Haemolytic uraemic syndrome complicated with norovirus-associated gastroenteritis

Sir,
Norovirus infections run a short self-limiting disease, course characterized by sudden onset of nausea, vomiting and diarrhoea [1,2]. Dehydration is the most common complication, especially among the young and elderly, and may require medical attention; however, there is no evidence of any serious sequelae [1,2]. Here, we describe the occurrence of haemolytic uraemic syndrome in a patient with norovirus-associated gastroenteritis.

An 82-year-old Japanese man, with a history of chronic kidney disease (stage 3) due to hypertensive nephrosclerosis [3], was referred and admitted in December 2006, because of rapidly progressive renal dysfunction, consciousness disturbance and convulsion. He had been well until 1 week previously; however, abdominal symptoms (i.e. watery non-bloody diarrhoea, abdominal pain and vomiting) had developed in him and his family members. On admission, he showed no abdominal symptoms, but showed marked renal dysfunction with anaemia (blood urea nitrogen, 181 mg/dl; serum creatinine, 9.17 mg/dl); thus, we initiated emergent haemodialysis. Although he had not been noted with marked hypertension during the gastroenteritis, he showed marked hypertension (200/100 mmHg). Furthermore, he also showed thrombocytopenia (11 × 10^9/l), anaemia with red blood cell fragmentation (haemoglobin, 8.0 g/dl) and an undetectable serum haptoglobin level. Coagulation screening and liver biochemistry results were normal. Further laboratory tests (i.e. hypocomplementaemia, direct Coomb’s test, hepatitis B/C, anti-nuclear antibodies, anti-double-stranded-DNA antibodies, anti-cardiolipin antibodies, blood/urine cultures, parvovirus B 19, cytomegalovirus and Epstein–Barr virus) showed negative results. In his fecal specimens, the cultures of enterohaemorrhagic-Esherichia coli, Clostridium difficile and Campylobacter species and the enzyme-linked immunoassay of verocytotoxins were negative, but norovirus antigen was identified with enzyme immunoassay, indicating norovirus-associated gastroenteritis. After six haemodialysis sessions, his clinical symptoms and laboratory abnormalities were completely improved; renal function, however, did not fully recover, and he was treated with maintenance haemodialysis.

We think our patient’s renal dysfunction might not have been caused by dehydration due to diarrhoea alone, but might have been caused by thrombotic microangiopathy, because he showed the marked hypertension, thrombocytopenia and microangiopathic haemolytic anaemia. Based on these clinical manifestations, laboratory data and the normal plasma activity of von Willebrand factor-cleaving protease (70%), we diagnosed a possible haemolytic uraemic syndrome with diarrhoeal prodrome [4]. Although we did not perform highly sensitive serum-serological assays, haemolytic uraemic syndrome associated with verocytotoxin-producing E. coli might be clinically unlikely because he had not showed bloody diarrhea or the positive results of fecal assays [5]. Reported other causal/associated factors of this syndrome (e.g. Streptococcus pneumoniae, drugs, malignancy, autoimmune diseases or viral infections) were not identified in our patient [4]. He had norovirus-associated gastroenteritis before admission; thus, the norovirus infection might have contributed to the development of his haemolytic uraemic syndrome. Norovirus-associated gastroenteritis is typically a non-inflammatory small bowel infection and disease manifestations generally last 48–72 h with a full and rapid recovery [1,2]; however, norovirus infections reportedly can lead to an increased duration of diarrhoea in elderly patients, and to severe consequences (e.g. increased levels of C-reactive protein and creatine phosphokinase, hypokalaemia and renal dysfunction) in patients with underlying conditions (e.g. cardiovascular disease and immunosuppression) [6]. To our knowledge, ours is the first case of the occurrence of haemolytic uraemic syndrome in norovirus-associated gastroenteritis. The question remains as to whether our patient’s norovirus infection was a root cause, a simple coincidence or a precipitating factor of haemolytic uraemic syndrome. Further, there is a possibility that his chronic kidney disease and hypertension might also have contributed to the development of endothelial cell damage, resulting in haemolytic uraemic syndrome, even in the mild norovirus-associated gastroenteritis.

Norovirus infections have been emerging this winter and up to 40 deaths of elderly patients associated with these infections have already occurred in Japan. Our observation merits presentation, because further accumulation of clinical studies including case reports is necessary to confirm whether haemolytic uraemic syndrome is a real association in patients with norovirus-associated gastroenteritis.

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Quality of life assessment in a recent haemoglobin trial in CKD (CHOIR)

Sir,

We read with interest the editorial comment by Levin [1] on methods and lessons learned from recent haemoglobin trials in chronic kidney disease (CKD). Levin identifies a number of issues on the design, reporting and conclusions of one of these trials, the Correction of Haemoglobin and Outcomes in Renal Insufficiency (CHOIR) study, published in the New England Journal of Medicine [2]. Improvement in quality of life (QOL) is an anticipated benefit of correcting anaemia, but in the CHOIR study there were no differences in QOL in the high Hgb group, in contrast to any other study to date [1]. Levin notes that it is not clear when QOL was measured in the CHOIR study [1], and we noted additional issues.

One measure used in the CHOIR study to assess QOL was a disease-specific instrument, the Kidney Disease Questionnaire (KDQ). Unfortunately, the correct reference for the KDQ, developed by Laupacis et al. [3], was not provided. The purpose of the KDQ is to assess five distinct QOL domains found to be salient for CKD patients: physical symptoms, fatigue, depression, relationships with others and frustration. Instead of reporting results for each of the five KDQ domains, however, a ‘KDQ total score’ was reported for CHOIR participants (Table 2) [2]. In the absence of a well-validated composite score, summing across discrete domains of a QOL measure is meaningless. Moreover, important information on QOL differences among patients participating in the CHOIR study may have been obscured. Change may occur in some domains but not in others, as Foley et al. [4] showed when they used the KDQ in their study of the normalization of Hgb in haemodialysis patients. Continued study of Hgb targets, epoetin alfa use and associated clinical outcomes among CKD patients is important [1], and QOL perceptions, appropriately measured and analysed, can furnish valuable information.

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