A Clinical Approach to Lysosomal Storage Disorders

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The presentation of lysosomal storage disorders are quite variable. The common presentations include hepatosplenomegaly, neurological deterioration, coarse facies, dysostosis, cardiomyopathy, angiokeratoma, etc. Less well appreciated presentations include non-immune hydrops fetalis and psychiatric symptoms meriting elaboration in the following lists:

Non-immune hydrops:
Mucopolysaccharidosis (MPS) VII, Sialidosis, Niemann-Pick A, Niemann-Pick C, Galactosialidosis, MPS I, Wolman's disease, MPS IV, Salla and sialic acid storage disease, Farber's disease.

Psychiatric symptoms:
MPS III, Adult onset MLD

Currently, antenatal diagnosis is possible for lysosomal storage disorders and is an important aspect of management to be noted. Treatment modalities include conventional supportive therapy, enzyme replacement therapy and bone marrow transplant. Cervical spine fusion in MPS IV is an example of useful treatment that could be offered. Currently enzyme replacement therapy is available for Fabry disease and Gaucher disease. There are clinical trials going on for mucopolysaccharidosis I, Niemann-Pick B and glycogen storage disease II.

Bone Marrow Transplantation for Lysosomal Storage Disease

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Bone marrow transplant as a form of treatment for lysosomal storage diseases offers hope for amelioration of the course of the disease. However, it carries high morbidity and/or mortality. This is an important modality of treatment when there is no alternative therapy available.

In lysosomal storage diseases, enzyme deficiency results in accumulation of substrate. Bone marrow transplant works by repopulating the marrow with enzyme-producing cells, which then disseminate into the reticulo-endothelial systems in different parts of the body. There is also evidence that enzyme is transferred from these cells to other enzyme-deficient cells. Enzyme-producing marrow stem cells also turn into microglial cells in the brain and potentially prevent neurological deterioration in some transplanted patients.

The experience of bone marrow transplant is most abundant in mucopolysaccharidosis I (MPS-I). There is adequate response in central nervous system, heart, respiratory system and hearing. However, the response in the eyes, bone and cartilage remains inadequate. With accumulation of experience, it is generally agreed that bone marrow transplant in MPS-I should be done if the following criteria are satisfied:

1. Age <18 months and preferably <12 months.
2. Absence of significant hydrocephalus.
3. Parental understanding of limitation of bone marrow transplant.

Cardiomyopathy is not a contraindication for transplant although the mortality of transplant in its presence is increased. The genotype and residual enzyme activity need to be studied as these offer some prediction as to the severity of the disease progression.

In mucopolysaccharidosis II (MPS-II), the value of bone marrow transplant is less clear. Unlike MPS-I, the diagnosis of MPS-II tends to be delayed. Outcome of some previously transplanted cases is not impressive. In mucopolysaccharidosis III, bone marrow transplant is incapable of altering its course. Bone marrow transplant has a definite role in the treatment of adrenoleukodystrophy preventing progressive deterioration.

In conclusion, bone marrow transplant does not result in normality. It works better in slowly progressive disorders. Alternative therapy like enzyme replacement therapy may complement BMT in the management of lysosomal storage disorders.