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Clinical and pathological features of nodular gastritis in adults

Aim: Data on antral nodularity in adults are sparse. Although the association of nodular gastritis with *Helicobacter pylori* infection is well known, its potential as a premalignant lesion and its association with other gastroduodenal diseases are questionable.

Materials and methods: The medical records of the patients between 2003 and 2006 were retrospectively reviewed to analyze their demographics, clinical characteristics, and endoscopic and pathological features.

Results: Of 9949 adult patients who underwent endoscopy, 185 (1.86%) were diagnosed with nodular gastritis, 167 (90%) of whom had dyspepsia. The presence of *Helicobacter pylori* was demonstrated in 65.4% (121/185). There were 16 cases (8.7%) of associated peptic ulcer, not more frequent compared to the *Helicobacter pylori*-positive control group without nodular gastritis and no case of gastric cancer was detected. Lymphoid follicle formation was not more prevalent either.

Conclusion: The presence of nodular gastritis does not necessitate a new therapeutic approach in addition to the current measures for *Helicobacter pylori* infection.

Key words: *Helicobacter pylori*, nodular gastritis

Erişkin hastalarda nodüler gastritin klinik ve patolojik özellikleri

Amaç: Erişkinlerde antral nodülarite üzerine bilgiler yetersizdir. Nodüler gastritin *Helicobacter pylori* enfeksiyonu ile ilişkisi iyi bilinmekle beraber premalign olma potansiyeli ve diğer gastroduodenal hastalıklarla birlikteliği tartışmalıdır.

Yöntem ve gereçler: 2003 ve 2006 yılları arasındaki hastaların tıbbi kayıtları demografik, klinik, endoskopik ve patolojik özellikler açısından retrospektif olarak analiz edildi.

Bulgular: Endoskopik inceleme yapılan 9949 hastanın 185 (% 1,86)' inde nodüler gastrit tanımlandı. Bunların 167 (% 90)' sinde dispepsi mevcuttu. *Helicobacter pylori* varlığı % 65,4 (121/185)'ünde gösterildi. Bu olgulara eşlik eden 16 (% 8,7) peptik ülser vakası vardı. Bu oran *Helicobacter pylori* pozitif olan ancak nodüler gastrit tanımlanmayan kontrol grubu hastalarında daha yüksek değildi. Nodüler gastrit olgularına eşlik eden gastrik kanser saptanmadı. Lenfoid folikül oluşumu da bu grupta kontrol grubuna göre daha sık değildi.

Sonuç: Nodüler gastrit varlığı *Helicobacter pylori* enfeksiyonu için mevcut tedavinin ötesinde bir terapötik yaklaşım gerektirmemektedir.

Anahtar sözcükler: *Helicobacter pylori*, nodüler gastrit

Introduction

Nodular gastritis (NG) is an unusual type of gastritis in children and it is frequently found in association with *Helicobacter pylori* infection (1). On the other hand, data on antral nodularity in adults are sparse. NG is not classified as endoscopic gastritis according to the Sydney classification system but it is increasingly used as a descriptive term (2). Some authors also attribute a pathologic

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correlation (1). Although the presence of NG was found to show high positive predictive value for the presence of *H. pylori* infection (3) its potential as a premalignant lesion and its association with other gastroduodenal diseases are questionable.

In this study, we describe the demographics and some clinicopathological features of NG among the patients admitted to Hacettepe University Hospital for adults (a 800-bed tertiary care hospital located in Ankara) and try to answer the question of whether the presence of NG poses clinical implications further than having been associated with *H. pylori* infection.

Materials and methods

There were 9949 Turkish adults (>17 years) who underwent endoscopy between 1 June 2003 and 1 January 2006. One hundred eighty-five patients (mean age 48.05 years, 72 men and 113 women) were diagnosed with NG and were included in this study. NG was defined as antral gastritis with endoscopic findings characterized by a miliary nodular appearance. The medical records of the patients were retrospectively reviewed to analyze their demographics, clinical characteristics, endoscopic features, pathological features, erythrocyte sedimentation rates (ESR), treatment, and treatment outcomes. The age- and gender-matched controls, patients without NG [184 patients (mean age 48.9 years, 84 men and 100 women)], were chosen at random from the medical records. The presence of *H. pylori* infection was determined by urea breath test (UBT), urease test, or histology. Thirty-one patients with NG were treated by *H. pylori* eradication using triple therapy (lansoprazole 60 mg, amoxicillin 2000 mg, clarithromycin 1000 mg per day for 2 weeks). In 31 *H. pylori*-positive patients with NG follow-up endoscopy was performed 3-6 months after the eradication therapy was completed.

Descriptive statistics were generated for all study variables, including mean and SD for continuous variables and relative frequencies for categorical variables. Relations between subgroups were analyzed using a chi-squared test for categorical variables and a t-test for continuous variables. One-sided values of $P < 0.05$ were considered statistically significant. The statistical analyses were performed with SPSS 11.0.

Results

The prevalence of NG in adults who underwent endoscopy was 1.86% (185/9949) and consisted of 72 men (0.49%) and 113 women (1.38%). Patient age ranged from 19 to 85 years (mean age, 48.05 years). Ninety-four patients (51%) were between 40 and 60 years old. The presence of *H. pylori* was demonstrated by histology, urease test, or urea breath test in 65.4% (121/185) of the patients with NG and in 59.2% (109/185) of the patients without NG ($P > 0.05$). Ninety percent (167/185) of the patients with NG had dyspepsia, significantly higher than the patients without NG, 68.5% (126/184) of whom had dyspepsia ($P < 0.001$). Dyspepsia as an indication for endoscopy was more frequent in the *H. pylori*-positive patients with NG 91.7% (169/185) than the *H. pylori*-positive patients without NG 69.7% (128/184) ($P < 0.001$). Among the 185 patients with NG, regarding the endoscopic findings, 16 (8.7%) had peptic ulcers (9 had duodenal ulcers and 7 had gastric ulcers), 9 (4.9%) had atrophic gastritis, 98 (53%) had erosive gastritis, 18 (9.7%) had duodenitis, 4 (2.2%) patients had gastric polyps, and no patient had gastric cancer (Table 1). Within the NG group 15 patients (8.1%) had gross appearance of pangastritis while 9 patients (4.9%) had nodules in other parts of the stomach beside the antrum. The mean ESR was 12.87 ± 12.36 mm/h in the patients with NG and 8.68 ± 7.97 mm/h in the control group ($P > 0.05$). Antral nodular gastritis was still present in 39% (12/31) of the *H. pylori*-positive patients with NG despite the triple eradication therapy.

Antral biopsy specimens (present in 161/185 of the patients with NG) showed that the prevalence of lymphoid follicle formation and/or marked lymphoid aggregates was higher in the *H. pylori*-positive patients (25%) than the prevalence in the *H. pylori*-negative patients (10.9%) ($P = 0.001$). Lymphoid follicle formation was more prevalent in the patients without NG (24%) than in the patients with NG (15%) ($P < 0.05$) (Table 2).

Discussion

This is one of the few reports to describe the characteristics of NG in adults and the first report on a Turkish adult population. The prevalence of NG

Table 1. Endoscopic features in patients with and without nodular gastritis.

| Gastroduodenal Disease | NG (+) patients (%) | NG (-) patients (%) | P value |
|------------------------|---------------------|---------------------|---------|
| Gastric Ulcer | 7 (3.8) | 13 (7.1) | >0.05 |
| Duodenal Ulcer | 9 (4.9) | 13 (7.1) | >0.05 |
| Atrophic Gastritis | 9 (4.9) | 22 (12) | <0.05 |
| Erosive Gastritis | 98 (53) | 120 (65.2) | >0.05 |
| Duodenitis | 18 (9.7) | 8 (4.3) | <0.05 |
| Gastric Cancer | - | 2 (1.1) | >0.05 |
| Gastric Polyp | 4 (2.2) | 1 (0.5) | >0.05 |
| None | 40 (21.6) | 5 (2.7) | <0.05 |
| Total | 185 (100) | 184 (100) | |

Nodular gastritis (NG)

Table 2. Histologic features in patients with and without nodular gastritis.

| | | Lymphoid follicle (%) | |
|--------------|-----------|-----------------------|----|
| | | | |
| NG (+) (161) | Hp+ (108) | 18* | 15 |
| | Hp- (53) | 8 | |
| NG (-) (184) | Hp+ (114) | 32** | 24 |
| | Hp- (70) | 13 | |

*P > 0.05 compared with NG (Hp-) patients; **P < 0.05 compared with NG (-) (Hp-) patients
Helicobacter pylori (Hp); Nodular Gastritis (NG)

among our patients was 1.86%. Miyamoto et al. reported that the prevalence of NG was 0.19% (1) while it was 2.3% in another series from Japan (3). The prevalence was found to be 7.2% in Peru (4) and 10% in Spain (5). There is no widely accepted histopathological definition for NG and it remains an endoscopic finding. On the other hand, there is no common definition for the characteristics of the nodules regarding appearance either, and the term “nodular gastritis” needs further clarification. The large difference in the prevalence of NG among various studies mainly originates from the subjective definition by endoscopists rather than the different *H. pylori* prevalence among the study groups.

The prevalence of *H. pylori* was 65.4% among the patients with NG, higher than that in the control group (59.2%). *H. pylori* was reported to be positive in 67%-98.5% of the patients with NG (5-7). Several

studies suggested that the presence of antral nodularity is highly predictive for *H. pylori* infection (6,8). Previous *H. pylori* eradication therapy and recent use of H2 receptor antagonists and/or proton pump inhibitors may explain the relatively low prevalence of *H. pylori* positivity among the patients with NG in our series. The antral nodularity persisted in 39% of the patients despite triple therapy. Although there is no suspicion about the association of *H. pylori* infection and NG, other infectious agents, environmental, nutritional, or other individual factors may contribute to the formation and persistence of nodules as well.

Dyspepsia, as an indication of endoscopy, was more prevalent in the patients with NG compared to the control group but there was no difference between the 2 groups regarding the association of peptic ulcer. The prevalence of peptic ulcer in the patients with NG

was 8.7% (Table 1). Miyamoto et al. found this prevalence as 13% and speculated that there may be a causative relationship between antral nodularity and peptic ulcer (1). On the other hand, there was no control group in Miyamoto's series. Our results showed that other than being predictive for the presence of *H. pylori* infection NG is clinically not very meaningful regarding the association of gastroduodenal disease. Only 8.1% of our patients had pangastritis and less than 5% had nodules in other parts of the stomach and so topographically NG cannot be regarded as a type of pangastritis as some authors suggested (1).

Our histopathological examination revealed that lymphoid follicle and/or aggregate formation was more frequent in the *H. pylori*-positive patients. However, among the *H. pylori*-positive patients lymphoid follicles were not more prevalent in the patients with NG compared to the patients without NG (Table 2). Maghidman et al. also found in their 261-patient series that there was no relation of NG with the presence and number of lymphoid follicles (4). NG is a well known, frequent presentation of *H. pylori* infection in children, and macroscopic nodularity is suggested to be a reflection of the presence of lymphoid follicles in the gastric antrum (9,10). On the other hand, in adults with *H. pylori* infection, lymphoid follicles are frequently observed in stomachs without endoscopic nodularities (11). Miyamoto et al. (1) suggested that the size and depth of the lymphoid follicles may even explain the nodular or granular pattern of NG. We think that, because the description of the nodule is subjective, to correlate nodule formation with histopathology is difficult. On the other hand, although significant lymphoid

hyperplasia may be responsible for the nodule formation in some of the antral gastritis caused by *H. pylori*, it cannot solely explain the nodules because lymphoid hyperplasia is not observed in a significant number of the cases.

There are reports of gastric cancer associated with NG (12), but there were only 2 patients (1%) in Miyamoto's series (1) and no patient had gastric cancer and NG in our series. The controversy on the definition of NG as pangastritis, absence of association with increased lymphoid follicle formation, normal ESR in our series, and the low number of reports on association of gastric cancer and NG all counter the idea that NG is a precancerous lesion. *H. pylori* is well known to be a class I gastric carcinogen, but a comparison of *H. pylori*-positive patients with NG to the *H. pylori*-positive control group without NG in our series showed that the presence of NG as an endoscopic finding does not constitute an extra risk in addition to *H. pylori* as far as carcinogenesis is regarded.

To summarize, NG results from chronic *H. pylori* infection. *H. pylori* eradication decreases the risk of peptic ulcer and possibly gastric malignancy. On the other hand, regarding gastroduodenal disease and gastric malignancy the presence of NG does not necessitate a new therapeutic approach in addition to the current measures for *H. pylori* infection. Nodules are not homogeneous and various histopathological parameters may explain the antral nodularity. The definition and clinical importance of NG and associated histopathology will become clearer with prospective long-term-follow-up studies including large numbers of patients.

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