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Case Report

Hypergastrinemia in Children : A Case Report

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Abstract:
Gastrin is an important hormone in the gastrointestinal system that promotes gastric acid secretion. Gastrin hormone is produced by the G-cells in the antrum of the stomach. Besides stimulating gastric acid secretion, gastrin also induces the proliferation of the gut epithelial cells, tissue remodelling, and angiogenesis. Gastrin levels higher than 100-150 pg/ml are known as hypergastrinemia. Hypergastrinemia may cause the hypersecretion of stomach acid, which, if not treated properly, may leads to refractory peptic ulcer, severe gastroesophageal reflux disease (GERD), diarrhea, or death due to complications of refractory peptic ulcer. This case presented a 12 years old boy with a chief complaint of severe epigastric pain in the past month, accompanied by nausea, especially during supine position. The patient had a previous history of esophagitis. He showed no significant changes upon empirical PPI treatment. However, slight improvements were observed after the administration of Helicobacter pylori treatment. The gastrin level in this patient was 198 pg/mL. Upon discharge, the patient was still given PPI treatment. During the follow-up visitation, patient complaints had improved significantly, and the patient was planned to undergo routine evaluations of gastrin.

Keywords: hypergastinemia, children, stomach acid

Introduction

Gastrin is an essential hormone in the gastrointestinal system, particularly in promoting gastric acid secretion. The hormone is produced by G-cells located in the gastric antrum. The presence of gastrin helps stimulate the secretion of gastric acid, induce the proliferation of the epithelial cells, as well as promote tissue remodelling and angiogenesis. Hypergastrinemia is a condition in which the level of gastrin exceeds 100-150 pg/ml.[1] Gastrin functioned to stimulate pepsin and parietal cells, increases the blood flow in the gastric mucosa, and exerts trophic effects on gastric, duodenum, and colon mucosa.[1,2]

Gastrin is initially synthesized as pro-gastrin or pro-hormone, which binds to other gastrin molecules in varying lengths. The hormone is then secreted to the vascular system with different affinity toward the gastrin receptors. There are two types of gastrin receptors, Cholecystokinin-A (CCK A) and Cholecystokinin-B (CCK B).

Circulating gastrin will activate CCK B on the parietal cells, leading to gastric acid secretion. Gastrin is produced as a response to food. Protein and amino acids were one of the major stimulators of gastrin secretion.[1] Hypergastrinemia is frequently found in several conditions, such as Zollinger-Ellison syndrome, Helicobacter pylori (H. pylori) infection, or the use of proton pump inhibitor (PPI).[3] This study depicted the management of pediatric hypergastrinemia with atypical manifestation.

Case Report

A twelve-year-old boy came with a chief complaint of severe epigastric pain for the past month, accompanied by nausea, particularly when lying down. The patient had previous history of esophagitis and appendicitis. During the endoscopy examination, the mucosa in the proximal and middle part of esophagus was within normal limits; however, the distal part of esophageal mucosa was severely hyperemic, with the mucosal break in 70% of the circumference, partially confluence between the folds. One inflamed polyp was also found during the endoscopy. Furthermore, the gastric mucosa was severely hyperemic, especially in the cardia, fundus, corpus, and pylorus. Erosion was found in the corpus and fundus part of the gaster. The pyloric gap was found, while bile reflux was not found. The mucosa of duodenal bulb and descending part of duodenal were mildly hyperemic. Patients were then given PPI, prokinetic therapy, rebamipide, and sucralfate.

However, upon the follow-up examination, the patient still complained of severe epigastric pain with no significant improvement. The results of both the abdominal CT-scan using contrast and abdominal ultrasound were within normal limits, including the pancreas. Meanwhile, the H. pylori examination through biopsy displayed negative result. Patient did not undergo urea-breath test examination due to financial limitations. Despite being given the maximum treatment according to the one-month test results, the patient still exhibited no improvement. Thus, after careful consideration, the patient was given H. pylori treatment. The treatment includes a combination of PPI, clarithromycin, and amoxicillin.

Significant improvement was seen after the initiation of therapy. Gastrin hormone examination was conducted to rule out the possibility of Zollinger-Ellison syndrome. The result showed a high level of gastrin (198 pg/ml; normal value : < 65 pg/mL). As patient responded to the H. pylori treatment, the treatment was continued until completion, along with the PPI treatment. After six weeks of PPI treatment, patient symptoms improved significantly, and on the eighth week, all complaints were completely resolved.

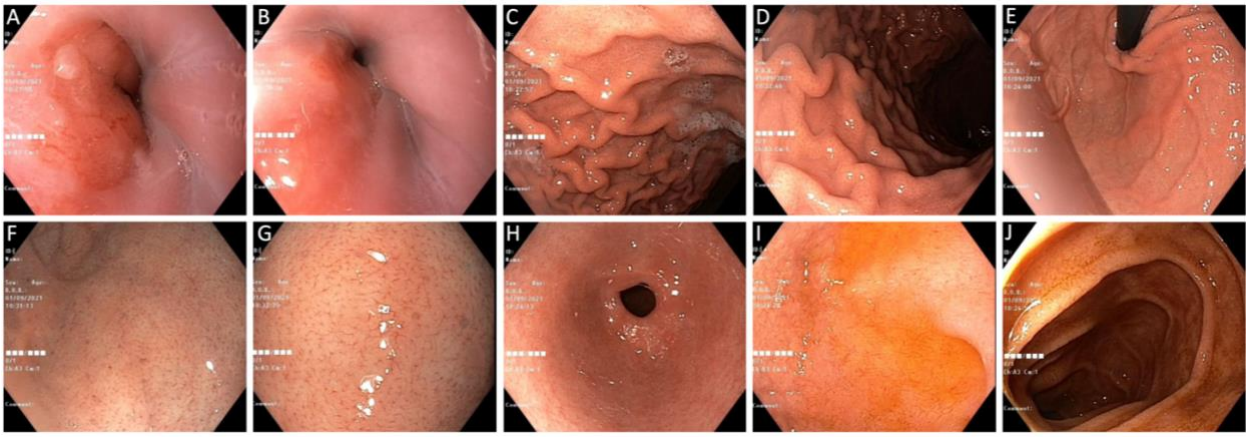

Figure 1. Endoscopic result. (a) and (b) showed severe hyperemia in distal esophageal mucosa with mucosal break and partial confluence between folds; (c) and (d) showed severe hyperemia and erosion in the corpus; (e) showed severe hyperemia and erosion in cardia and fundus; (f) and (g) showed severe hyperemia in antral; (h) showed severe hyperemia in pylorus; (i) and (j) showed mild hyperemia in duodenal bulb and descending part of duodenal.

Discussion

Hypergastrinemia was defined as serum gastrin level higher than 100-150 pg/mL.[1] The elevation of gastrin may occur in two conditions: during the decrease of gastric acid level (appropriate hypergastrinemia) and in the normal or high level of gastric acid (inappropriate hypergastrinemia). The increase of gastrin due to the low number of gastric acids was typically considered a normal body response in restoring the amount of gastric acid. Two of the most frequent causes of this situation include H. pylori infection and prolonged use of PPI or histamine H2 blocker. Meanwhile, the rise of gastrin despite the normal or high level of gastric acid is most likely pathological. The conditions that might cause hypergastrinemia despite the normal level of gastric acid are anatomical disturbances such as tumors, particularly Zollinger Ellison Syndrome (ZES).[1,2,4]

ZES is a neuroendocrine tumor that secretes gastrin and causes symptoms such as diarrhea and peptic ulcer.[4] The syndrome is rarely found in pediatric patients, accounting for only 1% of all ZES cases.[5] The tumor is frequently located in the duodenum or pancreas and causes ectopic secretion of gastrin. The diagnosis criteria for ZES are increased gastrin level > 10 times the normal value (> 65 pg/ml) or, in the other literature, increased level of gastrin > 1000 pg/mL.[6,7] Meanwhile, the radiological examination was considered less reliable in the case of ZES, as more than 60% of small tumors in the duodenum were not detected.[4] Based on previous studies, CT-scan and MRI could only detect tumors bigger than 2-3 cm.[6,8] In patients with ZES, the prescription of PPI was seen to be beneficial in controlling acid secretion

and improving the symptoms experienced by the patient.[4] In our case, the gastrin level of the patient was increased; however, it did not exceed > 10 times the normal value. Furthermore, despite the low diagnostic ability, the radiology examination results were within normal limits. This result decreased the possibility of ZES and eliminated other anatomical disturbances that might cause hypergastrinemia. Patient also did not exhibit any improvement after the administration of PPI during the follow-up examination. Based on these findings, we concluded that the diagnosis of ZES could be ruled out.

H. pylori infection disturbs the antral part of the somatostatin cells and causes the decreased production of somatostatin, an essential hormone inhibiting antral G cell secretion. This leads to the reduction of gastric acid secretion, which resulting in hypergastrinemia. In general, H. pylori infection only induces a subtle increase in gastrin level; however, the moderate elevation is deemed essential in causing the increase of gastric acidity and, ultimately, the risk of duodenal ulcer.[3] Furthermore, severe colonization of the pathogen in the gastric corpus may cause atrophic gastritis, which may further induce hypergastrinemia as it disrupts the function of somatostatin in inhibiting gastrin secretion.[1,7,9] Upon the initiation of H. pylori treatment, the hypergastrinemia typically resolved.[9]

In our case, the gastrin level in our patient was only moderately increased, and the number did not exceed more than ten times the normal value. Furthermore, upon treatment initiation for H. pylori, the patient showed clinical improvements. However, the H. pylori examination demonstrated a negative result. Interestingly, the positive result of H. pylori from biopsy examination were rarely observed in Indonesian children. The low accuracy of biopsy for H. pylori infection in Indonesian children could be caused by several factors. Study had shown that despite its high specificity, biopsy demonstrated varied number of sensitivity (85-95%).[10] Furthermore, the accuracy of biopsy is affected by several factors such as prior use of PPI, H2 antagonist, or antibiotic, gastritis, low number of pathogens, and poor specimen handle.[10] Based on a study by Shirin et al., the negative test might be induced by using PPI prior to the H. pylori examination, which might cause the misinterpretation as the PPI interferes with the pathogens' viability, morphology, and ability to produce urease.[11] Thus, the diagnosis of H. pylori was considered in this patient, and the initiation of treatment should be justified, especially in patients who exhibit no improvement with prior treatments.

The use of PPI was also one of the most frequently identified causes of hypergastrinemia. PPI inhibits gastric acid secretion, which subsequently induces the rise of serum gastrin level as the body tries to restore the amount of gastric acid. The increased gastrin level typically occurred only in the first four months after using PPI

and was constant in the following period. PPI was seen to only induce a moderate increase of gastrin level, at around 200-400 pg/mL. The gastrin level was commonly returned to normal after 5-7 days of PPI discontinuation.[1] Interestingly, studies have shown that the use of PPI may obscure not only hypergastrinemia due to H. pylori but also hypergastrinemia that ZES causes as it decreases the level of gastrin, leading to the misdiagnosis.[4] The patient in our case was known to consume PPI during the course of treatment. However, the knowledge of prior usage of PPI before the chief complaint was unknown. According to Ito et al., to confirm the etiology of hypergastrinemia, the administration of PPI must be discontinued first to prevent misdiagnosis.[4] Hence, upon managing other hypergastrinemia cases, we recommended terminating any PPI treatment with extensive observations of patient symptoms and manifestation prior to re-evaluating the gastrin level to reduce the risk of misdiagnosis.

The patient in our case, exhibited symptoms improvement after the initiation of H. pylori treatment along with the administration of PPI. A follow-up study by Sokic-Milutinovic et al. has demonstrated that the plasma gastrin level will declined to its normal level within six months in patients with successful eradication of H. pylori.[12] Furthermore, re-evaluating the gastrin level post-PPI discontinuation may be useful for our patient to further confirm the elimination of diagnosis related to PPI and inappropriate hypergastrinemia.[1,4] In addition, hypergastrinemia has been frequently associated with the occurrence of malignancy, particularly carcinoids.[1] Chronic hypergastrinemia has been associated with carcinogenesis and was seen to induce the proliferation of several types of cells, especially the gastric Enterochromaffin-like (ECL) cell.[1,9] Although the incidence was rare, the occurrence of carcinoid due to hypergastrinemia has been reported by several studies.[13-16] Fortunately, all of the reported cases were primarily among adult patients. Despite the lack of information on the occurrence of carcinoid in pediatric hypergastrinemia, the evidence of the increased risk of malignancy in patients with hypergastrinemia should be of concern. Thus, further evaluation of gastrin hormone was recommended in our case to confirm the diagnosis, monitor the therapy's effect, and further evaluate the level of gastrin hormone post-therapy.

Conclusion

Hypergastrinemia is a condition that may happen due to appropriate hypergastrinemia, often found in PPI or H2 Blocker therapy and H. pylori infection, or inappropriate hypergastrinemia, such as in ZES. Based on the examinations, we concluded that the patient did not suffer from ZES or any significant anatomical disturbances in the stomach. However, the evaluation of gastrin hormone level is still needed to confirm the diagnosis, therapy evaluation, and assessment for the risk of complications.

Conflict of Interest

None declared.

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