

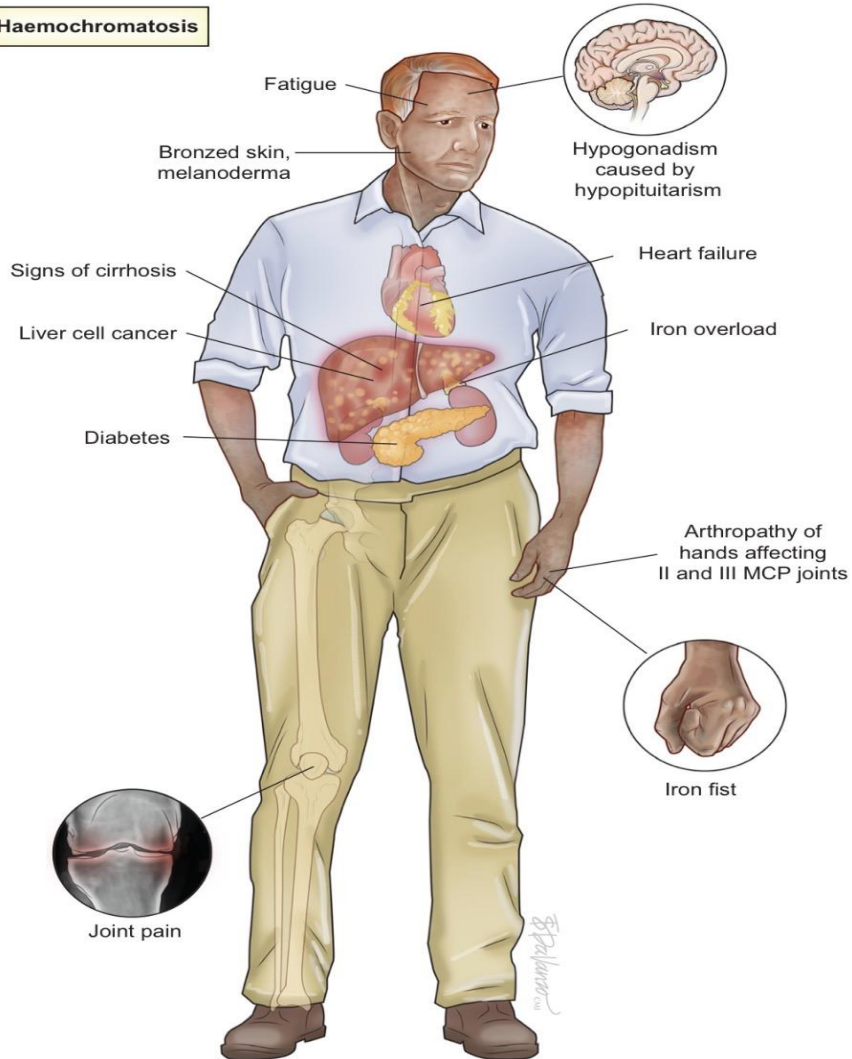
# *Case 3*



# *Hemochromatosis*



## Haemochromatosis



**Table 1**

Differential diagnosis of iron overload in humans.

### **Hereditary haemochromatosis**

HFE-associated hereditary haemochromatosis (type 1)

C282Y homozygosity

Or C282Y/H63D compound heterozygosity

Non-HFE-associated hereditary haemochromatosis

Type 2A haemojuvelin mutations

Type 2B hepcidin mutations

Type 3 transferrin receptor-2 mutations

Type 4 ferroportin mutations

Other

H-ferritin IRE (HHCS)

Hemoxygenase deficiency

Neonatal iron overload

Aceruloplasminaemia

Congenital atransferrinaemia or hypotransferrinaemia

DMT1 mutations

### **Secondary iron overload**

Iron loading anaemias

Ineffective erythropoiesis

Thalassaemic syndromes

Sideroblastic anaemia

Myelodysplastic syndrome

Congenital dyserythropoiesis

Increased erythropoiesis

Chronic haemolytic anaemia

Parenteral iron overload (including multiple blood transfusions)

Other

Metabolic syndrome

Obesitas

Hypertension

Insulin resistance

Chronic liver disease

Hepatitis

Alcohol abuse

Non-alcoholic steatohepatitis (NASH)

Porphyria cutanea tarda

Iron overload in sub-Saharan Africa

**Hereditary Spherocytosis :  
Chronic hemolytic anemia**

<b>Organ</b>	<b>Manifestation In Hereditary hemochromatosis</b>	<b>Manifestation in Thalassemia</b>	<b>Screening</b>
<b>Pituitary gland</b>	1.Hypogonadotropic hypogonadism 2.GH def -rare 3.others -rare	1.Hypogonadotropic hypogonadism 2.GH -common 3.others-rare	Testosterone (M) Estradiol(F) LH FSH
<b>Pancreas</b>	Common Prevalence 13-23%	Prevalence 5%	FBS , HbA1c
<b>Primary Gonadal</b>	Rare (mostly central)	Rare (mostly central)	Testosterone (M) Estradiol(F) LH FSH
<b>Adrenal gland</b>	AI-rare	AI-rare	8 AM cortisol
<b>Thyroid gland</b>	Hypothyroid -rare 1-2%	Hypothyroid 5-6%	TSH +- FT4
<b>Parathyroid gland</b>	Hypoparathyroid -rare	Hypoparathyroid 3-4%	PTH, Ca, P, ALP, 25 hydroxyvitamin D

# Endocrinopathy in Hemochromatosis

## ORGAN-SPECIFIC MANIFESTATIONS & PREVALENCE

### HEREDITARY HEMOCHROMATOSIS (HH) (PRIMARY IRON OVERLOAD)

**HYPOGONADISM:**  
Hypogonadotropic hypogonadism is the most common non-DM endocrine issue.  
**GH DEFICIENCY: RARE**



**THYROID:**  
Hypothyroidism is rare (1-2%).  
**PARATHYROID:**  
Hypoparathyroidism is rare.



**PANCREAS:**  
Diabetes Mellitus is common (13-23%).



**ADRENAL:**  
Adrenal Insufficiency is very rare.



### THALASSEMIA (SECONDARY IRON OVERLOAD)

**HYPOGONADISM:**  
Hypogonadotropic hypogonadism.  
**GH DEFICIENCY: COMMON (20-30%)**



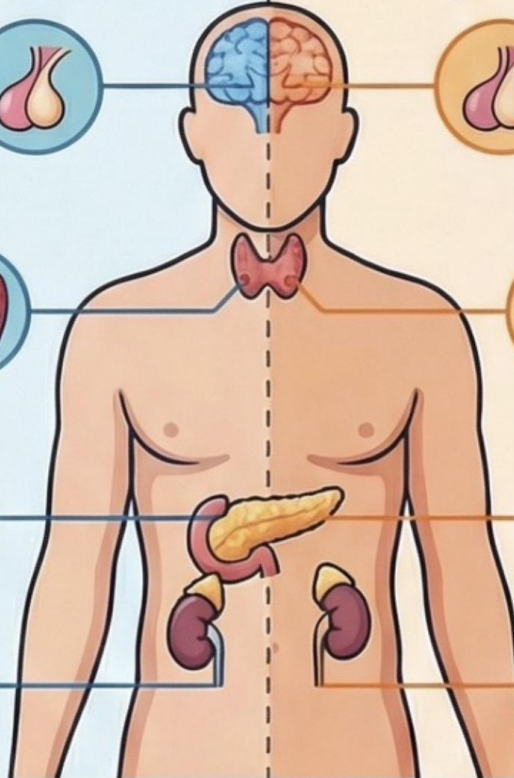
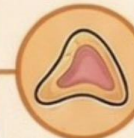
**THYROID:**  
Hypothyroidism is more frequent (5-6%) with common subclinical presentations.  
**PARATHYROID:**  
Hypoparathyroidism occurs in 3-4%.



**PANCREAS:**  
Diabetes Mellitus is less common (5%).



**ADRENAL:**  
Adrenal Insufficiency is very rare.



## MANIFESTATION COMPARISON DATA TABLE

Organ	Manifestation in HH	Manifestation in Thalassemia
Pituitary	Hypogonadotropic hypogonadism (most common); GH deficiency is rare.	Hypogonadotropic hypogonadism; GH deficiency is common (20-30%).
Pancreas	Diabetes Mellitus is common (13-23%).	Diabetes Mellitus is less common (5%).
Thyroid	Hypothyroidism is rare (1-2%).	Hypothyroidism is more frequent (5-6%).
Parathyroid	Hypoparathyroidism is rare.	Hypoparathyroidism occurs in 3-4%.
Adrenal	Adrenal Insufficiency is very rare.	Adrenal Insufficiency is very rare.

## CLINICAL SCREENING GUIDELINES



**PITUITARY & GONADAL LABS**  
Screen using Testosterone (males), Estradiol (females), LH, and FSH.



**PANCREATIC & ADRENAL LABS**  
Monitor Pancreas with Fasting Blood Sugar (FBS) and HbA1c; screen Adrenal gland with an 8 AM cortisol test.



**THYROID & PARATHYROID LABS**  
Check Thyroid with TSH and Free T4; Parathyroid requires PTH, Calcium (Ca), Phosphorus (P), Alkaline Phosphatase (ALP), and 25-hydroxyvitamin D.



# *Hemochromatosis : pituitary imaging*

**Brain is usually protected** by the blood–brain barrier (BBB)

However, some CNS structures are **outside the BBB**, allowing iron deposition:

- **Pituitary gland**
- Choroid plexus
- Circumventricular organs

**Iron deposition** in these areas causes:

- Magnetic field inhomogeneity on MRI
- Resulting in **signal loss on T2\*-weighted images**



# *MRI in Hemochromatosis*

**Iron** is paramagnetic ,causing magnetic field inhomogeneity which leads to **signal loss (hypointensity)** on MRI

## **MRI Sequences**

### **Conventional**

- T1-weighted (Spin Echo)
- T2-weighted (Spin Echo)

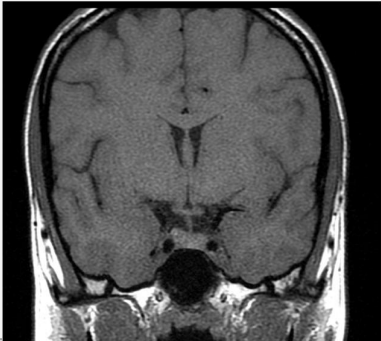
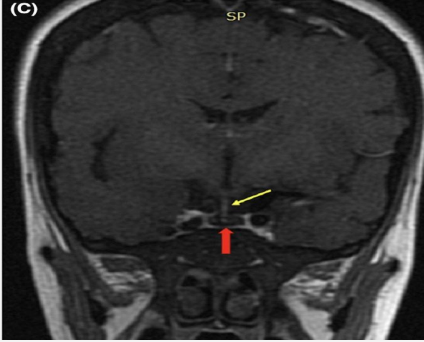
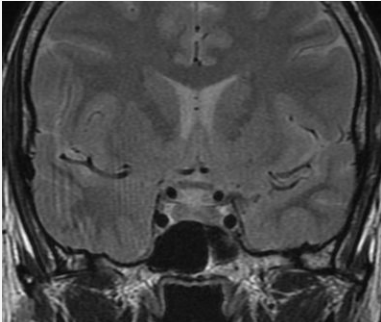
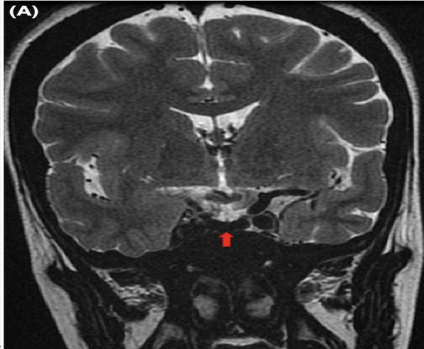
### **Advanced**

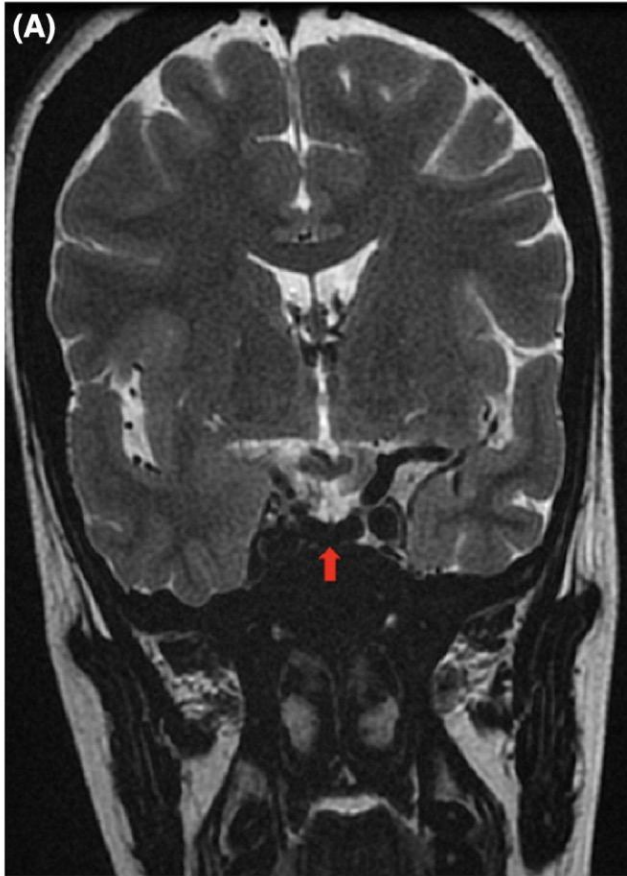
- T2\* (Gradient Echo, GRE)
- Multi-echo T2\*



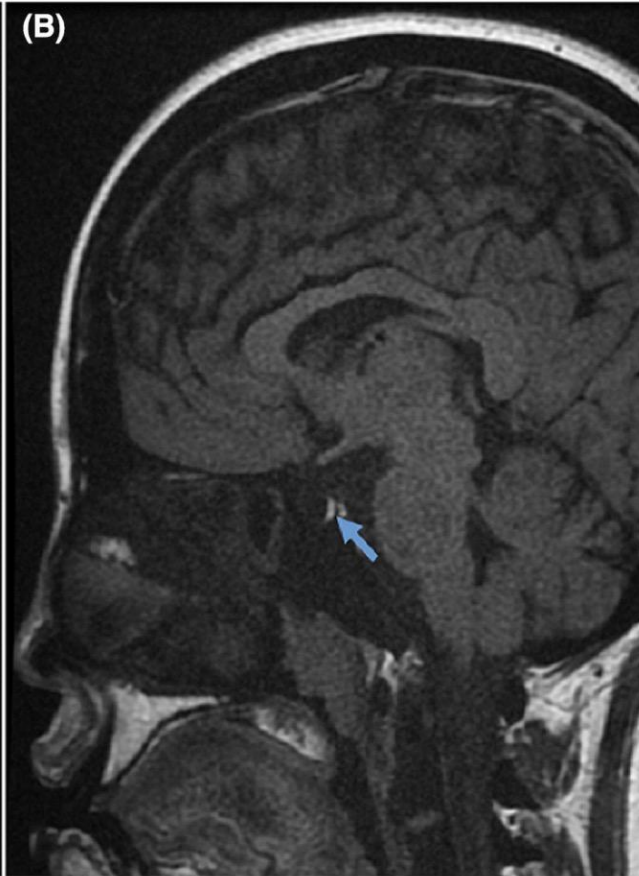
# *MRI in Hemochromatosis*

Pituitary—usually normal size, no mass lesion

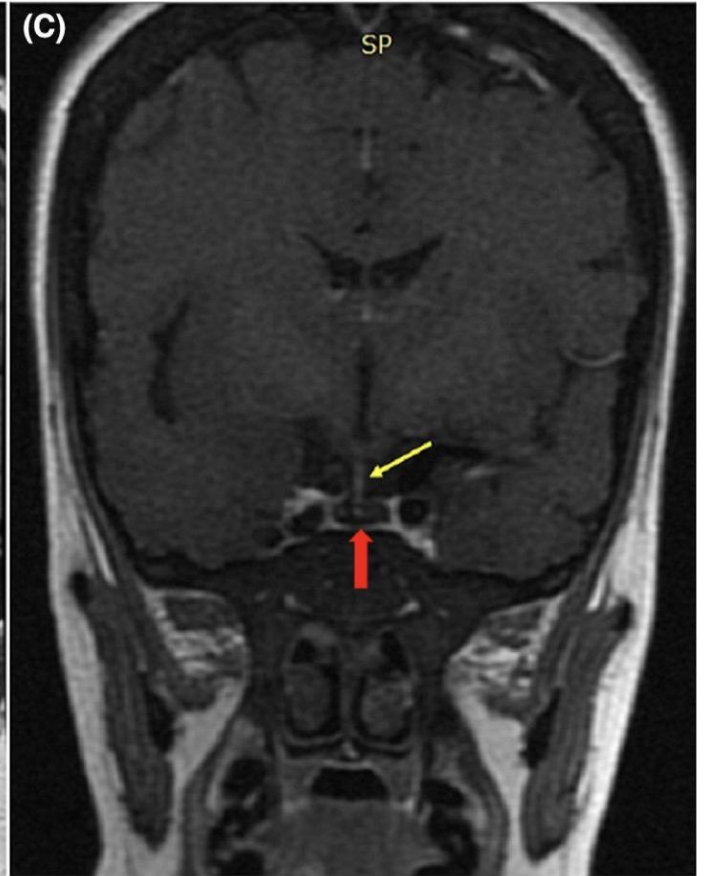
Hemochromatosis	Normal anterior Pituitary	Hemochromatosis
T1-weighted (SE)	Isointense 	slightly hypointense  (C) SP A yellow arrow points to the pituitary gland, and a red arrow points to a slightly hypointense area within it.
T2-weighted (SE)	Isointense 	low signal (dark)  (A) A red arrow points to the dark pituitary gland.



✧ T2 -Hyposignal of anterior pituitary gland

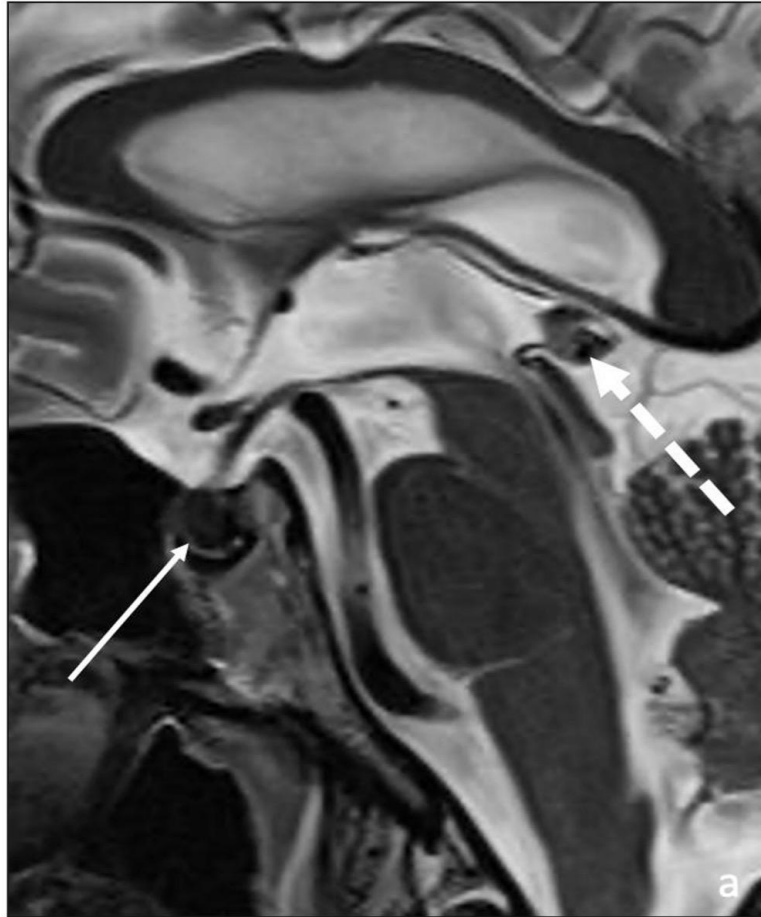


Physiological T1 hypersignal of posterior pituitary gland (blue arrow)



T1 with Gd  
Pituitary stalk enhancement (yellow)  
Lack of enhancement of hypophysis (red)

# *MRI in Hemochromatosis*



# *MRI in Hemochromatosis*

**T2\* is Gold standard MRI sequence for iron overload**

- Most sensitive to **susceptibility effects**
  - Detects **early iron deposition**

***T2 (GRE) in hemochromatosis***

Anterior pituitary : **dark**

Posterior pituitary : **normal bright**

No mass, no enhancement



# *Hereditary Spherocytosis*

- Inherited hemolytic anemia due to **RBC membrane defects** : reduced surface to volume ratio
- Clinical presentation
  - Asymptomatic to severe symptom
  - Chronic anemia, jaundice, splenectomy
  - Pigmented gallstones
- Common complications :
  - Anemia
  - Cholelithiasis
  - Aplastic crisis
- Treatment
  - Aim to improve quality of life, PRC transfusion to maintain Hb at a minimum 7-8 mg/dL, folic acid supplement
  - Splenectomy for moderate to severe disease
- Long term complication
  - Risk of iron overload (**Chronic hemolysis** -> increased iron absorption -> iron accumulation)



# *Hereditary Spherocytosis*

- Iron overload in HS is uncommon but clinically significant
- The exact mechanism remains unknown
- Potential causes :
  - **Chronic hemolysis**
  - Increased erythropoiesis of spherocytosis
  - Increased intestinal iron absorption
  - Altered iron metabolism
  - Repeated transfusion



Ann Hematol (2002) 81:202–209  
DOI 10.1007/s00277-002-0432-0

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CASE REPORT

**J. B. Brandenburg · F. Demarmels Biasiutti**  
**H. U. Lutz · W. A. Wuillemin**

# **Hereditary spherocytosis and hemochromatosis**

Received: 22 May 2001 / Accepted: 8 January 2002 / Published online: 26 March 2002  
© Springer-Verlag 2002



# *A 37-year-old man*

Splenectomized at the age of 1 year.

History of hypogonadotropic hypogonadism since 34 years old

Admit due to severe chest pain, cardiogenic shock

Echo : LVEF 20%, CAG : no significant stenosis of any coronary artery

U/S : Liver steatosis and cholecystolithiasis with multiple concrements.

Lab : Ferritin 6,243 mcg/L, Tsat 100%

Liver biopsy : portal cirrhosis with considerable fibrosis and extensive amounts of iron, especially in hepatocytes and epithelial cells of the bile ducts and vessels.

## Mechanism of Iron Overload

- Chronic hemolysis increases iron absorption
- HFE mutation predisposes to iron accumulation
- Splenectomy may contribute

## Management

- Phlebotomy reduced ferritin levels -> Ferritin 6243 -> 115
- Improved cardiac function and diabetes control, however hypogonadism not improved.





The Lancet

Volume 253, Issue 6557, 30 April 1949, Page 736



ORIGINAL ARTICLES

## HÆMOCHROMATOSIS IN THREE FAMILIES AND IN A WOMAN

R.D. Lawrence M.A., M.D. Aberd., F.R.C.P. (PHYSICIAN IN CHARGE OF DIABETIC DEPARTMENT, KING'S COLLEGE HOSPITAL, LONDON)



The American Journal of the Medical Sciences

Volume 292, Issue 5, November 1986, Pages 320-324



Case Reports

## Case Report: Hemochromatosis Heterozygotes May Have Significant Iron Overload When They Also Have Hereditary Spherocytosis

Daniel N. Mohler MD , Munsey S. Wheby MD



The Lancet

Volume 292, Issue 7566, 31 August 1968, Pages 481-485



ORIGINAL ARTICLES

## HEREDITARY SPHEROCYTOSIS WITH SECONDARY HÆMOCHROMATOSIS

Michael Barry M.B. Cantab., M.R.C.P. (LECTURER IN MEDICINE), P.J. Scheubr M.D. Lond., M.C.Path. (SENIOR LECTURER IN PATHOLOGY), Sheila Sherlock M.D. Edin., F.R.C.P., F.R.C.P.E., Hon. F.A.C.P. (PROFESSOR OF MEDICINE ROYAL FREE HOSPITAL MEDICAL SCHOOL, LONDON W.C.1), C.F. Ross M.D., B.Sc. Lond., F.C.Path. (CONSULTANT PATHOLOGIST, GROUP LABORATORY, ST. PETER'S HOSPITAL, CHERTSEY, SURREY), Roger Williams M.D. Lond., M.R.C.P. (CONSULTANT PHYSICIAN, KING'S COLLEGE HOSPITAL, LONDON S.E.5)

 Published via Lake Erie College of Osteopathic Medicine (LECOM)

Open Access Case Report

## A Rare Case of Iron Overload in Hereditary Spherocytosis: A Case Report

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Year	Author	Country	No. of Cases	Key Features	Genetics
1968	Barry	UK	1	Secondary hemochromatosis in HS	Not reported
1973	Berry	USA	1	HS + diabetes + iron overload	Not reported
1980	Zimelman	USA	1	Primary hemochromatosis with HS	Not reported
1982	Edwards	USA	1	Iron overload in HS	HLA-linked HH suspected
1984	Takegoshi	Japan	1	HS with hepatoma due to iron overload	Not reported
1986	Mohler	USA	3	Family with HS and iron overload	Possible genetic interaction
1986	Fargion	Italy	2	Siblings with HS and severe iron overload	Not reported
1987	O'Mahony	Ireland	1	Genetic hemochromatosis with HS	Not reported

Year	Author	Country	No. of Cases	Key Features	Genetics
1997	López	Spain	1	Multi-organ iron overload	Not reported
2002	Brandenberg	Switzerland	1	HS with hereditary hemochromatosis	C282Y homozygous
2004	Ichiche	France	1	HS with iron overload	HFE negative
2009	Höblinger	Germany	1	Cirrhosis reversed after phlebotomy	C282Y homozygous
2018	Gao	China	1	Secondary hemochromatosis in HS	Not reported
2018	Fujino	Japan	1	Fatal cardiac iron overload	Not reported
2019	Tole	UK	4	Mild HS with significant iron overload	HFE negative
2024	Soldin	UK	1	Coinheritance HS and hemochromatosis	Genetic interaction
2024	Bui	USA	1	Iron overload after splenectomy	HFE negative

# *Summary*

Total reported cases  $\geq$  33 cases worldwide

Characteristics:

- Rare complication
- Often long-standing HS
- Frequently post-splenectomy
- May occur without transfusion
- May occur without genetic mutation



# *Take home message*

- Always review MRI images yourself in referred cases; do not rely solely on reports.
- Monitor iron overload in chronic hemolysis, especially endocrine complications.
- Pituitary hemochromatosis typically shows **T2-signal loss** with **preserved gland volume** in the **anterior pituitary** and **preserved neurohypophysis bright spot on MRI**.



*Thank you!*