

PRESENTATION BY DR PRIYA KISHNANI OF DUKE UNIVERSITY TO TYPE I FAMILIES

Dr Kishnani began her presentation with a list of some of the issues that affect the long term survival of patients with Type I.

Prevention of hypoglycaemia,
Provision of optimum nutrition
Good control of uric acid and lipids
Close monitoring of kidneys and liver.

For Type I patients who have been managed well since birth normal growth and becoming adults is expected.

Duke has the oldest cohort of GSD survivors some of whom have had inadequate management or late diagnosis.

HEPATATIC CELLULAR ADENOMAS

50% of adolescents and adults develop these which tend to present in the second and third decade of life. Though patients tend to be over 20 years of age before they develop these. The complications arising from adenomas are bleeding which leads to anaemia and turning cacogenic.

Management of these complications

Cut off blood supply and thus shrink the adenoma
Cut off the adenoma
Liver Transplant as the final option

Adenomas will reappear within two years in GSD patients after they have been cut out. Research is being undertaken at Duke to develop a biomarker which will identify those adenomas that will turn into carcinomas. Removing adenomas does help anaemia.

Duke has done five transplants, all the patients were adults with poor metabolic control and there had been a recurrence of adenomas.

All five are doing well with most of the symptoms of GSD disappearing.

Kidney problems could arise from the prescribed medicines but so far none have been detected in the five patients

The UK has also done five transplants, four of which are doing well, the fifth sadly unsuccessful due to technical complications.

Summary

One should not worry too much about adenomas but they should always be monitored regularly so that if they turn into carcinomas action can be taken swiftly.

Duke uses ultrasound, CT and MRI scans to monitor the liver

The outcome of transplants in adults is very positive, though this appears to be less so with children.

GENE THERAPY

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Dr Kishnani is responsible for cloning the GSD gene of the Maltese dogs that have GSD Type I. The dogs have been cross bred with Beagles to increase their size and the results are known as Malteagles.

An AaV vector with the gene is being developed which can be injected into the dogs at three days of age and will last for a year. So far the results have been very promising, though it is important to stress that the amount and timing of the dosage is critical

Research is being carried out at Duke, Florida and Boston with the puppies. It will be some time before the AaV vector will be in production. Several years are needed to demonstrate the safety of the technique.

New survey

A comprehensive report on Type I will be published next year. Doctors from many countries have collaborated and have logged in their patients details onto a central data base to provide the information for the report. It is hoped to have the details of 250 to 300 patients.

In April 2008 Prof Smit., Dr Lee, Dr Walters and Dr Weinstein met at Manchester during a clinical course for medics with an interest in metabolic diseases. They went over all the present guide lines for the diagnosis and treatment of Type I and adjusted them accordingly. These will be published in 2009 along with the results of the Type I survey.