Autonomic neuropathy and coeliac disease

C H Gibbons, R Freeman

Coeliac disease ( gluten sensitive enteropathy) is the
commonest manifestation of gluten sensitivity, how-
ever, diverse manifestations may accompany the dis-
order.1 2 Several recent reports have drawn attention to
the association between gluten sensitivity and elevated anti-
gliadin antibodies and neurological disorders. Neurological
manifestations associated with gluten sensitivity include
cerebellar ataxia, myelopathy, myopathy, and peripheral
neuropathy.1 3 Although the prevalence of antigliadin anti-
bodies in patients with idiopathic peripheral neuropathy
may be as high as 40%, a recent study suggested that the
prevalence of biopsy proven coeliac disease in a referral
population of idiopathic peripheral neuropathy patients
is approximately 2.5%.2

Dysautonomia is seen in disorders of the central and
peripheral nervous systems. In many patients, however, no
underlying cause is found.3 In one series, patients with
known coeliac disease had subclinical abnormalities of
autonomic function when tested but no autonomic symp-
toms other than the gastrointestinal symptoms characteristic
of coeliac disease.4 We report four patients with biopsy
proven coeliac disease and symptomatic, laboratory con-
ﬁrmed dysautonomia from a group of 164 patients referred
for autonomic testing.

PATIENTS AND METHODS

We retrospectively reviewed the history, physical examina-
tion, and autonomic testing of all patients referred to the
Autonomic Function Laboratory for suspected autonomic
dysfunction during a one year period. Four patients were
identiﬁed among 164 to have coeliac disease and autonomic
dysfunction. The patients’ details are summarised in table 1.

Other identifiable causes of dysautonomia were excluded.
One patient with positive IgA antigliadin antibodies without
conﬁrmatory biopsy was excluded. A sixth patient with
elevated antigliadin antibodies and a positive biopsy was
excluded due to a history of diabetes as a possible cause of
dysautonomia.

All four patients initially presented to their general
practitioner with nausea, were diagnosed as having coeliac
disease by IgA antigliadin antibodies, and had characteris-
tic ﬁndings on small bowel biopsy. All had a diagnosis of biopsy
conﬁrmed coeliac disease prior to neurological evaluation.

Initiation of a gluten free diet did not improve the nausea.
Patients were referred for autonomic evaluation due to
symptoms of nausea and lightheadedness on average one
year (range 8–14 months) from the diagnosis of coeliac
disease.

All patients described nausea that occurred while sitting or
standing but was absent while supine. All gave a history of
syncopal or presyncopal episodes pre-dating the diagnosis of
coeliac disease. Other autonomic symptoms included palpita-
tions and lightheadedness. None of the patients experienced
traditional symptoms of coeliac disease such as diarrhoea,
and only one (patient 4) experienced constipation.

All patients had normal cognitive, cranial nerve, motor,
reflex, coordination, sensory, and gait examinations. Auto-
nomic testing included inspiratory to inspiratory heart
rate variability, Valsalva manoeuvre with blood pressure and
heart rate analysis, tilt table testing to 60˚ for 45 minutes,
and ﬁve minute stand. We compared the results to age
related normative values.5 The results of the autonomic tests
are shown in table 1. Abnormalities in parasympathetic and
sympathetic function were present. The heart rate response to
the Valsalva manoeuvre, a measure of cardiac parasympa-
thetic nervous system function, was abnormal in three of
the four patients. In addition, abnormal measures of sympathetic
nervous system function were present. The blood pressure
response to the Valsalva manoeuvre was abnormal in all
patients (ﬁg 1). Two patients had orthostatic hypotension on
tilt table testing and active standing (a fall greater than
20 mm Hg systolic or 10 mm Hg diastolic blood pressures).6
The other two patients had a postural tachycardia syndrome
(defined as rise in heart rate of 30 beats per minute or more
without a signiﬁcant fall in blood pressure).7

The patients did not notice a change in symptoms while
following a gluten restricted diet, however, they all indicated
poor compliance. In two of the four patients repeated testing
for antigliadin antibodies demonstrated a reduction, but not
an absence, of antibodies. Treatment with volume expansion
and α-adrenoreceptor agonist therapy gave some relief of
symptoms but none of the patients returned to baseline level
of functioning.

DISCUSSION

We report four patients with antigliadin antibodies, coeliac
enteropathy, and dysautonomia. Although the association
between neurological disease and gluten sensitivity has been
reported frequently,1 2 given the high percentage of anti-
gliadin antibodies in the general population (6–12%) the
aetiological signiﬁcance of this association is uncertain in
most patients.6 8 Still less is known about the potential
mechanisms whereby gluten sensitivity might result in
neurotoxicity. Nutritional factors and other disorders, such
as diabetes and Sjögren’s syndrome, that are associated with
coeliac disease and may cause neurological illness were
excluded in our patients. It is speculated that in genetically
predisposed individuals antigliadin antibodies or other
associated antibodies may cause nerve injury.6 9 Although
antigliadin antibodies have been associated with ataxia and

http://jnnp.bmj.com/ on September 14, 2016 - Published by group.bmj.com
peripheral neuropathy, the relation between these antibodies and dysautonmia is not established. In a single report of patients with coeliac disease and oesophageal dysmotility, subclinical abnormalities of cardiovascular reflexes were present in 19% (5/27) of patients.4

In our patients, nausea, which was postural in nature, was the primary symptom for referral. Other reported autonomic symptoms included lightheadedness, palpitations, fatigue, presyncope, and syncope. Autonomic test results revealed abnormalities in sympathetic and parasympathetic nervous system functions. These symptoms and test findings are not unique to coeliac disease patients and can be seen in other patients with dysautonomia. Our patients did not improve on a gluten restricted diet, an experience reported by other investigators.2 There are several possible explanations for this. Firstly, the patients were not closely monitored, and all admitted to dietary indiscretion. The two patients with repeated antibody testing had titres that, although reduced, remained elevated, suggestive of continued dietary intake of gluten. Secondly, it is possible that structural nerve damage, once present, is not responsive to dietary measures.9

Patients with gluten sensitivity and symptomatic dysautonomia have not been previously described. At our laboratory, 2.4% of 164 patients referred for autonomic evaluation had idiopathic dysautonomia and biopsy proven coeliac disease, a frequency similar to that reported in patients with idiopathic

### Table 1 Characteristics and autonomic test results of patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age/Sex</strong></td>
<td>38/M</td>
<td>78/F</td>
<td>54/F</td>
<td>63/F</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td>Postural nausea; lightheadedness; presyncope</td>
<td>Postural nausea; lightheadedness; syncope</td>
<td>Postural nausea; lightheadedness; syncpe</td>
<td>Postural nausea; lightheadedness; weakness; fatigue; syncope</td>
</tr>
<tr>
<td><strong>Baseline heart rate (beats per minute)</strong></td>
<td>75</td>
<td>66</td>
<td>72</td>
<td>85</td>
</tr>
<tr>
<td><strong>Baseline blood pressure (mm Hg)</strong></td>
<td>121/64</td>
<td>142/74</td>
<td>128/66</td>
<td>180/92</td>
</tr>
<tr>
<td><strong>Heart rate variation with respiration (average max-min)</strong></td>
<td>23 (/&gt;12 nl)</td>
<td>10 (&lt;7 nl)</td>
<td>11 (&gt;9 nl)</td>
<td>6* (&gt;7 nl)</td>
</tr>
<tr>
<td><strong>Heart rate response to Valsalva manoeuvre</strong></td>
<td>1.33* (&gt;1.5 nl)</td>
<td>1.44 (&gt;1.39 nl)</td>
<td>1.19* (&gt;1.47 nl)</td>
<td>1.07* (&gt;1.39 nl)</td>
</tr>
<tr>
<td><strong>Highest heart rate response to tilt</strong></td>
<td>112*</td>
<td>86</td>
<td>104*</td>
<td>108</td>
</tr>
<tr>
<td><strong>Lowest blood pressure response to tilt</strong></td>
<td>112/60</td>
<td>105/52*</td>
<td>122/72</td>
<td>114/62*</td>
</tr>
<tr>
<td><strong>Highest heart rate response to five minute stand</strong></td>
<td>106</td>
<td>84</td>
<td>116</td>
<td>110</td>
</tr>
<tr>
<td><strong>Lowest blood pressure response to five minute stand</strong></td>
<td>116/68</td>
<td>115/68*</td>
<td>132/70</td>
<td>128/64*</td>
</tr>
</tbody>
</table>

*Abnormal response.

Figure 1 The response of each patient to a Valsalva manoeuvre is shown. In each graph, the beat to beat blood pressure is shown on the top and the expiratory pressure on the bottom. All patients had reduced pulse pressure during phase II, and no late phase II recovery of blood pressure. Patient 2 showed an abnormal phase I of the Valsalva. Only patient 4 showed a phase IV overshoot.
peripheral neuropathy.\textsuperscript{2} If corroborated by additional studies, this report could suggest that screening for coeliac disease should be considered in selected patients with autonomic neuropathy of uncertain aetiology. A prospective study evaluating patients presenting with idiopathic dysautonomia for coeliac disease is warranted.

\textbf{Authors’ affiliations}
\begin{itemize}
  \item \textbf{C H Gibbons, R Freeman,} Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA
\end{itemize}

Competing interests: none declared

Correspondence to: Dr R Freeman, Autonomic and Peripheral Nerve Laboratory, Department of Neurology, Beth Israel Deaconess Medical Center, 1 Deaconess Road, Boston, MA 02215, USA; rfreeman@bidmc.harvard.edu

Received 11 June 2004
Revised version received 26 July 2004
Accepted 14 August 2004

\textbf{REFERENCES}
\begin{enumerate}
  \item Cross AH, Golumbek PT. Neurologic manifestations of celiac disease: proven, or just a gut feeling? Neurology 1994;(suppl).
  \item Cross AH, Golumbek PT. Neurologic manifestations of celiac disease: proven, or just a gut feeling? Neurology 2003;60:1566–8.
\end{enumerate}
Autonomic neuropathy and coeliac disease

C H Gibbons and R Freeman

*J Neurol Neurosurg Psychiatry* 2005 76: 579-581
doi: 10.1136/jnnp.2004.047480

Updated information and services can be found at:
http://jnnp.bmj.com/content/76/4/579

These include:

References
This article cites 7 articles, 5 of which you can access for free at:
http://jnnp.bmj.com/content/76/4/579#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

- Neuromuscular disease (1268)
- Peripheral nerve disease (614)
- Brain stem / cerebellum (655)
- Muscle disease (247)
- Musculoskeletal syndromes (519)
- Radiology (1685)
- Spinal cord (520)
- Surgical diagnostic tests (378)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/