

# A Case of Diabetic Nephropathy with Refractory Gastroparesis and Review of the Literature

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## Abstract

**Background:** Gastroparesis is one of the complications of diabetes mellitus, and long-term gastroparesis seriously affects patients' quality of life. Most of the patients can be relieved after lifestyle improvement and medication, but refractory gastroparesis is difficult to relieve, and is still a challenge in clinical treatment. **Aim:** To report a case of a patient with diabetic nephropathy combined with refractory gastroparesis, and to analyse the mechanism, diagnosis, severity grading, treatment of refractory gastroparesis in conjunction with a review of the literature, and to investigate the causes of recurrent nausea and vomiting in diabetic nephropathy patients with refractory diabetic gastroparesis and the possible effective treatment options. **Case Presentation:** The patient was hospitalised for recurrent nausea and vomiting and diagnosed with diabetic nephropathy and gastroparesis. Symptoms recurred after medication and peritoneal dialysis, and the patient's symptoms were relieved after multifaceted interventions. **Conclusion:** Diabetic nephropathy and refractory gastroparesis can both manifest as digestive tract symptoms, and in the face of this complex disease, it is necessary to analyse the various etiological factors and take comprehensive treatment measures.

## Keywords

Diabetic Nephropathy, Refractory Gastroparesis, Nausea, Vomiting

## 1. Introduction

Diabetic gastroparesis (DGP) occurs in patients with a long history of diabetes mellitus and poor long-term glycemic control, and is characterised by loss of appetite, early satiety, delayed gastric emptying, nausea, vomiting, abdominal

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distension, and malnutrition, with the exception of mechanical gastrointestinal obstruction. The persistence of gastroparesis symptoms despite dietary modifications and the use of gastroparesis as a first line of treatment is called refractory gastroparesis (except for pharmacological factors) [1]. DGP is not uncommon in patients with type 1 diabetes mellitus and type 2 diabetes mellitus, with a prevalence of 40% and 30% respectively [2]. After dietary control and symptomatic treatment, most patients with diabetic gastroparesis can relieve their symptoms, but the treatment effect of refractory gastroparesis is not significant. The aim of this paper is to investigate the causes of recurrent nausea and vomiting in diabetic nephropathy patients with refractory diabetic gastroparesis and the possible effective treatment options.

## 2. Case Information

The patient was a 41-year-old female. She was hospitalised more than 40 times for nausea, vomiting and other symptoms. She was diagnosed with type 1 diabetes mellitus in 2005 and was treated with long-term subcutaneous insulin injections without monitoring her blood glucose. In 2015, she was admitted to an outpatient hospital due to intermittent nausea, vomiting, epigastric fullness and discomfort, and poor appetite, and was diagnosed with: diabetic ketoacidosis, diabetic gastrointestinal and phytophysial neuronopathy, and diabetic nephropathy. She was discharged from the hospital with symptomatic relief after treatment. She had poor glycaemic control outside the hospital, and visited the hospital several times because of the worsening of the above symptoms. In 2017, she visited our hospital because of the inability to eat and the gradual worsening of double lower limb oedema with decreased urine output. The test showed that the glomerular filtration rate was  $6.25 \text{ ml}\cdot\text{min}^{-1}$ , and the blood creatinine was  $918.0 \text{ }\mu\text{mol}\cdot\text{L}^{-1}$ , and the haemoglobin was  $109 \text{ g}\cdot\text{L}^{-1}$ . The diagnoses were chronic renal failure uremic stage, renal anemia, and diabetes gastrointestinal vegetative dysfunction. Symptoms were slightly relieved after administration of acid suppression, diuretic, antiemetic, sedation, neurotrophic, haemodialysis and peritoneal dialysis placement. Regular out-of-hospital peritoneal dialysis has been performed since 2017, with 2 sets of 2 L of 1.5% low-calcium peritoneal dialysis daily, each with 3 hours of abdominal preservation, and 2 sets of 2 L of 2.5% low-calcium peritoneal dialysis daily, each with 3 hours of abdominal preservation. Gastrointestinal symptoms remained recurrent. In October 2019, she was consulted for frequent episodes of nausea and vomiting with bilateral lower limb oedema, and the total gastrointestinal angiography showed increased retention of fluid in the stomach and slowed peristaltic emptying; signs of chronic gastritis; and no obvious organic pathology in all segments of the intestinal tract. Considering the symptoms of gastroparesis, the peritoneal dialysis protocol was changed to 1.5% low-calcium peritoneal dialysis solution 2 L, 2 groups per day, 3 hours of abdominal storage in each group, and 2.5% low-calcium peritoneal dialysis solution 2 L, 2 groups per day, 3 hours of abdominal storage in each

group, and was given out-of-hospital oral mosapride, but the symptoms were still recurring, and the frequency of hospitalization did not change significantly compared with the previous one. The examination on admission to hospital in July 2020 showed edema of an eyelid, moderately depressed edema of both lower extremities, and BNP 2252.0 pg·mL<sup>-1</sup>, pleural, pelvic-abdominal and pericardial effusion. Considering the patient's volume load, adjust the dialysis regimen to 2.5% low-calcium peritoneal dialysate 2 L, 4 groups per day, 3 hours of abdominal storage in each group, nausea and vomiting were slightly relieved. September 2020 examination showed moderate oedema of the bilateral lower extremities, BNP decreased in retest compared with the previous one, and there were still effusions in the thoracic cavity, pericardium and abdominal cavity, and the dialysis regimen was adjusted: 1.5% low-calcium peritoneal dialysis solution 2 L 1 group per day, each group of abdominal storage for 3 hours, 2.5% low-calcium peritoneal dialysis solution 2L 3 groups per day, each group of abdominal storage for 4 hours, adjusting the regimen after the fluid retention significantly improved, the digestive symptoms are relieved. During the course of the disease, the patient was given pantoprazona, lansoprazole, ondansetron, tropansetron, gastroparesis, chlorpromazine, diazepam, mosapride, methylcobalamin tablets, intermediate-frequency electrotherapy, physiotherapy and other treatment for the patient's digestive symptoms, and at the same time was given the treatment of correcting anaemia, improving cardiac function, replenishing albumin, maintaining electrolyte balance, adjusting peritoneal dialysis programme and other treatments, and the brand of dialysis fluid was changed from "Chang Fu" to "Chang Fu". The brand of dialysate was changed from "Changfu" to "Baxter". Symptoms could be relieved for a short period of time after the above treatments, but it was difficult to maintain the effect in the long term.

In March 2022, the patient again showed obvious fluid retention, gastrointestinal symptoms were still recurrent, and it was considered that it was related to the poor adequacy of its peritoneal dialysis, and after many times of changing the peritoneal dialysis programme the effect was unsatisfactory, and it was changed to haemodialysis, and the programme was 3 times a week, 4 hours each time. After regular peritoneal dialysis, the patient's frequency of admission to the hospital was reduced, and the degree of nausea and vomiting was relieved, but the nausea and vomiting symptoms worsened after the intermittent occurrence of medium-large amount of ascites, which could be relieved by the administration of intensified dialysis and peritoneal tube drainage, but the discomfort in the epigastric region was more significant, and the patient was still suffering from lethargy, loss of appetite, and early satiety, and so on. He is still under follow-up.

### 3. Discussion

The pathogenesis of diabetes mellitus refractory gastroparesis is complex and has yet to be fully clarified, and may include gastrointestinal neuropathy, gastrointestinal hormonal disorders, hyperglycaemic damage, alterations in ga-

stointestinal Cajal mesenchymal stromal cells, and mental and psychological factors [3] [4] [5]. The mechanism of gastrointestinal palsy is complex and has not yet been fully clarified.

According to the Abell score, diabetic gastroparesis can be classified into 3 grades: Grade 1 has mild symptoms and intermittent episodes, which can be controlled by dietary adjustments and avoidance of triggers; Grade 2 has obvious symptoms without significant weight loss, which need to be treated by prokinetic drugs combined with antiemetic drugs; Grade 3 has severe symptoms and oral drugs are ineffective, which require frequent hospitalisation, enteral nutrition, parenteral nutrition, endoscopic therapy, and surgical treatment [6]. This patient was frequently hospitalized and could not be fully relieved by the usual antiemetic and gastrointestinal stimulant drugs, and was prone to recurrent exacerbations, eating less, and wasting away, with an Abel classification of 3, which makes him a severe patient.

Current pharmacological treatments for DGP include dopamine receptor antagonists, gastric motility receptor agonists, 5-HT<sub>4</sub> receptor agonists, gastric growth hormone receptor agonists, antihistamines, 5-HT<sub>3</sub> receptor antagonists and phenothiazines [7]. In recent studies, the pharmacological treatment of refractory gastroparesis has been explored with some of the most commonly used drugs, which are not effective in this condition. Transdermal patch of granisetron can reduce the symptom score of patients with refractory gastroparesis by 50% [8]. Mirtazapine, a tetracyclic antidepressant that enhances central norepinephrine and 5-hydroxytryptamine activity, was shown to be effective in a study of 30 patients with refractory gastroparesis [9], with 80% of patients taking oral clozapine experiencing improvement in symptoms of nausea, vomiting, dry heaves, and loss of appetite, but with a high incidence of adverse effects. Gastric emptying rates were significantly higher after cisapride-based administration of lipoic acid intravenously compared with cisapride alone [10].

Gastric electrical stimulators (GES) provide symptomatic relief for refractory gastroparesis, but their effectiveness remains controversial. Patients with gastroparesis who underwent a combination of GES and pyloroplasty showed significant improvements in symptom severity, frequency, and time to gastric emptying compared with GES alone, and GES plus pyloroplasty holds promise for achieving better long-term symptom control while improving delayed gastric emptying [11].

Gastric per-oral endoscopic endoscopic myotomy (G-POEM) is an emerging treatment that was first used to treat patients with gastroparesis in 2013, and patients experienced significant symptomatic relief after the procedure. The effective rate of G-POEM surgery in patients with diabetic gastroparesis is 89% [12]. A recent multicentre study reported a 56% improvement in the Gastroparesis Basic Symptom Index (GBSI) at 12 months after surgery in patients with refractory gastroparesis [13]. A recent multicentre study reported a 56% improvement in the basic symptom index of gastroparesis at 12 months after surgery. Another

study reported [14] G-POEM patients with gastroparesis had an effective rate of 81.1% at 3 - 6 months, recurrence rate of 7.1% at 6 months, 8.3% at 12 months, 4.8% at 24 months, and 14.3% at 36 months. High BMI and prolonged gastroparesis may lead to an increased chance of surgical failure, but the rate of adverse events is low and the extent of gastroparesis is mild, which makes the risk of surgery low. A few successful cases of G-POEM surgery have been reported in China [15] [16] [17].

In addition, there are other surgical procedures such as pyloroplasty and sleeve gastrectomy, and Rouxen-Y gastric bypass surgery. Although gastrectomy improves symptoms, body mass, and hospitalisation rates in patients with DGP, there is a risk of dumping syndrome, malnutrition, and weight loss, and the occurrence of postoperative complications should be taken seriously [18] [19]. The occurrence of postoperative complications should be taken seriously.

In this case, nausea and vomiting persisted for many years, and although refractory diabetic gastroparesis was the main cause, it is important to consider whether other factors were present in combination. The patient's poor glycaemic control led to recurrent ketoacidosis, which can lead to significant gastrointestinal symptoms. Uremia can lead to ischaemia in the digestive system, gastrointestinal hormone imbalance which can damage the gastric mucosa and prolong the gastric emptying time, and there is also a correlation between body mass index, haemoglobin level, and vitamin B deficiency and gastrointestinal symptoms [20] [21]. The patient had low haemoglobin, which could be a potential cause of exacerbation of gastrointestinal symptoms. During the treatment, vitamin D and iron supplementation, erythropoietin, sarostat and iron sucrose were given successively, and the haemoglobin could be increased but it was difficult to maintain the normal level. Existing studies have shown that vitamin E-coated polysulfone membrane dialyzers and selenium supplementation can help improve renal anaemia in haemodialysis patients [22].

Studies have shown that peritoneal dialysis nausea and vomiting are more prominent than haemodialysis [20] [21]. The nausea and vomiting are more prominent in peritoneal dialysis than haemodialysis. The increase in intra-abdominal pressure and glucose intake due to peritoneal dialysis can lead to further exacerbation of gastroparesis. If regular oral gastrointestinal stimulant medication fails to improve the symptoms, metoclopramide or erythromycin can be added to the dialysis solution, but its long-term effect has not been effectively verified and it has the risk of operating infections, so it should be used with caution [23]. Gastrointestinal symptoms also occur in haemodialysis patients, but they are usually of low severity, mainly mild, and gender, parathyroid hormone, and diabetes mellitus are factors influencing gastrointestinal symptoms in haemodialysis patients [24]. In this case, although the number of ketoacidosis was reduced after peritoneal dialysis, the symptoms still did not improve significantly, and the nausea and vomiting symptoms were relieved more than before after changing to haemodialysis, so we consider that peritoneal dialysis

may be one of the reasons for the aggravation of gastroparesis symptoms. Repeated peritoneal fluid accumulation during haemodialysis also reduces the patient's symptoms after intensive dialysis to reduce the accumulation of fluid, so it is necessary to ensure the adequacy of dialysis to improve the fluid retention caused by hypoproteinaemia. Superficial gastritis and cholecystitis also cause abdominal discomfort, nausea, and vomiting. Symptomatic treatments such as regular diet and acid-suppressing gastric protection can improve symptoms. In addition, patients suffering from pain for many years need to consider the emotional factors and improve the psychological assessment, and appropriate psychological counselling may help the patient's condition.

#### 4. Conclusion

In summary, both diabetic renal failure and refractory gastroparesis can have gastrointestinal symptoms. For such patients with complex conditions, the treatment process is based on a combination of therapeutic protocols. In addition to direct symptomatic treatment such as acid suppression, prokinetic and sedative drugs, other underlying causes such as anaemia, malnutrition, dialysis and fluid retention also need to be intervened. Chronic discomfort also leads to depression, which also requires appropriate psychotherapy. In patients with limited efficacy after aggressive dialysis treatment and pharmacological therapy, surgical treatment may be attempted to achieve long-term symptomatic relief and improve the patient's quality of life.

#### Fund Projects

A study of the clinical characteristics of patients with chronic kidney disease admitted to the ICU (202011).

The application of joint mind mapping based on the case library of the learning through platform in the teaching of internal science apprenticeships (J20231055).

Research on the Application of Integrated Medical Model in Chronic Disease Management in the Context of New Medical Reform (DJKZXKT2023143).

Analysis of the correlation between the expression of autophagy-related molecules in podocytes and hypoxia-inducible factor 1 alpha in diabetic nephropathy (2020MX56).

#### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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