loss, short stature, anorexia, irritability and vomiting. In CEC patients, CD usually presents as silent or latent or paucisymptomatic form, which are characterized - in absence of gastrointestinal symptoms - by dermatitis herpetiformis, dental enamel defects or autoimmune thyroiditis. Epilepsy's onset is between infancy and adulthood; most cases occur in early childhood. Most patients present with occipital epileptic seizures, the evolution being highly variable, with benign, drug-resistant, or epileptic encephalopathy forms. In the latter, severe intellectual disability and/or learning disorders have been reported while a mild mental deterioration is observed in only one third of all CEC cases. CC are seen in subcortical parieto-occipital regions. CC size does not change significantly over time, but in several cases, new CC appeared in other regions. Patients with CC and CD without epilepsy are considered as having an incomplete form of CEC. Some patients with epilepsy and CC without CD are supposed to have a CEC with latent CD.

It has been supposed that epilepsy and/or CC are a consequence of an unrecognized (or late recognized) CD. In fact, CD is an immune auto-inflammatory disorder which may induce autoimmune responses outside the gastrointestinal tract. In CEC patients it has been supposed that circulating activated T cells may cross the blood-brain barrier and be toxic to myelin or myelin-producing cells. Recently, high levels of immunoglobulin-A directed against transglutaminase isoenzyme 6 (TG6) have been found in the CEC patient's serum. More over, as for isolated CD, CEC is associated with *HLA-DQ2* and *HLA-DQ8* genes. Finally, studies revealed that early CD diagnosis and good compliance of GFD greatly improve patients' outcome. On the contrary, if treatment is delayed, epilepsy may be more severe and epileptic encephalopathy may develop.