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Case Studies in Thyroid Diseases; Case Studies in Chronic Hepatitis C

Series Editor and Contributor:

Richard J. Simons, MD, FACP

Professor of Medicine, Assistant Dean for Medical Education, Associate Director, Internal Medicine Residency Training Program, Staff Physician, Department of Medicine, Milton S. Hershey Medical Center, Pennsylvania State University College of Medicine, Hershey, PA

Contributors: Christopher J. Bero, MD, PharmD

Resident, Department of Medicine, Milton S. Hershey Medical Center, Pennsylvania State University College of Medicine, Hershey, PA

Alfredo Mendoza, MD

Gastroenterology Fellow, Division of Gastroenterology, Milton S. Hershey Medical Center, Pennsylvania State University College of Medicine, Hershey, PA

Table of Contents

Chapter 1—Case Studies in Thyroid Diseases. 2

Contributors: Christopher J. Bero, MD, PharmD
Richard J. Simons, MD, FACP

Chapter 2—Case Studies in Chronic Hepatitis C . . . 16

Contributors: Alfredo Mendoza, MD
Richard J. Simons, MD, FACP

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Chapter 1—Case Studies in Thyroid Diseases

Christopher J. Bero, MD, PharmD, and Richard J. Simons, MD, FACP

I. INTRODUCTION

Thyroid disorders are a common problem in adult medicine. Hyperfunction or hypofunction, goiter, nodules, and neoplasia can affect the thyroid gland. Based on population screening studies using serum thyrotropin or thyroid-stimulating hormone (TSH) levels, the prevalence of hypothyroidism in patients older than 18 years is estimated to be approximately 7.5% for women and 2.8% for men. The incidence of hypothyroidism is 3.5 cases per 1000 persons annually for women, and 0.6 cases per 1000 persons annually for men. Hyperthyroidism, typically diagnosed as a suppressed TSH, is estimated to have a prevalence of 10% of the population and primarily affects women.¹ The incidence of hyperthyroidism in women is low (0.8 cases per 1000 persons per year) and much lower in men.¹ Goiter is more common in women.

Thyroid nodules also are common, especially in women and individuals who received head and neck irradiation at a young age. The prevalence of thyroid nodules in the general population varies depending on the diagnostic modality used, with estimates ranging from 3% to 5% by palpation, 30% to 40% by ultrasound, and 40% to 50% at autopsy. Approximately 4% of thyroid nodules are cancerous. Interestingly, autopsies of military men aged 18 to 39 years documented a prevalence of thyroid nodules of 13%.¹ The mean prevalence of thyroid carcinoma is 3.6%, and most are papillary carcinomas. The incidence of thyroid cancer ranges from 3 cases per 100,000 persons annually at age 20 years to 8 cases per 100,000 per year at age 50 years, with women more often affected than men. The incidence of thyroid cancer in individuals who received head and neck irradiation is approximately 0.5% per year.¹

This article will review recommendations for screening asymptomatic patients for thyroid disease, discuss laboratory investigations used in its diagnosis and management, delineate the etiology and management of hypothyroidism and hyperthyroidism (including their subclinical variants), and outline the evaluation of goiter and thyroid nodules.

II. SCREENING ASYMPTOMATIC ADULTS

CASE PATIENT I PRESENTATION

Patient 1 is a 49-year-old man who presents as a new patient to a primary care practice. His medical history includes hypertension and depression for many years. Family history is negative for thyroid disease, coronary artery disease (CAD), and diabetes mellitus. His medications include fluoxetine, amlodipine, and hydrochlorothiazide. The review of systems is negative for lethargy, constipation, and heat/cold intolerance. On physical examination, his pulse is 68 bpm and his blood pressure is 142/84 mm Hg. There is no goiter or exophthalmos. The cardiac examination is normal, tremor is not detected, and normal deep tendon reflexes are present.

- According to the American College of Physicians (ACP), what is the appropriate screening modality for thyroid dysfunction for this patient?
 - A) Check serum TSH now
 - B) Check serum TSH at age 50 years
 - C) Check free thyroxine (T₄) now
 - D) Check free T₄ at age 50 years
 - E) Not indicated at present

DISCUSSION

The correct answer is E. Several organizations have published guidelines for screening asymptomatic adults for thyroid dysfunction. The ACP recommends^{2,3} that women age 50 years or older undergo TSH evaluation. If the TSH is undetectable or the level is at 10 mIU/L or higher, then free T₄ should be obtained. This recommendation is based on epidemiologic data indicating that unsuspected but symptomatic overt hypothyroidism or overt hyperthyroidism is common and will respond to therapy in most cases. Screening women younger than 50 years and men of any age is unnecessary given the low prevalence of unsuspected, symptomatic thyroid disease in these populations. Cooper⁴ recommended screening men older than 65 years, women older than 35 years every 5 years, and all women at their first prenatal visit. All pregnant women should be

Chapter 2—Case Studies in Chronic Hepatitis C

Alfredo Mendoza, MD, and Richard J. Simons, MD, FACP

I. INTRODUCTION

Hepatitis C is caused by infection with the hepatitis C virus (HCV), a small RNA virus from the Flaviviridae family. It is an important human pathogen initially known as the cause of non-A non-B post-transfusional hepatitis until 1989 when Houghton and colleagues cloned and sequenced the genome of HCV. This virus is one of the major causes of end-stage liver disease, cirrhosis, and hepatocellular carcinoma. HCV cirrhosis is the leading indication for liver transplantation in the United States.¹

HCV has a remarkable ability to establish persistent infections characterized by increased genetic diversity in the form of quasi-species of closely related but distinct viruses within infected individuals.² Commonalities within viral sequences have allowed the classification of viral isolates into 6 distinct genotypes and numerous subtypes. The most common genotype in the United States is genotype 1; genotypes 2 and 3 are also present. These genotypes are also found worldwide.

HCV antibodies are detected 7 to 31 weeks after infection and targeted against epitopes in all viral proteins. The existence of neutralizing antibodies to HCV and their role in the outcome of infection is still controversial. An early, vigorous, and multispecific immune response of CD4+ and CD8+ cells has been associated with self-limited HCV infection and viral clearance. In contrast, if the immune response is weak and not maintained for a sufficient time, HCV infection may become persistent, resulting in chronic hepatitis. In chronic HCV infection, the cellular response is insufficient to eradicate HCV completely. Although the cellular response may control the viral load, it may also contribute to chronic inflammatory liver disease.

Approximately, 170 million people (3%) worldwide are chronically infected with HCV. In the United States, the prevalence of anti-HCV is 1.8%, of which 74% have HCV RNA corresponding to an estimated 2.7 million individuals with chronic hepatitis C.³

The development of an effective viral vaccine against HCV is a high priority. However, HCV poses several potential obstacles to vaccine development, including its great heterogeneity and its high propensity for mutation. HCV vaccine approaches now undergoing preclinical evaluation include virus-like particles, synthetic peptide vac-

cines, recombinant viral subunit vaccines, naked DNA vaccines, and gene delivery via viral vectors.⁴

II. CASE PATIENT 6

PRESENTATION

Patient 6 is a 39-year-old female health worker who complains of increasing tiredness over the past several months, such that she now naps on a daily basis. She drinks 2 to 3 beers over the weekends, admits to having abused intravenous drugs, and had been sexually promiscuous 20 years ago. She denies having had blood transfusions, and her medical history is otherwise non-contributory. Her husband and son are healthy. The physical examination is unremarkable. She has a mildly elevated alanine aminotransferase (ALT) of 74 units/L, prompting an HCV antibody (anti-HCV) test that was positive. HIV, hepatitis B surface antigen (HBsAg), and antibody to HBsAg (anti-HBsAg, commonly referred to as anti-HBs) are negative.

RISK FACTORS

This patient has mildly elevated aminotransferases and a positive anti-HCV in the setting of a known risk factor for acquiring HCV. Risk factors (**Table 8**) include transfusion of infected blood or blood products, which was the main mode of transmission until 10 years ago. Blood banks have been screening for hepatitis for nearly 30 years. Since the introduction of blood donor screening and surrogate hepatitis tests, the proportion of post-transfusional HCV has declined. Parenteral exposure by sharing contaminated needles among injection drug users is currently the most important mode of transmission.^{5,6} Other risk factors include use of contaminated dialysis equipment, transplantation of infected organs, and occupational exposure from needle stick injuries in health workers. Perinatal exposure and sexual contact are associated with HCV infection; however, transmission is relatively inefficient by these routes. Breast feeding does not appear to increase the risk of HCV transmission.⁷ Approximately 10% of patients have no apparent risk factor; however, they admit to having used intranasal cocaine, which has been associated with HCV transmission through the use of contaminated straws.⁸ Other