ABSTRACT

There is increasing evidence that H. pylori strain diversity is associated with variable host immune responses and may influence the clinical outcome of infected patients. Some investigators have confirmed the association between H. pylori and cITP in adults, although studies in pediatric patients are few and have produced conflicting results.

So, the present study aimed to detect the prevalence of H. pyloria in patient with ITP and its correlation with the duration of disease, response to therapy and association with other autoimmune manifestations.

Key Word

Helicobacter Pylori in Immune Thrombocytopenic Purpura

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Presented by

Omar Mahmoud Soliman
(M. B. B. Ch)
Faculty of Medicine, Cairo University

Under supervision of

Dr. Mona Eltagui

Professor of Pediatrics

Faculty of Medicine

Cairo University

Dr. Mona Hamdy

Professor of Pediatrics

Faculty of Medicine, Cairo University

Dr. Ayman Emil

Assistant Professor of Pediatrics
Faculty of Medicine, Cairo University

Faculty of Medicine, Cairo University

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LIST OF ABBREVIATIONS

AEIOP	Associazione Italiana di Ematologia e Oncologia Pediatrica
CagA	cytotoxin associated gene A
EE	erosive esophagitis
FD	Functional Dyspepsia
GERD	Gastroesophageal Reflux Disease
GI	Gastrointestinal
IBD	inflammatory bowel disease
ITIM	immunoreceptor tyrosine-based inhibitory motif
ITP	Immune thrombocytopenic purpura
IVIg	intravenous immunoglobulin
JAK	Janus kinase
KIR	killer cell immunoglobulin-like receptor
MALT	Mucosa -associated lymphoid tissue
MAP	Mitogen-activated protein
MMR	measles, mumps and rubella
NK	natural killer
NSAID	nonsteroidal anti-inflammatory drugs
PPARd	peroxisome proliferator-activated receptor d
RB	Russell body
SMO	spermine oxidase
STAT	signal transducers and activators of transcription
T4SS	type 4 secretion system

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INTRODUCTION

Immune thrombocytopenic purpura (ITP) is the most common cause of isolated thrombocytopenia and it occur in two forms : acute self limited disease and a chronic form ***(McMillan, 2007).***

ITP is an autoimmune disorder in which thrombocytopenia results from the action of anti-platelet antibodies. Platelets coated with these antibodies have a shortened life span and rapidly cleared from the circulation. Recently it has been suggested that Helicobacter pylori may contribute to the pathogenesis of immune thrombocytopenic purpura, since partial or even complete remission of thrombocytopenia has been reported in some patient after eradication of H. pylori infection ***(Hayashi et al., 2005).***

Although no established mechanism to explain how H.pylori could be implicated in the pathogenesis of ITP, several theories have been proposed to explain that including molecular mimicry, platelet aggregation and the induction of T helper 1 phenotype that favor the onset and/or persistence of ITP ***(Loffredo et al., 2007).***

H. pylori has been considered a central etiologic agent for gastritis, peptic ulcer and gastric adenocarcinoma for many years. H. pylori ulcer has been also implicated in other disease such as vascular diseases, Henoch Schonlien purpura and certain skin diseases ***(Chen et al., 2013).***

AIM OF THE STUDY

Our aim of this work is to detect the prevalence of H. pylori in patient with ITP and its correlation with the duration of disease, response to therapy and association with other autoimmune manifestations.

IMMUNE THROMBOCYTOPENIC PURPURA

Definition

Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by a low circulating platelet count caused by destruction of antibody-sensitized platelets in the reticuloendothelial system ***(Blanchette and Bolton-Maggs, 2010).***

Epidemiology

In a systematic review, four were determined to have the strongest estimates for ITP incidence in children based on the method of patient identification and study design. The lowest incidence estimate in these four studies was 2.2 per 100000 children/year and the highest incidence estimate was 5.3 per 100000 children/year ***(Terrell et al., 2010).***

Pathophysiology

- **Humoral mechanisms**

Whereas classical helper T cell driven B cell activation is central to ITP ***(Kuwana et al., 2009)***, platelets in some patients with ITP express sufficient CD154 to be capable of directly activating B cells to produce antiplatelet antibodies ***(Solanilla et al., 2005).***

It has been demonstrated that platelet autoantibodies in ITP demonstrate constrained heavy and light chain pairings and appear to derive from somatic mutation in a clonally restricted B cell population ***(Roark et al., 2002).***

Fc receptors on reticuloendothelial phagocytes then recognize the Fc regions of the antibodies coating platelets, with subsequent uptake and degradation of the platelets in the reticuloendothelial system, with a preponderance of activity in the spleen ***(Kuwana et al., 2009).***

Following phagocytosis, processing of platelet antigens by antigen-presenting cells may then result in the presentation of

cryptic epitopes, further driving ongoing immune responses against the resulting neoantigens. Polymorphisms of FcγRIIIa genes may be implicated in the pathogenesis of ITP ***(Fujimoto et al., 2001)*** and monoclonal antibodies against FcγRIIIa have been effective in increasing platelet counts in case reports ***(Soubrane et al., 1993).***

However, amonoclonal antibody targeting FcγRI signaling has also been shown to inhibit the generation of T cell responses to the platelet antigen GPIIb/ IIIa ***(Kuwana et al., 2009).***

IVIG may derive its utility in ITP through activation of FcγRIIb, which is associated with an immunoreceptor tyrosine-based inhibitory motif (ITIM), and subsequent abrogation of signals transduced by other Fc receptors associated with immunoreceptor tyrosine-based activation motifs (ITAMs) ***(Samuelsson et al., 2001).***

A role for complement-mediated lysis has been further illustrated in reports demonstrating acquired deficiencies of complement regulatory proteins in ITP patients that are associated with the degree of thrombocytopenia but not with the

presence of detectable platelet autoantibodies ***(Ruiz-Arguelles and Llorente, 2007).***

- **Cell-mediated mechanisms**

The immunodysregulation that results in clinically apparent platelet destruction in ITP extends beyond purely B cell responses to include defects in the regulation of cellular immunity. Patients with primary ITP have been demonstrated to have a propensity for a Th0/ Th1 cytokine profile, suggestive of a defect skewed towards cellular mechanisms of immunopathogenesis ***(Cines et al., 2009).***

Autoreactive CD4+helper T cells drive the B cell response and are themselves activated by ongoing self-antigen uptake and presentation by antigen-presenting cells, permitting ongoing amplification and diversification of the autoreactive lymphocyte repertoire ***(Kuwana et al., 2009).***

In addition to driving the mechanisms of platelet destruction described above, however, CD3+ CD8+ T lymphocyte subsets may directly lyse platelets ***(Olsson et al., 2003).***

Increased expression levels of killer cell immunoglobulin-like receptor (KIR) genes, which function as negative regulators of cytotoxic NK and T cells, correlate with remission status in chronic ITP patients ***(Olsson et al., 2003).***

A role for natural killer (NK) cell involvement in ITP is also demonstrated by the presence of increased NK in patients with chronic active ITP and the absence of such increases in patients with ITP in remission ***(Garcia-Suarez et al., 1993).***

However, some series have failed to find evidence of CD3-CD16+CD56+ NK cell-mediated lysis, suggesting that either NK cells contribute to platelet destruction in only a subset of ITP patients or that the previously observed increases in CD56+ cells in ITP are associated with the disorder in a manner other than that of direct cytotoxicity ***(Olsson et al., 2003).***

- **Ineffective thrombopoiesis**

It is recognized that ineffective thrombopoiesis is as central to the pathogenesis of ITP as is the increased platelet destruction so convincingly demonstrated a half-century ago ***(McMillan and Nugent, 2005).***