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Case Report

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Hereditary hyperferritinemia cataract syndrome with iron deficiency : a case report

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ABSTRACT

Hereditary hyperferritinemia-cataract syndrome (HHCS) is a rare disease characterized by high serum ferritin levels, congenital bilateral cataracts, and the absence of tissue iron overload. HHCS is an autosomal dominant inherited rare genetic disease. In this case report, we aimed to present a young female patient with a history of cataracts in herself and her family members. Our patient had the dilemma of iron deficiency anemia and hyperferritinemia. As in our patient, patients with HHCS apply to many outpatient clinics and have difficulty in diagnosis. For this reason, we prepared our case to raise awareness.

Keywords: Cataract, hyperferritinemia, iron

INTRODUCTION

Hyperferritinemia-cataract syndrome is a disease characterized by ferritin (hyperferritinemia) in the blood, a protein that causes excessive accumulation of iron in the tissues of the body. The accumulation of this protein begins in the early hours of life and causes the lenses to become cloudy (cataracts). In affected individuals, as in the general population, it usually develops in infancy and after age 60. Cataracts that are not surgically removed cause progressive darkening and blurred vision because blurred lenses reduce and distort the incoming light. Our aim in this case is to increase the clinical awareness Hereditary Hyperferritinemia Cataract Syndrome (HHCS) as a cause of hyperferritinemia in the presence of iron deficiency anemia and in the absence of iron accumulation and to form a diagnosis scheme as possible.

CASE

A 39-year-old female without a known chronic disease has been suffering from joint pain, fever and fatigue since 1995. In 2004 she underwent cataract surgery. The patient was later diagnosed with iron deficiency anemia (low serum iron and low transferrin saturation) and received iron replacement. Due to ongoing complaints, the patient was treated for 2 years with an initial diagnosis fibromyalgia (there is no documented record of this issue). Later, in rheumatology outpatient clinics, it was determined that there was no rheumatologic pathology, patient's high serum ferritin levels was associated with iron replacement therapy (Table).

In follow-up with persistent high serum ferritin levels the patient was directed to our department of hematology. It was revealed that the patient had hyperferritinemia before iron replacement therapy (first documented value: 1469 ng/ml). The patient evaluated for hemochromatosis, but there was no family history and transferrin saturation was low. The patient had a family history of early-onset cataracts with her mother, two of her aunts, uncle and with her children (both daughter and son) all requiring cataract surgery at an early age. Molecular genetic analysis showed patient is heterozygous for the FTL: c-160G>A substitution (also known as + 40A>G). Also molecular genetic analysis of patient's children (both son and daughter) and mother (which was living in Norway) were consistent with hereditary hyperferritinemia cataract syndrome (Figure). The patient's 26-year-old daughter had iron deficiency anemia and was treated with iron.

DISCUSSION

HHCS is an autosomal dominant inherited rare genetic disease. HHCS is an example of deregulation of the iron regulatory element (IRE)- iron regulatory protein (IRP) system. Heterozygous mutations of the L-ferritin mRNA in IRE make it unresponsive to IRP binding and translation suppression.

Table. Laboratory values of the patient and daughter over time.

DATE (PATIENT)	Ferritin ng/mL	Hgb g/dL	RCB 10^6/mL	Hct** %	Iron mg/dL	UIBC* mg/dL
06/2010	1469					
08/2012		10	4.59	31		
02/2013	1585					
03/2013	1438	10.3	4.93	35		
09/2013	1545	8.9	4.57	30	14	458
06/2014	>2000	10.2	4.7	31	15	441
07/2014	1607	10.8	4.96	35	16	453
12/2014	>2000	9.7	4.6	30	17	385
09/2015	1516	7.4	4.20	27	12	448
04/2016	2296		4.7	40.3	64	375
DATE (DAUGTER)	**Ferritin ng/mL**	**Hgb g/dL**	**RCB 10^6/mL**	**Hct** %**	**Iron mg/dL**	**UIBC* mg/dL**
09/2012	1221	11.8	4.45	35.8	19	404
08/2013		12.6	4.69	38.4	104	469
05/2014	>2000	12.0	4.5	38.2	56	449
09/2015	1500	12.6	4.54	39.5	46	410
DATE (SON)	**Ferritin ng/mL**	**Hgb g/dL**	**RCB 10^6/mL**	**Hct** %**	**Iron mg/dL**	**UIBC* mg/dL**
07/2014	1632	15.2	4.9	43.3	91	333
09/2015	1366	14.8	4.89	44.1	116	344

*UIBC: Unsaturated iron binding capacity **Hematocrit

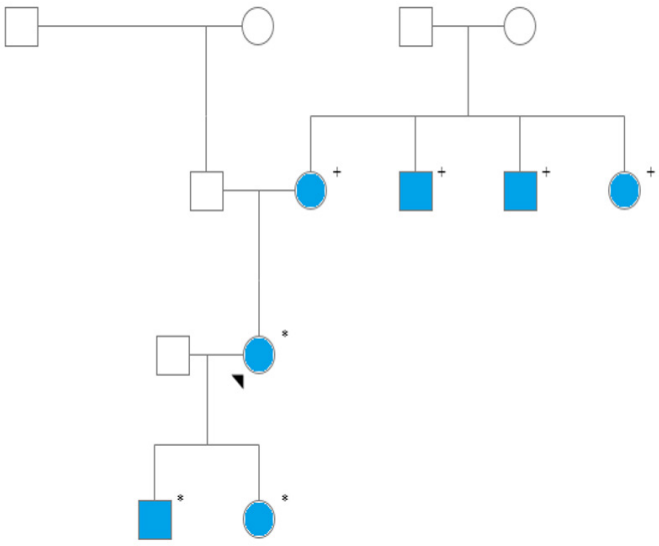

Figure. Family pedigree (plus: history of cataract , asterisk: genetically proven of HHCS)

Protein synthesis is continuous and iron independent. Serum ferritin levels are high, but total body iron and serum hepcidin levels are normal. In HHCS, ferritin accumulates in all cells in the body.[1] However, it causes cataracts by becoming toxic through forming L-ferritin crystal deposit formations only in the lens. Investigations of lens deposits with electronic microscopy revealed that lens deposits were crystals of L- ferritin. HHCS is usually not associated with anemia, and iron deficiency is usually not associated with an elevated serum ferritin. Distinguishing hyperferritinemia in HHCS with no iron overload from hyperferritinemia in hemochromatosis with iron overload is important.[2] In our case, the patient and her daughter had intermittent iron replacement therapy. HHCS may occur in patients with iron deficiency anemia without developed symptomatic cataract. So in this type of patients receiving iron replacement therapy could aggrevate the process of cataract formation. There is no specific treatment for HHCS. Cataracts are the only known complication of the disorder. Individuals are treated with corrective glasses, contact lenses and, if vision is impaired to the point of interference with daily activities, then cataract surgery is performed. Therapy involving the regular removal of blood via a vein (known as a phlebotomy) is a common therapy for disorders associated with excess iron in the blood, but is not recommended as a therapy for HHCS.[3]

CONCLUSION

HHCS should be considered in patients with family history, cataract, and hyperferritinemia, and genetic tests should be used for definitive diagnosis.

ETHICAL DECLARATIONS

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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