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ABSTRACT

Hereditary hemochromatosis (HH) refers to several inherited disorders of iron metabolism leading to tissue iron overload.

Classical HH is associated with mutations in HFE (C282Y homozygotes or C282Y/H63D compound heterozygotes) and is almost exclusively found in populations of northern European descent.

Target organs and tissues affected by HH include the liver,heart, pancreas, joints, and skin.

Recently, we have encountered the rare representation of this disease of the oral cavity associated with generalized burning sensation of the tongue.

To conclude, all patients with a chief complaint of burning sensation of the oral cavity and tongue should be adequately screened for hereditary hemochromatosis to prevent the associated mortality and morbidity with the hemochromatosis.

PATHOPHYSIOLOGY

Hereditary hemochromatosis is an adult-onset disorder characterized by inappropriately high iron absorption resulting in progressive iron overload. The organs involved are the liver, heart, pancreas, pituitary, joints, and skin.

The gene responsible for the disease is called HFE and is located on chromosome 6. When a mutant or nonfunctional variant of the HFE gene is present, ferritin levels(鐵蛋白濃度) are not under the influence of a normal and functional HFE gene, which leads to enhanced accumulation of iron in peripheral tissues.
Excess iron is hazardous because it produces free radical formation. The presence of free iron in biological systems can lead to the rapid formation of damaging reactive oxygen metabolites, such as the hydroxyl radical and the superoxide radical. These can produce DNA cleavage, impaired(缺陷) protein synthesis, and impairment of cell integrity(完整性) and cell proliferation, leading to cell injury and fibrosis.

DISCUSSION

Frequency

In the United States, the prevalence is approximately 1 case in 300 persons. Most are of northern European. The carrier state is estimated to be approximately 10%.

Mortality/morbidity

Mortality is estimated to be 1.7 cases per 10,000 deaths.

Race
Prevalence in whites is 6 times higher than in African Americans.
HFE C282Y mutation, a genotype seen in more than 90% of patients with typical hemochromatosis.

Sex
Men are affected more often than women, with an estimated ratio of 1.8:1.
who are homozygous for the C282Y mutation, especially when serum（血清） ferritin levels are 1000 u g/L (1mg/L) or more.

Age
Median age in women is 66 years. Median age in men is 51 years.

Table I. Clinical manifestations

Clinical manifestations associated with hemochromatosis
● Liver disease
● Skin pigmentation
● Diabetes mellitus
● Arthropathy
● Impotence in males
● Cardiac enlargement, with or without heart failure or conduction defects

In our cases the patients were asymptomatic with generalized burning sensation of the tongue.

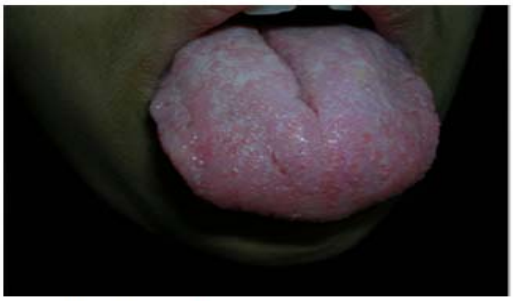

Fig. 1. Normal fissured tongue.

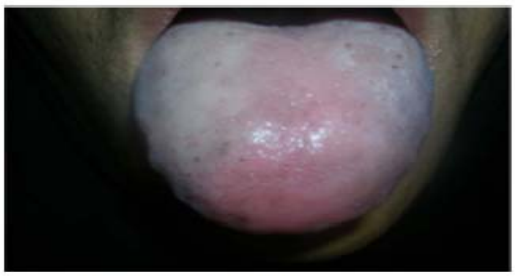

Fig. 2. Smooth and blanched tongue.

Table II. Symptoms and signs of hemochromatosis

Symptoms	*Signs*
Early	Hepatomegaly
Severe fatigue (74%)	Skin pigmentation
Impotence (45%)	Arthritis
Arthralgia (44%)	Abnormal liver function tests
	Susceptibility to bacterial infections
	Chondrocalcinosis of hand and wrists
Late	
Hyperpigmentation (70%)	
Diabetes mellitus (48%)	
Cirrhosis	
Asymptomatic (75%)	
Cardiomyopathy	
Dilated cardiomyopathy	
Hypogonadism	
Hypothyroidism	

早期：疲勞，性無能，關節痛　晚期：色素過多，糖尿病，肝硬化。(無症狀)
跡象：肝腫大，風濕，肝功能異常，容易細菌感染，軟骨鈣化。

Differential diagnosis
A history of documentation of cirrhosis and bronzing(燒灼) of skin should arouse suspicion of hemochromatosis of tongue.
A biopsy with demonstration of diffuse iron deposition, in conjugation with clinical findings and elevated serum iron levels allows for definitive diagnosis.
Laboratory studies
Measuring serum iron has no value in the diagnosis, but measuring transferrin saturation(轉鐵蛋白飽和度) is necessary. Transferrin saturation corresponds to the ratio of serum iron and total iron-binding capacity.The screening threshold for hemochromatosis is a fasting transferrin saturation of 45% to 50%.
The American College of Physicians found insufficient evidence to recommend for or against the use of transferrin saturation and serum ferritin levels to help identify the early stages of hereditary hemochromatosis. Genetic testing for the HFE mutation is indicated in all
first-degree relatives of patients with hemochromatosis and also in patients with evidence of iron overload

Treatment
The goal of therapy in patients with iron overload disorders is to remove the iron before it can produce irreversible parenchymal damage.
Once diagnosed, hemochromatosis is treated by phlebotomy to rid the
body of excess iron and to maintain normal iron stores.
Recently, deferasirox(拉羅司), which is a rationally designed oral iron chelator, has

been introduced to reduce chronic iron overload.
Patients should limit alcohol consumption and should not eat raw oysters.

CONCLUSIONS
Hemochromatosis is the most common genetic disorder among white populations.
Patients with hemochromatosis of the tongue are generally asymptomatic with generalized burning sensation of tongue.
Transferrin saturation, ferritin levels, and genotyping can often establish the diagnosis.
Iron depletion therapy with phlebotomy and deferasirox is helpful if initiated before organ damage occurs.

題號	題目
1	有關血鐵質沉著症（hemochromatosis），下列哪一敘述是不正確的？ (A) 慢性貧血中，Severe Aplastic Anemia較Cooley's anemia輸血頻繁，更容易合併此症 (B) 此症合併有皮膚色素沉著，糖尿病及肝硬化現象 (C) 螯鐵劑（iron-chelating agent）之使用為最有效之治療 (D) 在desferoxamine治療中同時服用vitamin C，可促進鐵之排泄
答案(A)	出處：九十三年度內科專科醫師考試筆試題
題號	題目
2	下列何者不是遺傳性血鐵質沉著症（hereditary hemochromatosis）的常見症狀？ (A) 尿崩 (B) 微小結節性肝硬化 (C) 糖尿病 (D) 皮膚色素沉積
答案(A)	出處：97 年第二次醫事放射師高等考試基礎醫學考試試題