MRI in Hemoglobinopathy and Storage Disorders

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MRI SZEREPE A HEMOGLOBINOPATHIÁKBAN ÉS RAKTÁROZÁSI BETEGSÉGEKBEN

Hermann professzor dolgozatának célja, hogy felhívja a figyelmet az MR vizsgálat szerepére a csontvelői elváltozások vizsgálatában. A csontvelő reconversiójára focusál haemoglobinopathiás (sarlósejtes anaemia, thalassemia), és lipid-tárolásos betegségek (Gaucher kór) eseteinek bemutatásával. Az MR jelmenet változásával demonstrálja az enzim therápia következtében létrejövő javulást a csontvelői, valamint a máj és lép elváltozásoknál. Megállapítja, hogy az MR a nagyon hasznos, korszerű módszer a korai csontvelői eltérések kimutatására anaemiában, sejtes expanzióban, infarctus esetén, vaslerakódás kimutatására, valamint az enzimtherapiára bekövetkező regressziós elváltozás demonstrálására Gaucher kórban.

MRI is an invaluable tool for detecting a wide range of focal and diffuse bone marrow changes reflected as signal alterations in the medullary cavity. To properly interpret MRI of the musculoskeletal system – particularly of the bone marrow – it is necessary to understand the anatomy and physiology of the bone marrow, which is one of the largest organs of the body. At birth almost the entire marrow space is filled with cellular red marrow.

Conversion from red to yellow marrow starts before birth at the terminal phalanges of the hands and feet and continues after birth to gradually extend through the long bones of the extremities toward the axial skeleton.

Marrow reconversion, reversal of the normal sequence, occurs at the time when increased hematopoesis exists in various types of anemia, infiltrative marrow disorders such as plasma cell myeloma, leukemia, myelofibrosis, and skeletal metastasis.

Abnormal hemoglobin in the blood represents hemoglobinopathies such as sickle cell anemia (Hb SS disease), sickle cell trait (Hb AS disease), or disease where the Hb S is combined with other abnormal Hb C, called sickle cell hemoglobin C disease.

Sickle cell anemia is the result of an inherited structural abnormality in one of the constituent globin chains.

Thalassemia is a disorder that is manifested by anemia of varying severity. It is an inherited defect in the rate of synthesis of one of the globin chains.

On T_1 WI focal or diffuse area of decreased SI represents the extended hematopoetic marrow.

On T_2 WI, depending on the cellularity and water content, the SI may vary: less than, equal to or higher than the subcutaneous fat. Marrow infarction usually involves the fatty marrow.

It is interesting to note that in sickle cell anemia marrow infarction occurs frequently in the cellular marrow.

Acute infarction accompanied by sickle cell crisis in SCA shows a zone of low to intermediate SI on T_1 WI due to replacement of fat cells by granulation tissue.

On T_2 WI the SI is homogeneous or peripherally high due to edema or hemorrhage.

In chronic infarction the area involved is characterized by low SI on both T_1 and T_2 WI.

Osteomyelitis is an important complication of sickle cell anemia. The signal changes of T1(T2(are similar to

Az ISS 31. máltai kongresszusán elhangzott referátum alapján sajtó alá rendezte és magyar összefoglalót írta Karlinger Kinga dr.

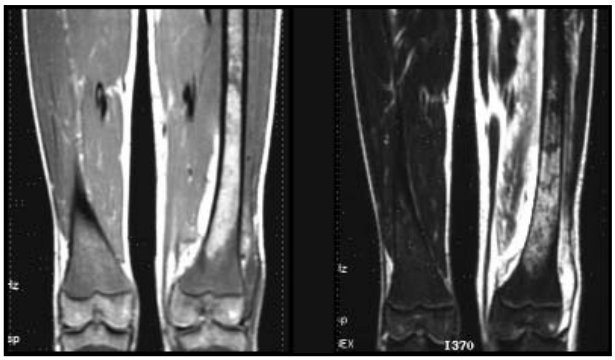

Fig 1./1. 19 year old patient with sickle cell crisis. [Pseudoosteomyelitis] MRI of the left thigh: A) T1 WI (TR/TE 700/18) reveals high SI in the middle 1/3 of the shaft. Note the high SI of the periosseal soft tissue (arrow). B) T2 WI (TR/TE 3000/96) the SI remains high (hemorrhagic infarct).

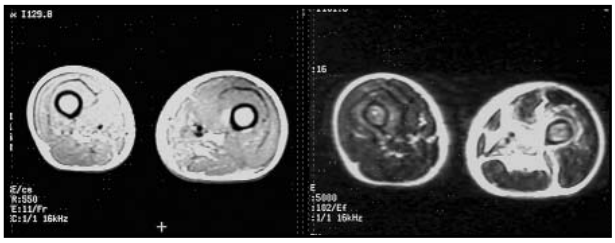

Fig. 2. 28 year old woman with left thigh pain Axial MR image T2 (TR/TE 5000/102) reveals increased SI in the medial aspect of the left thigh. Biopsy failed to demonstrate infection (sterile infarct).

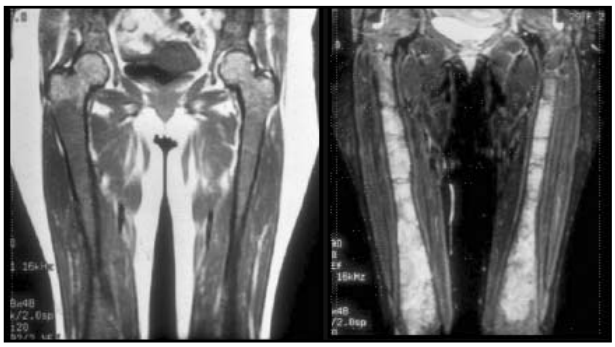

Fig 3.Fig. 35 year old male with Type I Gaucher disease MRI of both thighs MRI of the thighs: A) T1 WI (TR/TE 400/16) B) T2 WI (TR/TE 5000/68) Diffuse decreased SI involves the medullary cavity on T1 WI (A) that became higher on T2 WI (B)

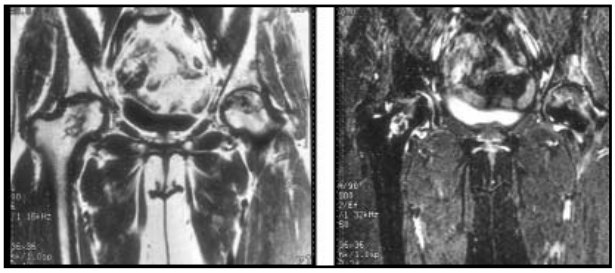

Fig. 4. 25 year old woman with Type I Gaucher disease and bilateral hip pain A) T1 (TR/TE 300/16) B) STIR (3000/90/52) reveals decreased SI at the epiphysis on both sides. (A) Note the decreased SI surrounded by high SI on both sides. (B) Ischemic necrosis of the hips

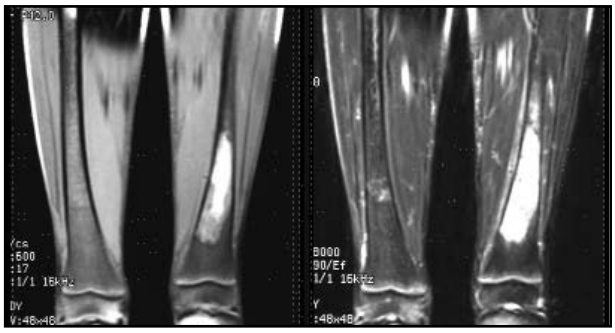

Fig 1. /2. One month later there is an improvement (T1) (TR/TE 600/17) T2 (TR/TE 8000/90)

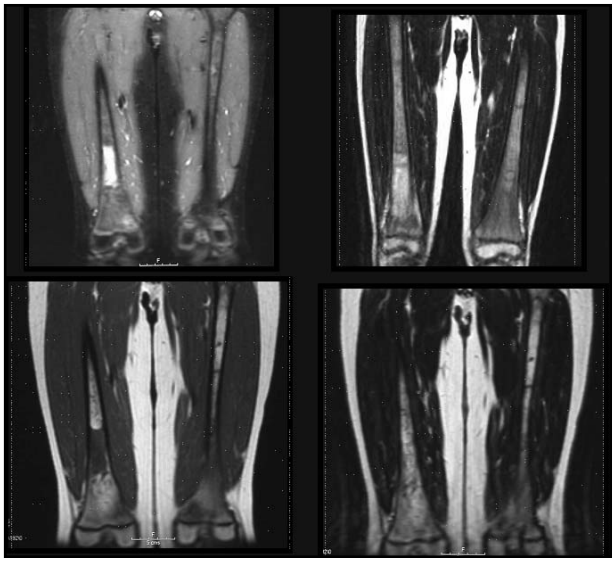

Fig. 5. Fig. 34 15 year old male with Type I Gaucher disease developed severe
pain in the right thigh A) On T1 WI (TR/TE 366/8) the distal femoral shaft shows increased SI. Two years later B) TR/TE 500/20 the involved marrow became low in SI. Note the rest of the marrow shows heterogeneously high SI.

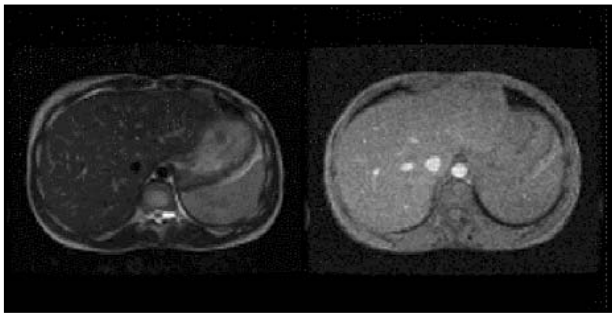

Fig.6. Axial T2 (left) and GRE (right) images through the upper abdomen demonstrated abnormally low signal in the liver and spleen secondary to iron deposition.

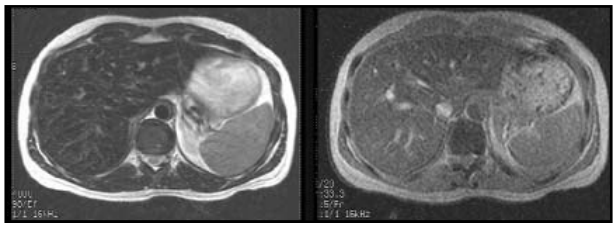

Fig 7. Axial T2 and GRE images through the upper abdomen in 1998 show very low signal in the liver and spleen secondary to iron deposition.

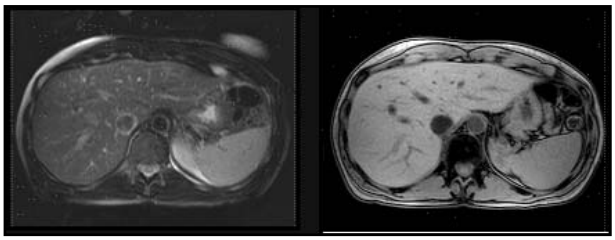

Fig 8. T2 and GRE images through the upper abdomen in 2000 after enzyme replacement therapy shows return of the liver and spleen signal to normal.

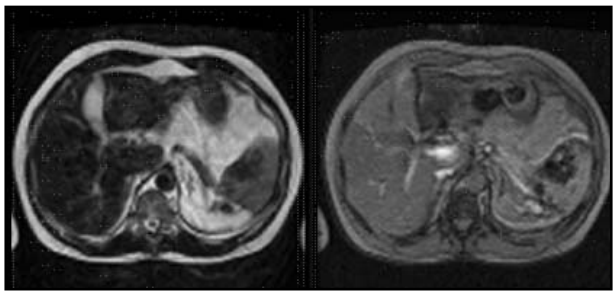

Fig.9. Axial T2 and GRE images through the upper abdomen in a patient with Gaucher disease demonstrates low signal in the liver and spleen consistent with iron deposition. In addition, there is a mass in the inferior spleen secondary to Gaucher infiltration. The mass exhibits low signal on both the T2 and GRE sequences due to iron within the Gaucher cells.

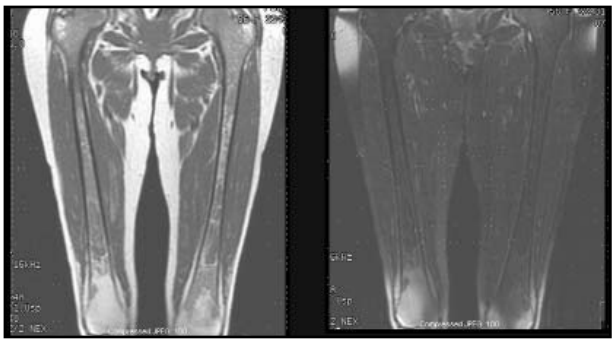

Fig.10. 45 year old patient with Type I Gaucher disease on Enzyme Replacement Therapy (ERT) A) T1 WI (TR/TE 360/16) There is an extensive decreased marrow signal in the femur (diffuse infiltration) Two years later: B) T1 WI (TR/TE 360/16) The marrow signal appears higher in SI – reconstitution of fat

acute infarction. To differentiate between the two entities on MRI is difficult or impossible.

Soft tissue abnormalities in sickle cell disease occur.

1. Extraosseous soft tissue changes without or with bone involvement can occur.
2. Soft tissue changes adjacent to the abnormal bone.
3. Distant to the abnormal bone in the same extremity or
4. Distant to the abnormal bone in a different extremity.

(F. Feldman: Skel Radiol 1993; 22:501-506 (modified)

Iron overload is an occasional complication of patients suffering from sickle cell disease and thalassemia treated with blood transfusion. Iron deposition in the marrow manifests as low SI in the marrow both on T_1 and T_2 WI.

In spite of deferoxamine chelation therapy that is used to reduce iron overload, iron deposition may be demonstrated in liver, kidney, pancreas, bone marrow.

While bony abnormalities are non-specific and well described in various lipid storage disorders, MRI images are extremely rare in the published literature. In Niemann-Pick disease the modeling deformity is similar to that of Gaucher disease. It has not been associated with Epiphyseal Osteonecrosis. Fabry's disease and Osteonecrosis may be observed in the femoral head, talus, etc., similar to Gaucher disease.

Gaucher disease is a rare familial autosomal recessive disorder caused by a deficiency of the lysosomal enzyme acid B-glucosidase. The major clinical manifestations

Lipid Storage Diseases usually include:

- Gaucher disease (glycosilceramide lipidosis)
- Niemann-Pick disease (sphingomyelin lipidosis)
- Fabry's disease (glycolipidosis)
- Refsum's disease (phytanic acid storage disease)
- Krabbe's disease (galactosylceramide lipidosis)
- Metachromatic leukodystrophy (sulfatide lipidosis)
- Farber's lipogranulomatosis (ceramidase deficiency)
- Gangliosidoses
- Sea-blue histiocytosis
- Tay-Sach's disease
- Fucosidosis

(Resnick: 56:2233-2251/Lipidosis, Histiocytoses and Hyperlipoproteinemia modified)

result from accumulation of the undegraded lipid glucosylceramide (glucocerobroside) in monocytes and macrophages of the spleen, liver and bone marrow.

The disease is divided into three clinical subtypes. They are distinguished on the basis of the absence (Type 1) or presence of neurological involvement (Type 2, Type 3).

Type 1 Gaucher disease is the most frequent. It primarily occurs in Ashkenazi Jews from the western hemisphere but it can involve other ethnic groups as well.

The onset of symptoms may be insidious. The common presentations include anemia, thrombocytopenia and hepatosplenomegaly.

Skeletal involvement is a major cause of morbidity. Conventional radiography is useful in assessing the overall pattern of Gaucher Type 1 disease.

MRI is a well established method to evaluate marrow infiltration. It is very sensitive in demonstrating alterations in the medullary cavity.

Bone marrow infiltration by Gaucher cells produces low SI on T_1 WI, T_2 WI and STIR images.

An increase in SI on T_1 WI and T_2 WI indicates active disease.

Iron deposition can occur in Type 1 Gaucher disease and can be detected in the liver and less often in the bone marrow. The iron accumulates in the Gaucher cells.

Hemosiderin granules may be subnormal in the erythroid precursors of the bone marrow.

Enzyme replacement therapy may decrease Gaucher cell infiltration and consequently decrease iron deposition and improve signal abnormality in liver, spleen and bone marrow.

Enzyme replacement therapy using placental derived (algluceraze) ceredase, and recombinant (imiglucerase) preparations has resulted in hemopoetic reconstitution and the resolution of hepatosplenomegaly.

CONCLUSION

MRI is the most useful imaging modality to-date to evaluate early marrow alteration in anemia, cellular expansion, marrow infiltration, infarction, iron deposition as well as regression of changes as a response to appropriate therapy such as enzyme replacement in Gaucher disease.