

Nodular gastritis: An endoscopic indicator of *Helicobacter pylori* infection in children

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La gastrite nodulaire : Indicateur endoscopique de l'infection à *Helicobacter pylori* chez l'enfant

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R É S U M É

Prérequis : L'infection à *Helicobacter pylori* (HP) est une infection bactérienne commune et universellement distribuée. Elle est majoritairement acquise pendant l'enfance.

But : Etudier la relation entre gastrite nodulaire et l'infection à HP.

Méthodes : Il s'agit d'une étude rétrospective concernant des enfants adressés à l'unité d'endoscopie digestive du service de médecine infantile C de l'Hôpital d'Enfant de Tunis pour douleurs abdominales chroniques. Tous ces enfants avaient bénéficié de cinq biopsies gastriques pour étude histologique, test à l'uréase et culture de l'HP. La spécificité, la sensibilité de la gastrite nodulaire ont été calculées. Plusieurs paramètres ont été étudiés en association avec la présence ou non de la gastrite nodulaire (âge, sexe, infection à HP, score de la gastrite et follicules lymphoïdes).

Résultats : Quarante neuf enfants, âge moyen $6,9 \pm 3$ ans (1-12 ans) ont été retenus pour l'étude. L'infection à HP a été diagnostiquée chez 35 enfants sur 49 (71,5%). La gastrite nodulaire a été rapportée chez 16 enfants sur 49 et chez 14 sur 35 enfants infectés (40%) et chez deux sur 14 non infectés (14%), $p=0,07$, 40% de sensibilité, 85,7% de spécificité, 87,5% de valeur prédictive positive et 36,4% de valeur prédictive négative. Les paramètres associés significativement à la présence de gastrite nodulaire étaient l'âge élevé ($p=0,04$), la gastrite chronique: $p=0,05$, l'activité de la gastrite ($p=0,02$), la gastrite folliculaire ($p=0,005$), un score de gastrite élevé ($p=0,005$). Une histologie normale n'a pas été trouvée chez l'enfant infecté et présentant une gastrite nodulaire. Parmi tous les enfants infectés, un score de gastrite élevé et la gastrite folliculaire étaient significativement associés à une gastrite nodulaire.

Conclusion : la gastrite antrale identifie nodulaire identifie les enfants atteints d'une infection à HP, et de gastrite folliculaire chronique.

S U M M A R Y

Background: *Helicobacter pylori* (Hp) infection is a common and universally distributed bacterial infection. It is predominantly acquired in childhood.

Aim: To assess the relationship between endoscopic nodular gastritis and Hp infection.

Methods: A retrospective study was conducted in children who underwent upper gastrointestinal endoscopy for chronic abdominal pain. All children who had five gastric biopsies for histologic analysis, urease test and Hp culture were included in the study. The Sensitivity and sensibility of nodular gastritis were determined and different parameters were studied according the presence or not of nodular gastritis (age, gender, Hp status, gastritis score and lymphoid follicles).

Results: 49 children, mean age 6.9 ± 3 years (range 1-12 years) were eligible for the analysis. Hp Infection was diagnosed in 35 out of the 49 children (71.5 %). Nodular gastritis was recorded in 16 out of 49 children and in 14 infected children and 2 out of 14 non infected children ($p=0.07$), 40% sensitivity, 85.7% specificity, 87.5% positive predictive value, and 36.4% negative predictive value.

The parameters associated significantly to the presence of nodular gastritis were older age: ($p=0.04$), Hp infection: ($p=0.01$), chronic gastritis: ($p=0.05$), active gastritis: ($p=0.02$), follicular gastritis: ($p=0.005$), higher gastritis score: ($p=0.005$). Completely normal gastric mucosal histology was never found in infected children with antral nodularity. Among all infected children, the gastritis score was significantly higher when there was a nodular gastritis and follicular gastritis was significantly associated to nodular gastritis.

Conclusion: The endoscopic pattern of antral nodularity identifies children with Hp infection, and active chronic follicular gastritis.

Mots-clés

Gastrite nodulaire, infection à *Helicobacter pylori*, enfant, gastrite chronique, gastrite folliculaire

Key- words

Nodular gastritis, *Helicobacter pylori* infection, child, chronic gastritis, follicular gastritis

Helicobacter pylori (Hp) infection is a common and universally distributed bacterial infection. It is predominantly acquired in childhood [1], and more than three fourth of the population in developing countries is infected during childhood. The inflammation that Hp causes in the gastric mucosa is not always observed macroscopically within endoscopy, but it is identified on the histological examination of gastric biopsies [2]. Endoscopic findings of nodularity can be seen in the stomach of children more frequently than in adults. This nodularity, more often observed in the gastric antrum, is called antral nodular gastritis, also named nodular antritis or gastric lymphonodular hyperplasia [3].

The aim of this study was to assess the relationship of endoscopic nodular gastritis and Hp infection.

METHODS

Patients

It's a retrospective study conducted during seven years in the digestive endoscopic unit of the paediatric department of the children hospital of Tunis between 2001 and 2007.

Inclusion criteria were the followings:

- Children aged between one and 16 years
- Children who had chronic abdominal pain
- Patients who had five biopsies: two antral and three in the corpus for histological study, urease test and culture.

Exclusion criteria: patients who had underlying disease, acute critical illness or used steroids or non steroidal anti inflammatory drugs or H2 histaminic blockers, antimicrobials, proton pump inhibitory patients taking immunosuppressive agents or chemotherapy drugs in the previous month.

Endoscopy

The materiel used was Olympus ® XP20 endoscope (outer diameter 7.5mm).The examination was not done under sedation. The endoscopic aspect of nodular gastritis was based on irregular appearance of the mucosa as a cobblestone pavement [4]. Five gastric biopsy specimens were collected from each patient for histological analysis: two from the gastric antrum (one from the distal lesser curvature and one from the distal greater curvature), two from the corpus (one from the lesser curvature and one from the greater curvature), and one from the area next to the incisura angularis for urease test and Hp culture.

Histological evaluation

The histological study consisted in Hematoxycilline and modified Giemsa coloration of the stain. Determination of Hp status was based on biopsy tests (histologic examination with Giemsa, rapid urease test, and/or culture). Patients in whom Hp tests did not fulfill these criteria were excluded from this study. The Hp infection was done when Hp was detected on histological sample and or by a positive culture of the biopsy. The histological findings were classified according to the updated Sydney system [1]. The degree of inflammation was divided into ? monocyte infiltration, ? neutrophil infiltration, ? glandular atrophy, or ? intestinal metaplasia, and scored as normal (0), mild (1), moderate (2), or marked (3) using the

visual analogue scale applied to microscopic examination results. The sum of the score obtained from each patient was used as the gastritis score. Firstly we studied epidemiological parameters, endoscopic aspect (nodular gastritis) and histological findings of patients according to their Hp status. Secondly the sensitivity and sensibility of nodular gastritis was determined. Thirdly we studied the occurrence of nodular gastritis in association with gender, age, Hp status, histologic findings and gastritis score. Finally we studied the characteristics of infected patients according the presence or not of nodular gastritis.

Statistics

Discrete variables were described by their medians and interquartile ranges, while quantitative variables were described by their means and standard deviations, and qualitative variables were described by proportions. The Kruskal-Wallis test was used to compare the score of each gastric region. In all statistical tests, a $p < 0.05$ was considered significant.

RESULTS

A total of 49 children, mean age 6.9 ± 3 years (1-12 years) were eligible for the analysis. Hp Infection was diagnosed in 35 out of the 49 children (71.5 %). Table 1 summarizes the clinical, endoscopic characteristics of patients according to their hp status. Nodular gastritis was recorded in 14 out of 49 hp infected children. We reported a low density of Hp in 26 cases moderate in 2 cases and high in 2 cases. Hp was not seen in five cases on histological findings. Chronic histological gastritis was reported in 31 out of 35 (88.5%) infected children versus three out of 14 non infected children (21.5%) ($p=0.001$).

Table 1 : Clinical, endoscopic and histological Characteristics of patients according to their Hp status (Hp +/Hp -)

	Hp + n=35 (%)	Hp - n=14 (%)	p
Mild age	8.5 ± 3 years	8 ± 3 years	NS
Gender male	14 (40)	5 (36)	NS
Nodular Gastritis	14 (40)	2 (14)	NS (0.07)
Histological patterns :			
Normal	4 (11.4)	11 (78.5)	< 0.0001
Chronic Gastritis	31 (88.5)	3 (21.5)	< 0.0001
Active Gastritis	22 (63)	0	0.0002
Atrophy	21 (60)	11 (70)	0.023
Follicular Gastritis	23 (65.7)	2 (14)	0.001
Mild Score gastritis	2.7 ± 1.6	0.4 ± 0.7	< 0.0001

Active gastritis was recorded in 22 out of 35 (63%) children with Hp infection versus none out of the 14 children without Hp infection. ($p=0.0002$). Follicular gastritis was present in 23 out of 35 (67.5%) patients with Hp infection versus two out of 14 (14%) patients without Hp infection ($p=0.001$). Score gastritis was 2.07 ± 1.6 in children with Hp infection versus 0.4 ± 0.7 in children without Hp infection ($p<0.0001$). Hp was not seen in five cases on histological findings. The diagnostic performance of nodular gastritis for Hp infection was as follow: sensitivity (40%), specificity (85.7%), positive predictive value (87.5 %), and negative predictive value (36.4%) (Table 2)

Table 2 : Diagnosis value of nodular gastritis in HP infection

	Sensitivity	Specificity	PPV	PNV
Nodular Gastritis	40 %	85.7 %	87.5 %	36.4 %

The table 3 summarized the characteristics of children according to the presence or the absence of nodular gastritis. The average age in the group with nodular gastritis was 10 ± 3 years versus 7.5 ± 3 years ($p=0.04$) without nodular gastritis. Hp infection was diagnosed in 14 out of 16 children with nodular gastritis (87.5%) versus 21 out of 33 (63%) without nodular gastritis ($p=0.01$). Chronic gastritis was described in 14 out of 16 children (87.5%) with nodular gastritis versus 20 out of 33 children without nodular gastritis (60.6%) ($p=0.05$). Active gastritis was recorded in 11 out of 16 children with nodular gastritis versus 11 out of 33 (33%) children without nodular gastritis ($p=0.02$). Follicular gastritis was reported in 13 out of 16 children (81.2%) with nodular gastritis versus 12 out of 33 (36.4%) in children without nodular gastritis ($p=0.005$). The gastritis score was 3 ± 2 in children with nodular gastritis versus 1.5 ± 1.5 in children without nodular gastritis ($p=0.005$). Among children with Hp infection, the different parameters summarized in (table 4), were studied according the presence or the absence of nodular gastritis.

Table 3: Characteristics of patients according to presence or absence of nodular gastritis (NG)

	NG+ n=16 (%)	NG – n=33 (%)	p
Age(yrs)	10 ± 3 y	7.5 ± 3 y	0.04
Sex (Boys/girls)	3/13 (18.7)	16/17 (48.5)	0.04
Chronic Gastritis	14 (87.5)	20 (60.6)	0.05
Active gastritis	11 (68.7)	11 (33.4)	0.02
Atrophy	9 (56.3)	10(30.3)	0.06
Follicular gastritis	13 (81.2)	12 (36.4)	0.005
Mild Score gastritis	3 ± 2	1.5 ± 1.5	0.005
Hp infection	14 (87.5)	21(63)	0.01

Follicular gastritis was found in 13 children out of 14 with nodular gastritis versus 10 out of 21 (47. 6%) children without nodular gastritis ($p=0.01$). The inflammation score was of 2 ± 0.8 in the group with nodular gastritis and 1 ± 0.7 in the group

without nodular gastritis ($p=0.001$). Gastritis global score was of 3.4 ± 1.6 in the group with nodular gastritis versus 2 ± 1.5 in the group without nodular gastritis ($p=0.02$).

Table 4: Characteristics of patients infected according the presence or absence of nodular gastritis (NG + / NG -)

	NG + n = 14 (%)	NG – n = 21(%)	p
Mild age	10 ± 3 y	8 ± 3 y	NS
Gender male	2 (14)	12 (57.2)	0.01
Histological findings :			
Chronic Gastritis	14 (100)	17 (81)	NS
Active Gastritis	11 (78.5)	11 (52.4)	NS
Atrophy	12 (86)	15 (71)	0.096
Follicular Gastritis	13 (93)	10 (47.6)	0.01
Inflammation Score	2 ± 0.8	1 ± 0.7	0.001
Activity score	0.9 ± 0.6	0.6 ± 0.7	NS
Gastritis global score	3.4 ± 1.6	2 ± 1.5	0.02

Table 5 : Sensibility and specificity of nodular gastritis according to different authors

	Sensitivity	Specificity	PPV	NPV
Loffeld 1999 [7] adults	19.6 %	98.6 %	93.9 %	53.3 %
Luzza 2001 [8]	40.5 %	100 %	100 %	64 %
Da G.S Bahu 2003 [2]	44 %	98.5 %	91.7 %	82.5 %
Prasad (2008)[10]	42%	85.7 %	42.4%	36.4 %
Our study	40 %		87.5 %	

DISCUSSION

Prevalence of Hp infection (71.5%) is high in our study as it was reported in previous study concerning asymptomatic children and symptomatically ones [5]. Chronic gastritis, active gastritis, follicular gastritis and score gastritis were significantly higher in infected children, than in non infected children as it was reported by different authors [3]. In 11.4% of cases the histology was normal in infected children as it was reported in literature [6]. In our study nodularity in the stomach showed a high specificity 85.7% and positive predictive value (87.5%) for the diagnosis of Hp infection. The same results were found in other studies (table 5). However, Prasad et al [10] concluded that antral nodularity is a poor predictor for Hp infection in children (positive predictive value = 46, 4%, sensitivity = 42%). He also insisted that during endoscopy, gastric biopsies should always be obtained in children to establish the presence of Hp infection.

In our study nodular gastritis was statistically associated to increasing age, to active gastritis and to a higher global score gastritis ($p=0.005$). Rafey et al [11] and Bahu Mda et al [9] found the same results. They also recorded Hp density as a

parameter statistically associated to nodularity. Logistic regression in a study conducted in children and young adults with Hp infection [12] revealed a significant increase in the incidence of nodular gastritis with gastritis score ($p=0.008$), but not an association with sex, age, or Hp density. Gastritis score was the only significant factor influencing the occurrence of nodular gastritis.

Follicular gastritis was significantly associated to nodular gastritis in our study ($p=0.005$). This histological entity seemed to be responsible for the nodular appearance in different studies [8, 9]. This fact was corroborated by Maghidman et al [13] who concluded that nodular gastritis was a chronic gastritis with superficial eosinophilic infiltration associated to an important inflammatory activity with the presence of Hp. The same author

reported that there is no relation with the presence and number of lymphoid follicles. For Sukmennier et al [14], it was the increase of intraepithelial lymphocytes that may contribute to formation of macroscopically nodules.

CONCLUSION

The relationships between nodular gastritis and Hp infection remain unclear. It was associated mainly to Hp infection and severe gastritis but we should study with more accuracy other parameters (clinical ones like nutrition, food allergy and histological ones as eosinophilic infiltration and intra epithelial lymphocytes) to understand better the therapeutic implication of this peculiar endoscopic aspect.

References

1. Dixon MF, Genta RM, Yardley JH, Correa P. Classification and grading of gastritis: the updated Sydney system. International Workshop on the Histopathology of Gastritis, Houston 1994. Am J Surg Pathol 1996; 20: 1161-81.
2. Warren JR, Marshall B. Unidentified curved bacilli on gastric epithelium in active chronic gastritis. Lancet 1983; 1:1273-5.
3. Prieto G, Polanco I, Larrauri J et al. *Helicobacter pylori* infection in children: clinical, endoscopic and histologic correlations. Pediatr Gastroenterol Nutr. 1992; 14:420-5.
4. Al-Enezi SA, Alsurrayei SA, Aly NY, et al. Endoscopic Nodular Gastritis in Dyspeptic Adults: Prevalence and Association with *Helicobacter pylori* Infection. Med Princ Pract 2010; 19:40-45.
5. Maherzi A, Bouaziz Abed A, Fendri C et al. *Helicobacter pylori* infection: prospective study for asymptomatic Tunisian children. Arch Pediatr 2003; 10 :204-7.
6. Gottrand F, Cullu F, Turck D et al. Normal gastric histology in *Helicobacter pylori* -infected children. J Pediatr Gastroenterol Nutr 1997; 25:74-8.
7. Loffeld RJ. Diagnostic value of endoscopic signs of gastritis with special emphasis to nodular antritis. Neth J Med 1999; 54:96-100.
8. Lizza F, Pensabene L, Imeneo M et al. Antral nodularity identifies children infected with *Helicobacter pylori* with higher grades of gastric inflammation. Gastrointest Endosc 2001; 53: 60-4.
9. Bahú Mda G, da Silveira TR, Maguilnick I et al. Endoscopic nodular gastritis: an endoscopic indicator of high-grade bacterial colonization and severe gastritis in children with *Helicobacter pylori* . J Pediatr Gastroenterol Nutr 2003; 36:217-22.
10. Prasad KK, Thapa BR, Sharma AK et al. Reassessment of diagnostic value of antral nodularity for *Helicobacter pylori* infection in children. Minerva Gastroenterol Dietol 2008; 54:1-6.
11. Rafeey M, Jafari Rouhi AH, Gassemi BA, Rouhi AJ. Relationship between endoscopic nodular gastritis and *Helicobacter pylori* infection in children. Indian J Gastroenterol 2004; 23:138-9.
12. Koh H, Noh TW, Baek SY, Chung KS. Nodular gastritis and pathologic findings in children and young adults with *Helicobacter pylori* infection. Yonsei Med J 2007; 48 :240-6.
13. Maghidman S, Cok J, Bussalleu A. Histopathological findings in nodular gastritis. Experience at the Cayetano Heredia National Hospital. Rev Gastroenterol Peru. 2001;21 :261-70.
14. Sokmensuer C, Onal IK, Yeniova O et al. What are the clinical implications of nodular gastritis? Clues from histopathology. Dig Dis Sci. 2009; 54:2150-4.