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Episodic vomiting and pseudo-obstruction like syndrome associated with mitochondrial DNA 3243 point mutation

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General Note
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ABSTRACT

A 55-year-old woman with mitochondrial DNA 3243 point mutation developed episodic vomiting repeatedly. Abdominal radiography revealed small intestinal gas like adynamic ileus or pseudo-obstruction. She presented with short stature as physical characteristics, hearing loss, and diabetes mellitus. Her predominant clinical symptom, however, has been only episodic vomiting

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with adynamic ileus or pseudo-obstruction and it is quite uncommon. Mitochondrial DNA 3243 point mutations cause episodic vomiting similar to adynamic ileus and sometimes it may be called pseudo-obstruction.

Keywords: 3243 point mutation, MELAS (mitochondria encephalopathy, lactic acidosis, strokelike episode), hearing loss, episodic vomiting, pseudo-obstruction

Abbreviations: MELAS-mitochondria encephalopathy, lactic acidosis, strokelike episode; MNGIE: mitochondrial neurogastrointestinal encephalomyopathy

1. INTRODUCTION

MELAS (mitochondrial encephalopathy, lactic acidosis, strokelike episodes) is a multisystem disorder with onset typically in childhood and short stature is common (DiMauro and Hirano, 2001). The most common initial symptoms are generalized tonic-clonic seizures, recurrent headaches, anorexia, and recurrent vomiting. Exercise intolerance or proximal limb weakness can be the initial manifestation. Seizures are often associated with stroke-like episodes. Sensorineural hearing loss is common. Presenting with only episodic vomiting especially with adynamic ileus or pseudo-obstruction is, however, quite uncommon. We encountered a patient presented with episodic vomiting associated with mitochondrial DNA 3243 point mutation. Here we report clinical features of the patient.

2. CASE REPORT

A 55-year-old woman admitted to the hospital because of vomiting. She had been well until approximately 3 days before admission, when she developed common cold and vomiting. She continued vomiting from 2 days before. She was unable to eat and drink because of vomiting. She developed faintness. She admitted to the hospital.

Twenty years earlier, she was diagnosed as diabetes mellitus. Ten years earlier, she developed hearing loss, and mitochondrial DNA 3243 point mutation was revealed. Thereafter, she has developed nausea. She has developed episodic vomiting approximately once per year for 6 years. A few days after episodic vomiting began, she called ambulance and admitted to hospitals. Intravenous fluid improved her condition and she was discharged from 1 week to 10 days. She admitted due to episodic vomiting 2 years before and twice last year. Metoclopramide has been prescribed for 2 years. She has never developed lactic acidosis, seizure, headache, or stroke like episode.

Her father died of lung cancer at 9th decade. Her mother died of lung cancer at 8th decade. She has 1 brother and 3 sisters. Her brother died in infancy. Her 2 sisters developed diabetes. She has 2 sons and 4 daughters. One of her sons has hearing loss. She has neither drunk nor smoked. She has been a housewife.

Neurological examination showed as follows: short stature and high arched palate. Her height was 143cm and her weight was 35kg. She was oriented regarding place. She was unable to say the date. She was able to perform easy subtractions. Her auditory comprehension and repetition were good. Her visual acuity was normal. Her visual field was normal. Her ocular movements were normal. She presented with hearing loss. Her soft palate elevation was diminished. Her tongue did not show atrophy and did not deviate at protrusion. She showed normal muscle strength. Her extremities especially lower extremities were thin. Her muscle tonus was normal. She showed no involuntary movement. She showed generalized areflexia with normal triceps reflexes. She showed no pathological reflex. Plantar responses were indifferent. She showed mild ataxia of lower extremities: heal shin tests showed that bilateral heal flailed above the tibiae whereas finger nose tests and rapid alternative movements were normal. She presented with mild sensory abnormality: vibration senses of bilateral wrists were slightly decreased. The remainder examinations were normal. Auscultation of her abdomen showed no bowel sound.

Laboratory examination showed as follows: total protein 8.7 g/dL BUN 84.0 mg/dL creatinine 1.2 mg/dL Cl 94mEq/L CK 60 U/L glucose 305 mg/dL HbA1c 7.8% pyruvate 0.6 mg/dL lactate 17.0 mg/dL BNP 382.0 pg/mL. Urinalysis showed protein 2+ glucose 4+ ketone 1+ occult blood 1+. The remainder examinations were normal. Nerve conduction study showed only absence of H reflex and slightly delayed minimal latencies of F waves (right median nerve 25.2 m/s, right ulnar nerve 24.5 m/s, and right tibial nerve 44.4 m/s) and otherwise normal. Electrocardiography showed left axis deviation. Echocardiography revealed mild concentric left

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ventricular hypertrophy. Electroencephalography showed slowing basic rhythm (8-10Hz). Abdominal radiography revealed small intestinal gas like adynamic ileus or pseudo-obstruction (Figure 1). Magnetic resonance imaging (MRI) of brain revealed slight ischemic white matter lesions without findings suggesting MELAS. MRI of cervical spine revealed normal findings.

Intravenous fluid and metoclopramide improved her conditions. She was able to eat and discharged. However, three months later, she developed episodic vomiting again and admitted.

Figure 1
Abdominal radiography
Small intestinal gas like adynamic ileus or pseudo-obstruction

3. DISCUSSION

Summary of clinical features of present patient with 3243 mitochondrial DNA point mutation included as follows: episodic vomiting; short stature; hearing loss; diabetes mellitus; and no history of lactic acidosis, seizure, headache, or stroke like episode. She presented with short stature as physical characteristics, and also presented with hearing loss and diabetes mellitus, however, her predominant symptom has been only episodic vomiting.

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The most common initial symptoms of MELAS are generalized tonic-clonic seizures, recurrent headaches, anorexia, and recurrent vomiting (DiMauro and Hirano, 2001). Sensorineural hearing loss is common (DiMauro and Hirano, 2001). Presenting with only episodic vomiting especially with adynamic ileus or pseudo-obstruction is, however, quite uncommon. A familial occurrence of intestinal obstruction in children with the syndrome of MELAS has previously been reported (Shimotake et al., 1998). Three children, ages 11, 8, and 6, demonstrated acute onset of intestinal obstruction. The first female sibling underwent an emergent laparotomy because she was diagnosed to have intestinal strangulation. She had postoperative complications caused by progressive lactic acidosis and died. The second and third sisters had similar onsets of the disease and were treated with gastrointestinal decompression and intravenous administration of lactate-free fluid and coenzyme Q10. Accumulation of mitochondrial A3243G mutation in the stomach has been a contributory factor in gastric dysmotility and gastric syndrome in other patients with the mutation in their leukocytes (Fujii et al., 2004).

Furthermore, intestinal pseudoobstruction due to another mitochondrial disease, mitochondrial neurogastrointestinal encephalomyopathy (MNGIE), have been reported (Blondon et al., 2005; Oztas et al., 2010; Patel et al., 2011). The disease is clinically characterized by ptosis, progressive external ophthalmoparesis, gastrointestinal dysmotility, cachexia, peripheral neuropathy, and leukoenchephalopathy (Nishino et al., 2001). MNGIE, or Psuedo-Obstruction-Leukoencephalopathy-Intestinal-Pseudoobstruction Syndrome (POLIP), is a rare disease that associates chronic intestinal pseudo-obstruction (CIPO) and neurological symptoms (Blondon et al., 2005). This condition was associated with (a) a specific cluster of neurological symptoms including leukoencephalopathy (96%), polyneuropathy (96%), ophthalmoplegia (91%), and hearing loss (55%); (b) a CIPO syndrome with the presence of small bowel diverticlae (53%); and (c) mitochondrial cytopathy in 36 of the 37 tested patients, and thymidine phosphorylase gene mutations in all tested patients (Blondon et al., 2005).

Therefore, episodic vomiting similar to adynamic ileus or pseudo-obstruction is one of possible clinical manifestations of mitochondria encephalomyopathy such as MNGIE. Mitochondrial DNA 3243 point mutation, which usually causes MELAS, may also cause adynamic ileus or pseudo-obstruction like MNGIE. It seems to be unusual that episodic vomiting repeated frequently like present patient although we are unable to exclude the possibility of diabetic gastropathy. Moreover, autonomic neuropathy, which has caused diabetic gastopathy, seems to be associated with mitochondrial DNA 3243 point mutation. Episodic vomiting of present patient may be due to intestinal leiomyopathy, smooth muscle mitochondrial myopathy associated with mitochondrial DNA 3243 point mutation.

Mitochondrial DNA 3243 point mutations cause episodic vomiting similar to adynamic ileus and sometimes it may be called pseudo-obstruction.

4. CONCLUSION

Mitochodrial DNA 3243 point mutation may cause adynamic ileus or pseudo-obstruction like MNGIE. Episodic vomiting of present patient may be due to intestinal leiomyapathy associated with mitochondrial DNA 3243 point mutation.

SUMMARY OF RESEARCH

1.A patient with mitochondrial DNA 3243 point mutation patient presented episodic vomiting repeatedly and sometimes she presented adynamic ileus or pseudo-obstruction like syndrome.

2.3243 point mutation is usually associated with MELAS: mitochondrial encephalopathy, lactic acidosis, strokelike episodes. Intestinal pseudo-obstruction due to another mitochondrial disease, mitochondrial neurogastrointestinal encephalomyopathy (MNGIE), have been reported. This patient present with MNGIE-like pseudo-obstruction syndrome associated with MELAS mutation.

3.Episodic vomiting of present patient may be due to intestinal leiomyopathy associated with mitochondrial DNA 3243 point mutation.

FUTURE ISSUES

I believe that the cause of episodic vomiting associated with mitochondrial DNA 3243 point mutation will be apparent. Biopsy at surgery or autopsy of intestinal smooth muscles may clarify the cause of episodic vomiting associated with mitochondrial DNA 3243 point mutation.

DISCLOSURE STATEMENT

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