Helicobacter pylori in gastric biopsies—should you trust the pathology report?

ABSTRACT—The presence of Helicobacter pylori in gastric biopsies is closely associated with gastritis and duodenal ulceration. We have assessed the reliability of H pylori identification on haematoxylin and eosin (H & E) stained sections of gastric biopsies showing gastritis. A set of 20 slides was shown to 20 histopathologists (a total of 400 diagnoses); 11 of them were H pylori-positive, assessed using two special stains. Participants were asked to comment on the presence or absence of H pylori on H & E alone. The overall detection rate in positive cases was 66%. All pathologists missed at least one case, and there were 25 false-positive diagnoses overall. We conclude that identification of H pylori is unreliable in gastric biopsies if H & E alone is used. Clinicians who use the presence of H pylori as a basis for treatment should be aware of this problem.

Since Warren observed curved bacteria on gastric epithelium in 1983 [1], various staining methods have been used to visualise the organisms more clearly [2-4]. In diagnostic and experimental work, light microscopic identification of the bacteria, now known as Helicobacter pylori (previously Campylobacter pyloridis), is the method most frequently used. This compares favourably with the urease test and with direct culture [5]. In practice, many pathologists question the need for special stains and use haematoxylin and eosin (H & E) alone.

Specific treatment will often be initiated as a result of an H pylori-positive gastric biopsy, as the association between H pylori, gastritis, and duodenal ulceration is well documented [6,7]. The variability and accuracy of H pylori identification on H & E, however, has not been clearly defined. A previous study suggested an accuracy of 83%, using biopsies assessed independently by two pathologists with a special interest [8]. The accuracy of H pylori identification in routine biopsies may fall below this figure.

In this study, we have assessed interobserver variability and the reliability of H pylori identification on H & E alone.

Materials and methods

Haematoxylin and eosin stained slides from 20 gastric biopsies were used; all showed gastritis. The presence or absence of H pylori was assessed on special stains prior to circulation of the slides. The stains used were (i) modified Giemsa and (ii) Silver (Steiner), on subsequent levels of the same biopsies. Both have been shown to improve the detection of H pylori [2,9]. The stains were performed by one experienced technician in order to maintain consistency. The circulated slides were also critically reviewed in the light of the special stains.

The same set of 20 slides was seen by 20 pathologists (a total of 400 diagnoses). All were practising histopathologists from registrar (or equivalent) to consultant grade, with experience in reporting gastric biopsies. Participants were asked to record, on H & E alone, whether or not H pylori were present in each case. No time limit was given, but the participants were asked to spend the same length of time they would take to examine a routine gastric biopsy for H pylori. The time taken to complete the set of 20 slides was recorded.

Results

Of the 20 gastric biopsies, 11 were H pylori-positive, and 9 H pylori-negative, on special stains. In five of the positive cases H pylori were numerous; in two cases organisms were very sparse and focal. The time taken by participants to complete the set varied between 35 and 90 minutes.

Overall, the H pylori detection rate on H & E was 66% in positive cases. If the two cases with very sparse organisms were excluded, the detection rate was 76%. The results from the five cases where H pylori were numerous were more consistent, with a detection rate of 89%.

As expected, false-positive diagnoses were much less common than false-negatives. However, all nine H pylori-negative biopsies were given a false-positive diagnosis at least once. Of these, six cases were recorded as positive by three or more participants. Of the 20 pathologists in this study, 13 made at least one false-positive diagnosis on H & E. A total of 25 false-positive diagnoses were made—a specificity of 88%; 10% overlap-diagnosis.

Discussion

Our findings suggest that, except in cases where organisms are numerous, H & E alone is inadequate
for \( H \) \textit{pylori} identification. Interobserver variability is high, and the reporting of \( H \) \textit{pylori} on H & E staining only is unacceptably subjective. We found no relationship between accuracy in detection and time taken to examine the biopsies. Interestingly, the relative experience of the participants also proved to be unimportant. The main determinants appeared to be the number and focal clustering of the organisms in the biopsy. False-positive diagnoses were an occasional but recurrent finding in our study. All of the negative biopsies were recorded as positive at least once. False-positive diagnoses were made by almost two-thirds of the participants, constituting a total of 25 false-positive diagnoses.

Specific problems encountered were distinguishing \( H \) \textit{pylori} from strands of mucus in gastric pits, and from other micro-organisms. Special stains help to differentiate between mucus and micro-organisms and allow a more accurate assessment of bacterial morphology. Many stains have been described for \( H \) \textit{pylori} identification, most authors reporting good results [2–4]. However, it may be that the use of an additional stain is more important than the actual stain chosen.

Our results clearly have implications for patient treatment, where that depends on the \( H \) \textit{pylori} status. False-positive reporting of \( H \) \textit{pylori} may result in patients receiving inappropriate therapy. Gastric biopsies in which \( H \) \textit{pylori} are sparse, but clinically relevant, include re-biopsy following treatment for \( H \) \textit{pylori} gastritis associated with duodenal ulcer. Our results suggest that these are the biopsies in which \( H \) \textit{pylori} would be most likely to be overlooked if H & E alone were used. Due to the often focal nature of \( H \) \textit{pylori} infection, there will be occasional biopsy-negative cases, even following the use of special stains. Clinicians treating these cases should be aware of the limitations inherent in the histological diagnosis of \( H \) \textit{pylori} infection. Until definitive new techniques are established, liaison with the pathologist, who may otherwise be unaware of the clinical background and that small numbers of organisms may be present, is recommended, particularly if a patient is re-biopsied.

Acknowledgement

We are grateful to all of the pathologists who took part in this study, and to Simon Brown who performed the special stains.

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