Helicobacter pylori Link to Pernicious Anaemia
HG Desai*, PA Gupte**

Abstract
An immunological classification of chronic gastritis based on the detection of Helicobacter pylori (H. pylori) antibody, parietal cell antibody, intrinsic factor antibody, is reported. H. pylori chronic gastritis, slowly progresses to atrophic gastritis, in the majority of patients; in a few patients, with genetic susceptibility to form intrinsic factor antibody, it progresses to pernicious anaemia. In majority of patients of pernicious anaemia, H. pylori gradually disappears from the gastric mucosa, on development of intestinal metaplasia in them. Atrophic gastritis results from H. pylori or non H. pylori. H. pylori infection is diagnosed in the presence of H. pylori in the gastric mucosal biopsy and/or H. pylori antibody (IgG) in the serum. The presence of the genetic factor (intrinsic factor antibody) is essential for the diagnosis of pernicious anaemia. Pernicious anaemia patients without intrinsic factor antibody, should be correctly diagnosed as atrophic gastritis, in view of the absence of the genetic factor (intrinsic factor antibody) in them.

Diseases such as acute or chronic hepatitis, thyroiditis, glomerulonephritis, arthritis are all classified on the basis of immunological parameters. A significant progress in the classification of chronic gastritis will be achieved only when immunological parameters are given maximum importance (Fig. 1).

The immunological classification of chronic gastritis was independently reported from India (March 1973) and Australia (May 1973). It was based on the presence of parietal cell antibody (PCA: 1962) and intrinsic factor antibody (IFA: 1963) in the serum of patients of pernicious anaemia (autoimmune : Type A). Following the discovery of Helicobacter pylori (H. pylori) in endoscopic gastric mucosal biopsy of humans in 1983, the etiological agent in 80% of patients of chronic gastritis is H. pylori, was reported. An immunological classification based on H. pylori antibody (HPA:1986), PCA, IFA, to identify the environmental factor "H. pylori (or non H. pylori) and the genetic factor – IFA, is reported.

Immunological classification
Chronic gastritis should be divided in two groups (i) H. pylori induced (ii) non-H. pylori. The causes of non-H. pylori chronic gastritis are – eosinophilic, lymphocytic, granulomatous, reflux (post-operative), post-radiation, corrosive; they are not discussed, as typical gastric mucosal histology and history, establishes the diagnosis. The chronic gastritis (acquired) in a patient with a genetic susceptibility to form IFA, progresses to pernicious anaemia.

Helicobacter pylori and immunology
HPA – IgA, IgG indicates present and past infection respectively. HPA cross react with gastric autoantigens such as the alpha and beta subunits of proton pump and determines the progress and localization (body or antrum) of gastric mucosal damage.

PCA are formed against the parietal cell cytoplasm and the specific antigen identified is the alpha and beta units of the gastric H⁺K⁺ATPase (proton pump). A positive correlation between HPA and PCA was observed in patients of pernicious anaemia; these antibodies recognize different epitopes on H⁺K⁺ATPase.

Intrinsic factor antibody
IFA is against the amino acid sequence 251 – 256 of intrinsic factor, secreted by the parietal cells.
Blocking (type I) and Binding (type II) IFA are present in the serum and/or gastric juice of patients of pernicious anaemia. Initially Type II antibodies were considered rare but subsequently a high incidence of type II antibody in sera of patients of pernicious anaemia was reported. Estimation of total (type I and II) antibodies with enzyme linked immunosorbent assay (ELISA) is recommended. The prevalence of IFA in serum of patients of pernicious anaemia increased significantly during a follow up of 70 (14-137) months. The incidence of IFA in first – degree relatives of patients of pernicious anaemia was as high as 22%. Amongst 16 Indian patients of atrophic gastritis with histamine fast achlorhydria (HFA) with severe vitamin B12 malabsorption (< 5% excretion on Schilling test), IFA was present in only 2, indicating the rarity of IFA in Indian patients, due to a genetic factor. The development of IFA is independent of the sex, age, duration of disease, degree of atrophic gastritis or titre of PCA and is determined by a genetic factor.

**DISCUSSION**

Is there any link between H. pylori infection and pernicious anaemia?

Fifty percent of healthy control subjects with a positive HPA in serum showed a negative urea breath test, indicating absence of H. pylori (at present) in the gastric mucosa. In patients with atrophic gastritis, the difference of a positive serum HPA and a negative staining for H. pylori, is even more marked. In pernicious anaemia patients, the prevalence of H. pylori in the gastric mucosal biopsy is low, it was 11% (71% in controls), 21% (39% in controls), and 40% and was related to the development of intestinal metaplasia in them. In contrast, the prevalence of HPA in serum of pernicious anaemia patients was 57% (in patients > 60 years), indicating past exposure to H. pylori infection. In 30 patients of pernicious anaemia, the prevalence of HPA and PCA was 83% and 100% respectively. The first – degree relatives of pernicious anaemia and duodenal ulcer patients, showed a comparable prevalence of H. pylori in the gastric mucosal biopsy in young relatives but a markedly decreased prevalence H. pylori in the older age group relatives of pernicious anaemia patients. This observation indicates the role of H. pylori in the early stage of pernicious anaemia.

The immunological classification (HPA, PCA, IFA) of chronic gastritis is based on two questions: (i) whether H. pylori infection (present or past) is responsible for the atrophic gastritis? (ii) whether a genetic factor, indicated by IFA formation, has any contribution? The environmental and genetic factor earlier blamed for pernicious anaemia are now recognized as H. pylori (or non H. pylori) and IFA formation respectively. The presence of H. pylori in the gastric mucosa and / or HPA (IgG) in serum indicates H. pylori, as the aetiological agent of atrophic gastritis (acquired). The patients of atrophic gastritis with histamine fast achlorhydria, severe vitamin B12 malabsorption (<5% excretion on Schilling test) without IFA in serum, should not be labelled as pernicious anaemia. The presence of IFA (genetic factor) should be considered essential for the precise diagnosis of pernicious anaemia and its absence should exclude it.

**REFERENCES**


