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Comment on Yeh et al, page 1247

Triple play of H pylori in ITP

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In this issue of Blood, the meticulous study by Yeh and colleagues offers new insight into the mechanism of “immune” TP associated with H pylori infection.

Although association of H pylori infection with a subgroup of ITP is now widely recognized, little is known about the underlying mechanism of the thrombocytopenia (TP). In this issue of Blood, Yeh et al offer new insight on the mechanism of “immune” TP associated with H pylori infection. They document induction of platelet aggregation by H pylori in vitro and show that this effect is strain-dependent. Using both the proaggregatory strain (Hp49503) and nonaggregatory strains (Hp42504, Hp51932), they demonstrate an essential role for P-selectin and Hp IgG antibody (Hp IGs) in H pylori-induced platelet aggregation. This reaction was completely inhibited by anti-P-selectin antibodies. The presence of H pylori was shown by demonstration of Hp–specific urease gene fragment in the aggregates. They propose that binding of bacteria/Hp IGs to platelet FcyRIIA receptor activates platelets to release granules and to induce surface P-selectin and von Willebrand factor, leading to aggregation. They also looked into platelet apoptosis evidenced by annexin V binding and membrane blebbing, and observed that both proaggregatory and nonaggregatory strains induced apoptosis. Taken together, they conclude that platelet aggregation and apoptosis induced by certain strains of H pylori leads to thrombocytopenia.

As we see it, this “triple play” of H pylori is summarized in the figure. First, IgG antibodies to H pylori are generated. Second, H pylori with the IgG antibodies induce platelet activation and movement of P-selectin to the platelet surface. Third, interaction of H pylori with the IgG antibodies induce platelet activation and movement of P-selectin to the platelet surface.

IgG antibodies to H pylori are generated. (2) H pylori with the IgG antibodies induce platelet activation and movement of P-selectin to the platelet surface. (3) Interaction of H pylori, Hp IgGs, and P-selectin leads to platelet aggregation and apoptosis, reducing the number of circulating platelets. Professional illustration by Paulette Dennis.
IGs, and P-selectin leads to platelet aggregation and apoptosis, reducing the number of circulating platelets.

However, details of this interaction are not fully elucidated. Yeh et al studied 2 groups of healthy subjects with normal platelet counts, comparing the uninfected group to the group infected with *H pylori*. They did not investigate patients with thrombocytopenia with *H pylori* infection or perform sequential studies before or after eradication of *H pylori*.

Despite questions about details, they have taken an important step toward delineating the mechanism of *H pylori*–mediated immune thrombocytopenia. Better understanding of the mechanisms involved may be important not only in ITP but also in more serious and familiar diseases such as cancers and atherosclerosis. *H pylori* is implicated in the induction and progression of lymphomas, other neoplasm, and cardiovascular disorders. Early eradication of *H pylori* infection has resulted in favorable outcomes.

Among patients with *H pylori*–associated ITP, a significant percentage achieve lasting remission after eradication of *H pylori*. This fact heralds a definite sea change for hematologists in evaluating patients with “idiopathic” TP. Physicians must now dig deeper in searching out the etiology of “immune” TP, because the key to curing ITP is rooting out the underlying causes. This etiologic search must include serology of *H pylori* to detect its antibodies, and if positive, presence of the bacteria must be confirmed by appropriate tests such as 13C-urea breath test, stool test, or endoscopic biopsy, followed by antibiotic therapy if confirmed. After completion of the antibiotic course, eradication of the offending bacteria must be ensured by repeating the breath test or stool test.

ITP is often like an iceberg, signaling more serious underlying problems that could lead to progression of atherosclerosis and neoplastic transformation. It is the duty of the hematologist to catch the opportunity to detect potential serious problems and prevent grave consequences.

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Triple play of *H pylori* in ITP

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