

[ LETTERS TO THE EDITOR ]

**Gastro-intestinal Involvement in m.3243A>G-associated Mitochondrial Myopathy, Encephalopathy, Lactic Acidosis, and Stroke-like Episodes**

**Key words:** chronic intestinal pseudo-obstruction, mitochondrial DNA A3243G mutation, MELAS, familial occurrence, gastrointestinal symptoms

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**The Authors Reply** Thank you for your letter regarding our case report of three patients harboring the mitochondrial DNA A3243G (m.3243A>G) mutation, which manifested as chronic intestinal pseudo-obstruction (1).

The pathophysiology of chronic intestinal pseudo-obstruction caused by the m.3243A>G mutation was uncertain, and the presence of either myenteric plexus neuropathy or visceral myopathy was hypothesized. Supporting the presence of visceral myopathy, the accumulation of numerous enlarged abnormal mitochondria in intestinal smooth muscle cells and the mucosal layer was observed, and cytochrome c oxidase deficiency was specifically confined to smooth muscle cells of the muscularis mucosa, outer muscularis externa, inner muscularis externa, and smooth muscle lining of large arterioles. Furthermore, the m.3243A>G mutation was nearly homoplasmic at these sites (2). Unfortunately, because an autopsy was not permitted in any of the three cases, the pathophysiology of chronic intestinal pseudo-obstruction therein was unclear.

In a previous study, 80% of patients with mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) and more than 60% of m.3243A>G mutation carriers were found to present with 1 or more autonomic symptoms. Gastrointestinal symptoms are especially common in patients with MELAS, occurring in 66% of these patients, and have been found to occur in almost 40% of mutation carriers (3). In our studied cases, patients 1 and 2 did not present with any autonomic dysfunction, such as increased light sensitivity, dry mouth, dry eyes, orthostatic hypotension, abnormal heart-rate variability, urinary dysfunction, or dry skin, except for obstipation. Patient 3 presented with urinary retention and obstipation.

The autonomic function of these patients was not evalu-

ated using the head-up tilt test, ambulatory blood pressure and heart rate monitoring, thermoregulatory sweat test, urodynamics, or electrogastrography, because all patients presented chronic intestinal pseudo-obstruction at an advanced clinical stage.

With regard to gastrointestinal compromise, patients 1 and 2 had vomiting, diarrhea, poor appetite, and chronic intestinal pseudo-obstruction. Patient 3 had vomiting, diarrhea, poor appetite, dysphagia, a gallbladder stone, and chronic intestinal pseudo-obstruction. We agree that gastrointestinal symptoms are common in mitochondrial disorders, and intestinal pseudo-obstruction is the most severe form of mitochondrial disorders affecting gastrointestinal motility. A recent report indicated that, among eight deceased patients with the m.3243A>G mutation and intestinal pseudo-obstruction, four died of aspiration pneumonia associated with the intestinal pseudo-obstruction (4). In our cases, patients 1 and 3 died of aspiration pneumonia associated with intestinal pseudo-obstruction at an advanced clinical stage. Therefore, we consider intestinal pseudo-obstruction to be an important prognostic factor in patients harboring the m.3243A>G mutation.

**The authors state that they have no Conflict of Interest (COI).**

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