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ANATOMICAL PATHOLOGY

Gastric foveolar dysplasia: a survey of reporting habits and diagnostic criteria

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Summary

This study aimed to ascertain views, incidence of reporting and diagnostic criteria for gastric foveolar dysplasia.

A questionnaire, a post-questionnaire discussion and microscopic assessment of selected cases was conducted by gastrointestinal pathologists to explore the above-stated aims.

Fifty-four percent of respondents never or rarely diagnosed gastric foveolar-type dysplasia. The general consensus was that round nuclei, lack of nuclear stratification, presence of inflammation/damage and surface maturation favoured reactive change; while architectural abnormalities/complexity and nuclear enlargement mainly were used to separate low-grade from high-grade foveolar dysplasia. Immunohistochemistry was rarely used to make the diagnosis of dysplasia and was thought not to be of help in routine practice.

Inter-observer agreement in grading of dysplasia versus reactive, and the type of dysplasia (foveolar versus adenomatous), was substantial/almost perfect amongst 35.7% and 21.4% of participants, respectively. This reflects low reproducibility in making these diagnoses.

In conclusion, foveolar dysplasia was a rarely made diagnosis among 14 gastrointestinal pathologists, there are no uniform criteria for diagnosis and there is poor inter-observer agreement in separating low-grade foveolar dysplasia from reactive gastric mucosa and low-grade adenomatous dysplasia. Greater awareness and agreed criteria will prevent misdiagnosis of low-grade foveolar dysplasia as reactive, and *vice versa*.

Key words: Gastric dysplasia; foveolar dysplasia; reactive atypia; adenomatous dysplasia.

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INTRODUCTION

Dysplasia is a precursor to cancer and is of two major types in gastric mucosa: the more frequently known and encountered adenomatous-type (intestinal-type or type-I dysplasia) and the less common gastric foveolar-type (non-adenomatous or type-II dysplasia). Adenomatous-type arises in a background of intestinal metaplasia and is akin to dysplasia encountered in the colon. Adenomatous-type dysplasia consists of epithelium with a villo-glandular/tubulo-villous architecture, basophilic columnar cells with hyperchromatic, stratified and enlarged penicillate nuclei and variably conspicuous nucleoli. Architectural complexity and loss of nuclear polarity are key criteria used to separate low- from high-grade adenomatous dysplasia.[1] Foveolar-type dysplasia consists of cuboidal to columnar cells with pale-to-clear cytoplasm and hyperchromatic round-to-oval nuclei. There have been several studies on foveolar-type dysplasia in Barrett's oesophagus.[2–4] The distinction between foveolar low- and high-grade dysplasia is based mainly on nuclear size and architectural abnormalities.[2] Several morphological features help to discriminate between reactive changes and low-grade foveolar dysplasia in Barrett's oesophagus.[3] Although foveolar-type dysplasia in Barrett's oesophagus is morphologically similar to gastric foveolar-type dysplasia, the criteria applied in the oesophagus and its diagnosis have not been explored in the stomach to date.

Therefore, the aim of this study was to examine the diagnostic criteria for gastric foveolar-type dysplasia, its separation from reactive change and adenomatous-type dysplasia and to examine the strength of agreement amongst 14 pathologists in the diagnosis of gastric foveolar dysplasia.

MATERIALS AND METHODS

The participants were invited to complete an online questionnaire, designed by SS and RC (Table 1), to determine/ascertain participant practice habits regarding gastric foveolar dysplasia and, in particular, to suggest diagnostic

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criteria that were used and/or were thought to be important in making this diagnosis. Free text comments were also allowed.

Based on the diagnostic criteria emanating from the questionnaire, participants were invited to assess 11 representative cases without group discussion (round 1) and after discussion of criteria (round 2).

The 11 cases, consisting of nine gastric biopsies and two gastric resection specimens retrieved from the archives at UHN, were reviewed by SS and RC and classified as reactive (Fig. 1A,B), low- or high-grade dysplasia, and foveolar- or adenomatous-type (Fig. 2A–F), based on criteria available currently in the literature. For practical purposes and to simplify matters, we grouped reactive gastropathy and cases indefinite for dysplasia into one category. No clinical or other pathological information was provided to the participants, thus eliminating clinical bias. The assessment by SS and RC served as the 'gold standard' or baseline, as they had access to relevant clinical information and discussed each case using the criteria in Table 2 and other publications. The cases selected for the assessment included: four cases of reactive gastropathy, four cases of low-grade gastric foveolar-type dysplasia, two cases of high-grade gastric foveolar-type dysplasia and one case of low-grade adenomatous dysplasia.

Whole-slide imaging

High-resolution, whole-slide images were generated for all slides using an Aperio ScanScope CS scanner (Leica Biosystems, Germany) to allow viewing between ×0.17 and ×20 magnification. Selected whole-slide scanned de-identified images of H&E stained slides were uploaded to a secure file portal. The link to the scanned slides was circulated to the 14 pathologists. They were able to review the slides through a digital microscope interface allowing navigation from desktop computers. The participants were asked to record the type of lesion (reactive versus dysplastic), the degree of dysplasia (low-grade versus high-grade) and the type of dysplasia (foveolar versus adenomatous). Each pathologist was randomly assigned a study number. After the initial round of assessment, there was a discussion about the results and criteria used. Specifically, discussion points surrounded the diagnostic criteria to separate foveolar from adenomatous dysplasia, what constituted reactive change, the cytological and architectural features of low- and high-grade foveolar dysplasia. All features considered are in Table 2 and formed the basis of the initial 'gold standard'.[5]

Table 1 Questionnaire completed by participants

Questionnaire
1. How often do you make a diagnosis of foveolar dysplasia per year?
2. List and weight all the diagnostic criteria you use to make a diagnosis foveolar dysplasia
3. List the criteria separating low-grade from high-grade foveolar dysplasia
4. How do you distinguish low-grade foveolar dysplasia from reactive change?
5. How do you distinguish foveolar dysplasia from intestinal dysplasia?
6. Do you use immunohistochemistry in the diagnosis of foveolar dysplasia? If so, what stain?
7. Other comments.

SS and RC co-ordinated answers/responses, led the discussion and synthesised responses leading to the final document. The three other gastrointestinal (GI) pathologists from University Health Network, Toronto, did not discuss their responses hence avoiding any institutional bias.

Results were e-mailed to RC and SS and were entered into a standardised data collection form and inter- and intraobserver variability analysed using kappa statistics.

Kappa scores measure the degree of agreement of the nominal or ordinal assessments made by multiple appraisers when assessing the same samples. Kappa values range from −1 to +1. The higher the value of kappa, the stronger the agreement is. Kappa values were interpreted according to standardised criteria: <0 agreement is weaker than expected by chance (this rarely occurs); 0.01–0.20 slight agreement; 0.21–0.40 fair agreement; 0.41–0.60 moderate agreement; 0.61–0.80 substantial agreement; 0.81–0.99 almost perfect agreement; 1.0 perfect agreement. A kappa value of at least 0.70 is desirable, but kappa values close to 0.90 are preferred. A positive value indicates positive association while a negative value indicates a negative association. The higher the magnitude of the kappa score, the stronger the association.

RESULTS

A total of 14 pathologists were invited based on their practice being mainly or exclusively GI pathology; 13 responded to the questionnaire and 14 assessed the slides. The questionnaire is shown in Table 1.

Regarding the frequency of the diagnosis of gastric dysplasia, seven of 13 (54%) participants never or rarely (1–2 times/year) diagnosed gastric foveolar-type dysplasia, while six of 13 diagnosed it 4–12 times/year. Pertinent comments included: 'I do not subtype in clinical reports', 'I have assessed these changes previously as representing an unusual form of dysplasia, without using this terminology – or possibly as unusual reactive change'.

In terms of diagnostic criteria to diagnose gastric foveolar-type dysplasia (Table 2), nuclear features including the presence of nucleoli (8/13), enlarged/prominent nuclei (7/13), round monomorphic nuclei (6/13) and lack of nuclear stratification (7/13) were most commonly used. Additional diagnostic criteria included cytoplasmic features such as eosinophilic pale cytoplasm, cytoplasmic features of foveolar type mucin; full thickness/surface involvement (5/13), architectural complexity (1/13) and lack of surface inflammation (1/13). 'Exclusion of adenomatous dysplasia' before considering/making a diagnosis of foveolar dysplasia, was a recurring comment (8/13).

Criteria used to separate low-grade from high-grade gastric foveolar-type dysplasia included architectural abnormalities such as complexity (10/13) and gland crowding (7/13) and nuclear features such as nuclear enlargement (7/13), prominent

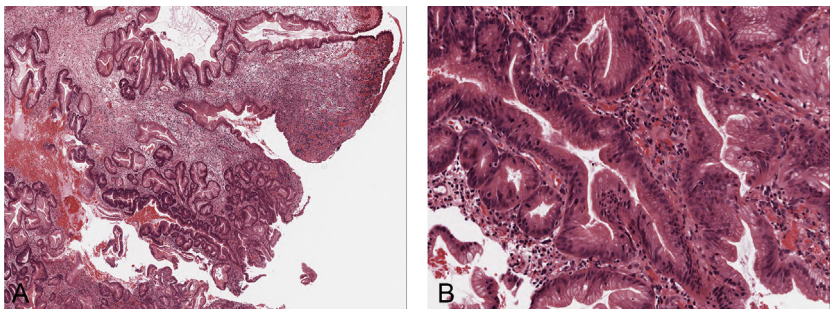

Fig. 1 Reactive gastric mucosa (A) that shows some degree of glandular crowding adjacent to an area of erosion. At higher magnification the glands consist of columnar cells with small basally polarised nuclei with dense chromatin. Nuclei are generally smaller than 1.5 times the size of a small mature lymphocyte. Nucleoli are inconspicuous and rare. There is surface maturation and the stroma is inflamed (B).