Gastrointestinal and Hepatic Disease in Rheumatoid Arthritis

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KEYWORDS

• Rheumatoid arthritis • Gastrointestinal disease • Hepatic disease
• Antirheumatic medications (DMARDs)

KEY POINTS

- Gastrointestinal and hepatic disease are rare extra-articular manifestations of rheumatoid arthritis.
- Treatment of rheumatoid arthritis can lead to digestive and hepatic dysfunction, either as a direct effect of medications, or from the infections to which patients with RA are susceptible.
- Although rare in the modern era, complications of long-standing, poorly controlled RA (including rheumatoid vasculitis, Felty syndrome, and amyloidosis) may be associated with significant GI morbidity.

INTRODUCTION

The importance of the gastrointestinal (GI) tract in development of autoimmunity has been increasingly appreciated in human diseases.[1,2] Many autoimmune diseases primarily affect the GI tract or the liver, including inflammatory bowel disease (IBD), celiac disease, and various autoimmune liver diseases. Rheumatoid arthritis (RA) is a systemic autoimmune disease that can affect multiple organ systems. Understanding the range and prevalence of GI manifestations associated with RA itself, with related autoimmune disorders, and with RA treatments is essential for rheumatologists and other clinicians caring for patients with RA. All organs of the GI tract can be affected either directly from RA, through related autoimmune diseases, or as consequences of treatment (**Fig. 1**). This article discusses the presentation, epidemiology, and diagnosis of GI disease in patients with RA.

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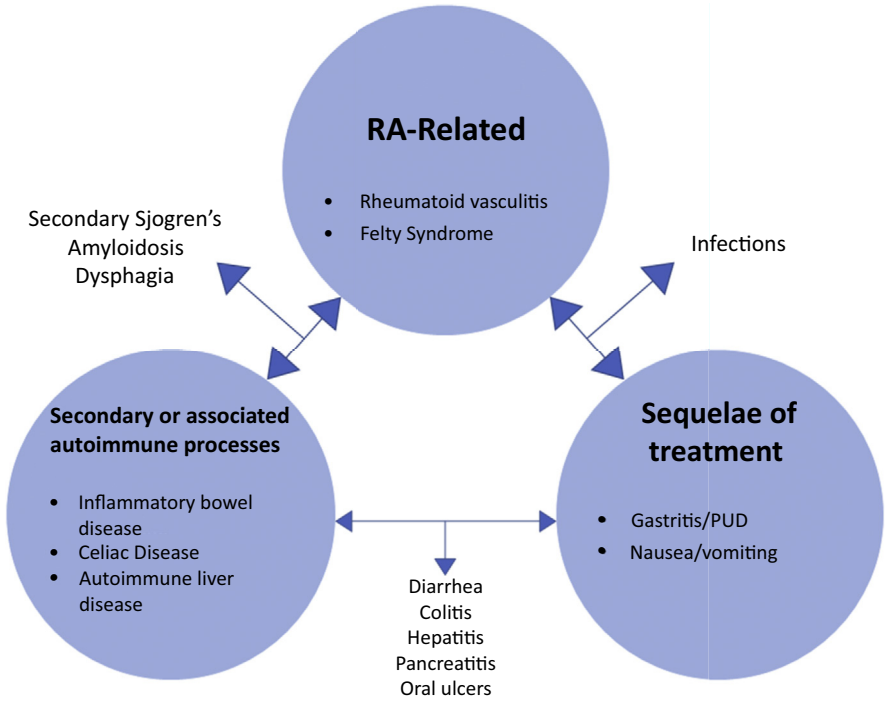

Fig. 1. An overview of digestive and hepatic complications from rheumatoid arthritis, its treatment, and related disorders. PUD, peptic ulcer disease.

EPIDEMIOLOGY OF RHEUMATOID ARTHRITIS

RA is a common rheumatologic disorder that affects up to 1.29 million adults in the United States.[3] Estimates of RA prevalence range between 0.5% and 1% of adults.[3] Lifetime risk among Americans has been reported as 1.7% for men and 3.6% for women.[4] The prevalence of RA seems to be decreasing since the early 1960s. In a 2008 study of RA in Olmstead County, Minnesota, prevalence had decreased over time for most age groups. An increased prevalence was noted only in older age groups, suggesting an increase in chronicity, and decrease in incidence.[3]

Several factors have been associated with an increased risk for RA, including female sex; smoking; and certain infectious agents, such as GI pathogens, as discussed later. Genetic risk has also been identified, with higher risk for RA among those with the shared epitope, a sequence of five amino acids in the hypervariable segment common to several HLA-DRB chains.[5] However, there remains considerable discordance even between identical twins in development of RA, speaking to a possible role of environmental risk factors.[6] Numerous other mutations have been identified that predispose to RA, although none as strongly as the shared epitope, and none that are necessary or sufficient for development of disease.[7,8]

THE GASTROINTESTINAL TRACT IN RHEUMATOID ARTHRITIS PATHOGENESIS

A growing literature suggests that the GI tract may play a major role in the pathogenesis of RA. This hypothesis was initially derived from an epidemiologic association