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MONITORING OF CASES WITH A CHRONIC PERSISTENT INFECTION WITH HELICOBACTER PYLORI.

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ABSTRACT:

Introduction: The patients with persistent forms of Helicobacter pylori (HP) infection are refractory to eradication treatment. They receive unsuccessful therapies, experience frequent recurrences and re-infections. One of the main reasons for the development of persistent forms is an inadequate and insufficient treatment. The persistent forms of HP infection create conditions for the maintenance of activity and for the progression of the induced chronic gastritis. In this aspect these cases will be at a higher risk for the development of gastric cancer.

The aim of this study is: to monitor and analyze the cases with persistent HP infection and to establish an approach for their management.

Clinical material and methods: The study includes 12 patients (8 female and 4 male) at a middle age of 63,7, with a persistent HP infection, who have been observed for a period of five years. Two methods for the detection of HP infection are used – one invasive and one non-invasive. Upper endoscopy with morphological examination was performed.

Results: In 9/12 patients HP was unsuccessfully treated for three times, in 2 patients – four times, and in 1 patient – five times. In all patients the initial treatment consisted of a standard triple therapy (STT). In 5 of them STT was conducted twice, with the same regimen for a period of seven days. Two patients received three courses of STT. In four patients an antibiotic resistance was established by means of a cultured assessment. In three cases an HP resistance to Clarithromycine and Metronidazole was demonstrated. Significant gastro-duodenal pathology with atrophic gastritis, intestinal metaplasia, and hyperplastic polyposis was found in all patients. The persistent clinical symptoms had 9 patients.

Conclusion: We believe that a devised and proposed step strategy which covers early detection of infection, reliable diagnosis, adequate and successful treatment, and dispensary monitoring, contributes to the prevention of gastric cancer.

Key words: HP infection, persistent forms, treatment, risk patient,

The patients with persistent forms of Helicobacter pylori (HP) infection are usually refractory to standard eradication treatment. They receive unsuccessful therapies, experience frequent recurrences and re-infections. One of the main reasons for the development of persistent forms is an inadequate and insufficient treatment. The persistent forms of HP infection create conditions for the maintenance of activity and for the progression of the induced chronic gastritis. In this aspect these cases will be at a higher risk for the development of gastric cancer.

The aim of this study:

· to monitor and analyze the cases with persistent HP infection

· to establish an approach for their diagnosis, management and treatment.

PATIENTS AND METHODS:

The study includes 12 patients (8 female and 4 male), at a middle age of 63,7, with a persistent HP infection, who have been observed for a period of five years.

HP infection was proven and unsuccessfully treated three times consequtively in 9/12 patients, four times in 2/12 patients and five times in 1/12 patients.

Two methods for the detection of HP infection are used – one invasive and one non-invasive (by histology and fecal antigen test). Upper endoscopy with morphological examination was performed. Cultured assessment for HP infection was performed in 7 patients. Was used a disk diffusion method, taking into account areas of dwarfed. Assessment for HP in the dental plaque was made by the PCR- DNA method. Quality of life in all patients by a questionnaire containing 14 questions was examined.

RESULTS:

Analysis of the treatment

All patients had initial treatment with standard triple therapy (STT). In 9/12 patients HP was unsuccessfully treated for three times, in 2 patients – four times, and in 1 patient – five times.

In 5 of them STT was conducted twice, with the same regimen for a period of seven days.

The next course after failed STT in 7/12patients was sequential therapy. The history for frequent antibiotic use had 7 patients. In four patients an antibiotic resistance was established.

In three cases a combined HP resistance to

Clarithromycine and Metronidazole was demonstrated.

In 5 patients side effects, mainly diarrhea, were reported. In 4 patients poor compliance was achieved.

Clinical data:

Persistent clinical symptoms were present in 75% (9/12) patients, predominantly epigastric pain. Episodes of rebleeding from the gastrointestinal tract (respectively 4 and 2 episodes) were observed in 2/12 patients. All patients had a poor quality of life (bellow 25 points). None of the patients had other risk factors. In 3/12 patients a combination of HP infection in the stomach and in the oral cavity (dental plaque) was found. In 4 patients (3 female, 1male) depressive symptoms were present. Two of all had a family history of gastric cancer.

Endoscopy and morphology data:

In all patients significant gastro-duodenal pathology was found.

• chronic atrophic gastritis in 3 patients.

• antral atrophic gastritis with intestinal metaplasia in 4 patients.

• antral atrophic gastritis with intestinal metaplasia and dysplasia in 2 patients.

• atrophic gastritis with intestinal metaplasia and hyperplastic polyposis was found in 1 patient

• MALT Lymphoma in 1 patient

• atrophic pangastritis with Vitamin. B12 deficiency anemia in 1 patient.

RESULTS OF TREATMENT:

In 4 patients .after antibiotic testing a quadruple personalized therapy was applied. In 4 patients quadruple sequential Levofloxacine based therapy was prescribed. Quadruple Rifabutine based therapy plus Levofloxacine was administred in 4 patients

A probiotic - Bio Gaia, was added as an adjuvant therapy for period of 1 month.

• Successful eradication was established in all patients after treatment

• The monitoring will continue

• All have been included in a register for gastric cancer risk patients

• HP infection is monitored every 6 months

• Sanitation of oral cavity and dental status is obligatory.

• Endoscopic surveillance of patients with premalignant lesions was carried out.

DISCUSSION:

Persistent forms of HP infection are those cases which are refractory to standard eradication regimes and proven for 2 years or more after unsuccessful therapy. According to literature data [1, 2] their frequency ranges between 15-30% of cases. Our data show nearly 12% incidence of persistent HP infection. We tend to assume that one of the main reasons for the development of induced persisting forms is an inadequate and/or insufficient treatment. Patients with persistent forms of HP infection are refractory to a series of antibiotic treatment. **C**ommon causes are insufficiency of treatment period, interruption mode, failure mode and the presence of side effects. Such causes and circumstances were found in our cases too. Our observation shows that frequent re-prescription of the same eradication regimen is one of the reasons for the development of secondary antibiotic resistance. According to our observations the most frequent practice is the repeated administration of STT. In one of our cases STT was appointed four times. Not by chance antibiotic resistance to Clarithromycin and Metronidasole occurs most frequently after this treatment pattern. Our results show that the best strategy for the diagnosis and successful treatment of persistent HP infection is a microbial culture with antibiotic testing, and a corresponding therapy.

According to J. Luther et al. [3] the treatment of persistent infection with H. pylori is a major challenge for clinical medicine today. Unfortunately the widely used triple combination for 7 days, and 14 days in developed countries, failed to successfully eliminate the infection and thus it persists in not less than 25% of the patients. Significant gastroduodenal pathology - chronic active inflammation and premalignant lesions. was found in all our patients

Muller et al [2] consider that persistent infection with HP worsens inflammation and predisposes to an increased risk of gastric cancer. According to the data of SS Kim et al. [4] and Alvi et al.[5], that H. pylori stimulates gastric neoplasia mainly by inducing intense and prolonged inflammatory response. This persistent state of chronic inflammation causes oxidative stress, and adaptations in the pathobiology of gastric epithelial and immune cells, which in a small number of subjects would result in a marked neoplastic transformation. S. Abdiev et al. [6] investigated the relationship between persistent infection with H. pylori and gastric atrophy, on the one hand, and the genetic polymorphism of cytokines on the other hand.

Persistent forms create condition for persistence of chronic inflammation, that stimulates gastric atrophy and in this aspect presents a risk of gastric cancer. Cervantes et al. [7] established that H. pylori infection of elderly relatives always precedes persistent infection in the younger ones. Study of the status of breastfeeding mothers, use of antibiotics and socioeconomic factors showed a strong effect of persistent infection in older brothers and sisters on younger siblings. Based on the results of our study, we register and follow up the patients with persistent forms of HP infection, because they have a higher risk for development of gastric cancer and are subject to active surveillance in order to prevent gastric cancer. Lee et al. [8] reported that HP-eradication has a substantially increasing importance especially for the primary and secondary prevention of associated serious diseases such as gastric cancer and gastric MALT lymphoma.

Based on our results, we consider that in order to prevent the development of persistent form of infection, it will be necessary to implement the following measures:

• more frequent check-up for HP infection at 6 months.;

• rehabilitation of potential sources of re-infection (oral cavity, tooth status)

• testing of family members and improved sanitation and hygienic status

• reliable verification of infection by at least two methods

• appropriate and timely treatment of HP infection, excluding re-administration of the same eradication regimen, administration with the inclusion of two new antibiotics.

• endoscopic and morphological verification of the associated gastro-duodenal pathology

• endoscopic surveillance of patients at risk for gastric cancer

• treatment of active gastric inflammation

CONCLUSIONS:

Based on our observation and analysis of cases with a persistent HP infection, we have worked out a step strategy for the management of persistent forms of infection with Helicobacter pylori.

Eighth step strategy

The first step – analysis of each clinical case taking into account all the circumstances in respect of the diagnosis and treatment.

The second step – verification of HP infection by 2 or 3 methods, preferably by culture assessment.

The third step – diagnosis and clarification of associated pathology and assessment of endoscopy control.

The fourth step – treatment by administration of an adequate eradication regimen. Therapy of choice – antibiotic testing, quadruple therapy, or alternative therapy – quadruple Levofloxacine - based therapy, or quadruple Rifabutine plus Levofloxacine therapy.

The fifth step – monitoring of HP infection every six months.

The sixth step - registration of patients at increased risk for gastric cancer.

The seventh step - endoscopic surveillance of patients with premalignant gastric conditions and lesions.

The eighth step - dispensary monitoring of patients with persistent HP infection.

We believe that devised and proposed step strategy for management of persistent HP infection which covers early detection of infection, reliable diagnosis, adequate and successful treatment and dispensary monitoring **is a step forward in the prevention of gastric cancer**

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