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Helicobacter Pylori Infection in Children with the Rescue Therapy; A Case Report

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ABSTRACT

Background: *Helicobacter pylori* infection affects more than half of the world population and it occurs generally in childhood. Risk factors include residence in a developing country, poor socio-economic status, overcrowding family, ethnic and genetic predisposition. There is a difficulty eradicating this bacterium due to its high antimicrobial resistance. We aim to discuss enforcement and management of Helicobacter pylori infection in children.
Case Presentation: A 5 year 10 months old girl diagnosed with recurrent abdominal pain due to *Helicobacter pylori* infection. The patient often had recurrent abdominal pain located specifically on epigastrium area. Laboratory findings demonstrated *H. pylori* IgM positive and negative IgG level. The result of endoscopy and biopsy revealed gastritis and mild intestinal metaplasia and moderate *Helicobacter pylori* density. The patient still experienced abdominal pain despite the standard therapy, and later received rescue therapy.
Conclusion: Eradication of *H. pylori* was failed with standard therapy and continued with rescue therapy.

Keywords: *Helicobacter pylori* infection, rescue therapy, standard therapy, case report

INTRODUCTION

Helicobacter pylori is a Gram-negative microaerophilic bacteria.[1,2] Infected patients may develop chronic gastritis, peptic ulcer disease 10%, gastric cancer 1%-3% and will present with mucosa associated lymphoid tissue lymphoma 0.1%. All these complications occur in their vast majority in adulthood.[2,3]

The progress of the disease is related to the virulence of the strain, the genetic predisposition, the host's immune response, the time of exposure and environmental factors. The CagA+ and VacA s1m1 strains are considered the most pathogenic and carry a higher risk of precancerous lesions. The risk seems higher if infection with these strains occurs simultaneously and in childhood.[4,5]

The diagnosis and treatment should not be considered in the same way in children and adults. The immune mechanisms against infection differ at both stages of life and therefore the decision to investigate and treat infection in childhood is indicated in a small proportion of patients in whom the benefits are greater considering that recurrence and complications largely occur from ineffective treatments.[2,3]

CASE PRESENTATION

A 5 year 10 month old girl was hospitalized in pediatric ward of Dr. M Djamil Hospital with recurrent abdominal pain that occurred every day. She often suffered from abdominal pain since 11 months ago, almost every day, 5 to 6 times a day, 1-5 minutes long, not associated with food. The abdominal pain was located specifically on

epigastrium area, not spreading to other abdominal area, and often felt like being stabbed. There was no loss of appetite, good feeding tolerance, no nausea and no vomiting. There was no fever nor seizure. No cough, runny nose, and breathlessness. There was no history of contact neither with long cough sufferer nor with the patient suspected of having a COVID-19. Urination frequency, color and volume remained unchanged. Defecation frequency, color, and consistency remained normal.

The patient had a history of outpatient clinic at RSUP Dr. M. Djamil Padang from March 2021 until recently and was diagnosed with recurrent abdominal pain due to *Helicobacter pylori* infection. Laboratory findings on march 2021 demonstrated *H. pylori* IgM level of 71,7 (positive) (normal limit <40) and IgG level of 5,7 (negative) (normal limit <20), abdominal ultrasound was normal. The patient received first line eradication therapy consisted of oral amoxicillin 250mg, oral proton pump inhibitor (PPI) 20 mg and oral metronidazole 500mg twice daily. After 2 weeks of treatment, patient still complaint of abdominal pain, then received other course of therapy consisted of oral proton pump inhibitor (PPI) 20mg twice daily, oral levofloxacin 125mg once daily, oral amoxicillin 500 mg twice daily during 2 weeks of treatment. The patient still complaint of abdominal pain and a re-evaluation of laboratory findings on April 2021 demonstrated *H. pylori* IgM level of 120,5 (positive) and IgG level of 9 (negative). This resukt suggests Eradication therapy failure, and the patient was recommended for endoscopy (esophagogastroduodenoscopy / EGD).

Her sister had the same complaint. Patient was a second child from three siblings, was delivered by spontaneous full term delivery, cried instantly, birth weight was 3,550 grams and birth length was 48 cms, vigorous. Patient received complete immunization, the last vaccine received was MR vaccine on 24th months old. Growth and development of patient was normal according to age.

Patient looked moderately ill, compos mentis, blood pressure 100/60 mmHg (P5:75/37; P50 92/55; P90 106/69; P95 110/73; P99117/80; Crisis 165/110) heart rate 92 times per minute, respiratory rate 22 times per minute, body temperature 36,7oC, body weight 17 kg, body length 108 cm, weight for age was 85%, height for age was 93%, weight for height was 94%, with impression well nourished. Skin was warm, no cyanotic, turgor was slowly returned. Head was round and symmetrical with head circumference was 50 cms (normocephal). Conjunctiva did not look pale, sclera was not icteric, pupil were isochoric with diameter 2mm/2mm, light reflex was positive normal. Ears and nose were normal. Tonsil was T1-T1, not hyperemic and pharynx was not hyperemic. Mouth's mucous was pink and moist. Chest and heart were normal. From the abdominal examination, we found no distension, supple palpated. The liver and the spleen were not palpable, there was epigastric tenderness but no pain, the bowel sound was normal. No abnormality found in genitalia and extremities. Laboratory finding were normal except APTT 33,7 second.

Patient was diagnosed with recurrent abdominal pain due to Helicobacter pylori infection. She received proton pump inhibitor (PPI) 2x20 mg/day. She was scheduled for an EGD examination and biopsy. The results of EGD examination were gastritis with hyperemic mucosa of gaster (figure 1). Gastric biopsy specimen on prepyloric region were mild chronic inflammation, no acute inflammation, no glandular atrophy, mild intestinal metaplasia and moderate H Pylori density (figure 2). Serology and biopsy results are consistent with refractory *H. pylori* infection, and later proceed to start rescue therapy.

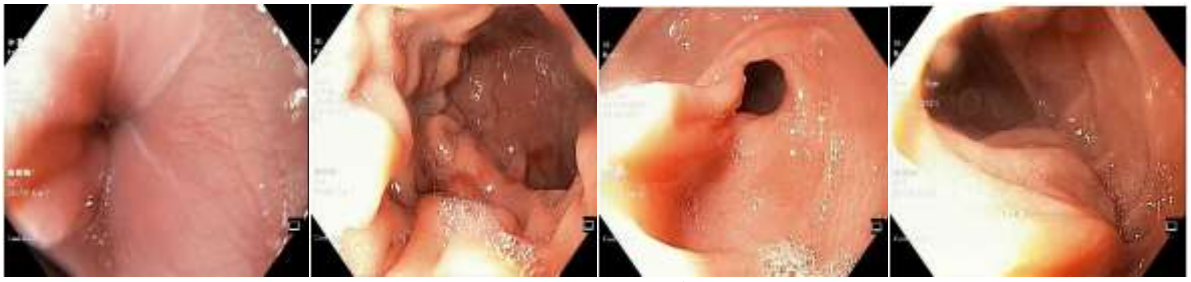
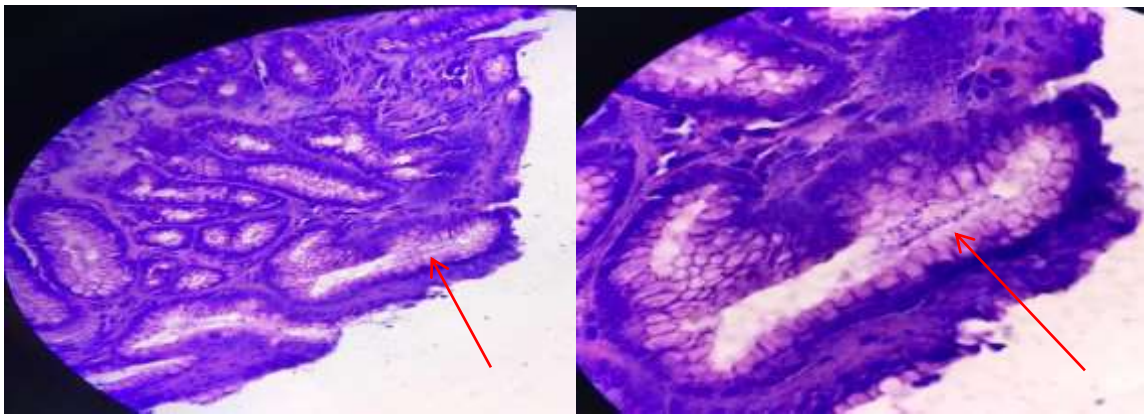


Figure 1. The endoscopy of gaster.



Pembesaran 40x Pembesaran 100x

Figure 2. Gastric biopsy specimen on prepyloric region

DISCUSSION

Helicobacter pylori is a Gram-negative microaerophilic bacteria. It has been found in mummies, but was first described when it was related to chronic gastritis and peptic ulcer disease in 1983 by Barry Marshall and Robin Warren. This discovery was the beginning of numerous investigations to amplify knowledge of this bacterium.[1]

The prevalence of Helicobacter pylori infection in paediatric age is high (approximately 50% of the total population)[1,6] and varies from country to country and in the same geographical area.[1] It is lower in high-income countries (34.7 %) than in low-income and middle-income countries (50.8 %), more prevalent in adults than in children and may also vary in a geographic area within a country.[6]

Patient was a second child from three siblings, spontaneous delivery, complete immunization, growth and development of patient was normal according to age. Her parents graduated from senior high school, lived in their own home with good hygiene and sanitation. Her sister had the same complaint. Several studies describe that person-to-person transmission among family members is frequent, with mother-to-child being the most predominant and the most important transmission route being oral-oral and oral-faecal.[7] Contaminated water can also be a source of infection, in which the bacterium can remain for long periods in a viable state. Many associate H. pylori infection with socioeconomic conditions and dietary habits, suggesting that foods such as milk, meat and vegetables may be an important route of transmission. Saliva is also another possible source of infection.[8]

She often had recurrent abdominal located especially on epigastrium area, not spreading to others area on abdomen, and felt like being stabbed. There was no loss of appetite, good feeding tolerance, no nausea and no vomiting. Defecation frequency, color, and consistency remained unchanged. Clinical manifestations are non-specific and some may be justified by the presence of complications. A statistically significant positive association with nausea, but no significant association between gastrointestinal symptoms, pain or pain

characteristics and infection has been documented.[9] Other studies have found that symptoms decrease in frequency and intensity or disappear with or without eradicating the bacteria. A meta-analysis attempted to establish a possible association between infection and symptoms, and concluded that it was not related to vomiting, diarrhoea, flatulence, chronic functional abdominal pain, halitosis, regurgitation, constipation or nausea. However, they documented a statistically significant association with epigastric pain.[10]

The patient was diagnosed with recurrent abdominal pain due to *Helicobacter pylori* infection. Laboratory findings on march 2021 demonstrated H. pylori IgM level of 71,7 (positive) (normal limit <40) and IgG level of 5,7 (negative) (normal limit <20). Laboratory re-examination findings on April 2021 demonstrated *H. pylori* IgM level of 120,5 (positive) and IgG level of 9 (negative), after receiving first line therapy of Helicobacter pylori for 14 days and second line therapy for another 14 days. Eradication therapy was failed, and later was recommended for endoscopy (EGD). Antibody based tests for *H. pylori* in serum, whole blood, urine and saliva are not modified by treatment with PPI or antimicrobials but their utility is more accurate for epidemiological purposes. The antibodies remain for a time after eradication and it does not allow differentiate between current and past infection.[2]

The initial point of investigation in children begins with upper endoscopy or oesophago-gastro-duodenoscopy (OEGD) for different indications. Although this procedure does not allow direct diagnosis, with high-definition endoscopic techniques like Blue Light Imaging and Linked Color Imaging are helpful in characterization of mucosal changes in chronic gastritis, allowing the selection of areas for sample collection.[11] Initially *H. pylori* colonises the antrum and can produce antral gastritis and if the infection persists nodular, pan gastritis.[7] In this context, the infection can be diagnosed and the first challenge begins, in deciding whether to treat or not. OEGD should be indicated to investigate the cause of symptoms, not the presence of H. pylori infection.[2]

The sensitivity of all invasive methods is compromised by the use of antibiotics, bismuth, proton pump inhibitors (PPI) and upper gastrointestinal bleeding. Culture has a specificity of 100% but the sensitivity is compromised by the use of antibiotics, H2-receptor antagonists, PPI, bismuth, alcohol drinking, digestive bleeding, high activity of gastritis, low bacterial load the quality of the sample collection, the patchy distribution of *H. pylori*, transport of biopsies, staff skills and culture media. For these reasons, it should not be used as the only diagnostic method. A negative culture does not exclude infection. This has the advantage of providing antimicrobial sensitivity data to offer strain-directed treatment. Ideal is to provide this method for initial diagnosis but when it is available generally is reserved for cases with a first time failure.[2,12,13]

The patient had performed endoscopy and biopsy. The endoscopy revealed following result: gastritis with hyperemic mucosa of gaster. Gastric biopsy specimen on prepyloric region was taken during endoscopy and revealing gastric mucus with mild chronic inflammation, no acute inflammation, no glandular atrophy, mild intestinal metaplasia and moderate Helicobacter pylori density. Gastroduodenal ulcers in children are infrequent. Samples should be taken for biopsy and the infection confirmed. Other causes, however, need to be considered. Gastric atrophy and intestinal metaplasia are less frequent as compared with adults and are more related to time exposure.[2,14] During the procedure and for the initial diagnosis, at least six samples must be taken. Two samples, of the antrum and the body taken for histopathological study, for which the Sydney classification should be used.[12]

She received first line eradication therapy, oral amoxicillin 500mg two times/day, oral proton pump inhibitor (PPI) 20 mg two times/day and oral metronidazole 250mg two times/day. After 2 weeks of treatment, patient still complained about abdominal pain, then change therapy with oral proton pump inhibitor (PPI) 20mg two times/day, oral levofloxacin 125mg one times/day, oral amoxicillin 500 mg two times/day during 2 weeks of treatment. The patient still complained with abdominal pain and second laboratory findings still revealed serum antibody IgM *Helicobacter pylori* in high titre. Adapting the first line of treatment according to susceptibility would be ideal, but we know that in practice it is difficult so therefore in many regions treatment is indicated empirically. Clarithromycin (CLA) is the choice of treatment in patients with susceptible strains. If the resistance rate exceeds 15%–20% in that region, it should not be used unless sensitivity to this antibiotic is known in the patient.[2,15] There is high resistance to CLA and Metronidazole (MET), mainly CLA in children and MET in adults. It varies with region and is an increasing trend.[2] Very little resistance to amoxicillin (AMO) and levofloxacin.[15–17] Multidrug resistance was a problem.[15,16,18] Resistance increases considerably in treatment failures.[16] The hetero-resistance in strains was described in children.[15] Studies demonstrated that triple therapy with PPI-AMO-CLA offers acceptable eradication rates when the strains are sensitive.[18,19] Authors reported patients with susceptibility guided treatment with adherence >90% of treatment achieved acceptable rates of eradication, the rates were significantly higher in those receiving sequential therapy.[17] PPI plays a key role in treatment; double doses are recommended to improve susceptibility to AMO and CLA and to overcome rapid degradation with individual differences of CYP450 cytochrome polymorphisms.[19]

After a failure in the second therapy, we can give rescue therapy which regiment should be given individualized considering antibiotic susceptibility, the age of the child, and available antimicrobial options. The choice of rescue therapy should consider initial antibiotic susceptibility status and the first-line regimens employed. She got oral amoxicillin 750mg two times/day, oral proton pump inhibitor (PPI) 20 mg two times/day and oral metronidazole 250mg two times/day during 2 weeks of treatment.[2]

CONCLUSION

Reports on successful H pylori eradication therapy in some countries are still limited due to lack of people's awareness to seek treatment. Inadequate therapy caused antibiotic resistance which urges the need to practice applicable guideline to reduce the failure eradication with first and second line therapy. Rescue therapy should be performed once failure therapy of the first and second line is assessed.

Declaration by Authors

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