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Causes of childhood epilepsy: A look for celiac disease?

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2 **Causes of childhood epilepsy: A look for celiac disease?**
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18 Conflicts of interest: none to declare.
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33 Key words: Children - Coeliac disease - Diet - Gluten - PRES
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1 Dear Editor,
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4 Epilepsy is a protean disease caused by many aetiologic factors like congenital syndromes, hypoxia,
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6 metabolic disorders, trauma. In a recent study Sanlidag et al. evaluated aetiologic factors and
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8 neurologic and/or psychiatric comorbidities among children affected by epilepsy in Cyprus. Two
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10 hundred and fifty-four children were enrolled. In most of the patients (78%) an aetiologic factor of
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12 epilepsy was not found. Neurologic insult (haemorrhage, ischemia or hypoxia) was the most prevalent
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14 identified aetiologic factor (10.6%), followed by genetic syndrome (4.7%), metabolic disorders (2%),
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16 neurocutaneous syndromes (1.2%) and a miscellanea of causes (tumours, central nervous system
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18 infections, autoimmune encephalitis) (3.5%). Regarding neurologic comorbidities, 12.4% of children
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20 suffered from migraine and headache too. Regarding psychiatric comorbidities, attention
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22 deficit/hyperactivity disorder (ADH) was present in 11.8% of children and autism spectrum disorders
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24 in 1.2%, at least one among anxiety or depression or aggression or oppositional defiant was reported in
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26 5.9% of cases.¹
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32 Celiac disease (CD) is a chronic, immune-mediated disorder, characterized by malabsorption and
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34 villus atrophy of the small intestine after ingestion of gluten (present in wheat) or related proteins
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36 (present in rye and barley), in genetically susceptible individuals expressing the HLA class II molecules
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38 DQ2 or DQ8. Furthermore, following strict adherence to a gluten-free diet in most of the patients a
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40 prompt clinical and histologic improvement is observed.² The overall prevalence of CD varies between
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42 0.7% and 2%. The clinical manifestations of the disease vary greatly, and range from typical
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44 gastrointestinal manifestations (diarrhoea, bloating, growth retardation, abdominal pain, vomiting,
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46 muscle wasting, nutritional deficiencies) to absent, minimal, or unusual intestinal complaints with
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48 extraintestinal manifestations or disorders (atypical CD).^{2,3} Neurologic manifestations have been
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50 reported in about 6-10% of patients with CD. In particular, the more frequent described diseases have
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1 been cerebellar ataxia, peripheral neuropathy, migraine, autism, dementia, multifocal
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4 leukoencephalopathy and epilepsy. The clinical spectrum of epilepsy associated to CD ranges from
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6 benign syndromes to intractable epilepsy with evolution to a severe encephalopathy, including
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8 progressive myoclonic epilepsy. Confirmed evidence of an association between temporal lobe epilepsy
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10 with hippocampal sclerosis and gluten sensitivity has been provided. Although the precise mechanism
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12 of association between CD and epilepsy remains unknown, several hypotheses have been proposed. For
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14 example, it has been suggested that the antibodies associated with CD may be themselves neurotoxic
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16 or, alternatively, these may be a marker for a neurotoxic immunological process.⁴ Children with CD are
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18 also at increased risk for mood disorders (relative risk, RR: 1.2; 95% confidence interval, CI: 1.0-1.4),
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20 anxiety disorders (RR: 1.2; 95% CI: 1.0-1.4), attention deficit hyperactivity disorder (ADHD) (hazard
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22 ratio, HR: 1.2; 95% CI: 1.0-1.4).⁵ Psychiatric disorders occurring before the diagnosis of CD may be
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24 attributed to active CD, resulting in cerebral hypoperfusion, presence of proinflammatory cytokines,
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26 and low folate levels. However, the exact mechanisms underlying the association between CD and
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28 psychiatric disorders have yet to be established.
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34 In conclusion, considering these data we suggest that measurement of anti-tissue transglutaminase
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36 and anti-endomysium immunoglobulin A should be performed in patients with epilepsy and psychiatric
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38 comorbidities (antibody-positive patients should be offered a duodenal biopsy), especially in children.⁶
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40 In this population, a gluten free diet in case of concomitant CD could have beneficial effects not only
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42 on seizures control but also in the management of the associated neurologic and psychiatric disorders.
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