
Bone Marrow Transplantation in a patient with type 1b Glycogen Storage Disease

Presentation

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Child in family

- Presented at 6 months of age
- Developed low blood sugar during diarrhoeal illness
- Also noted to have large liver and raised blood lactic acid

Diagnosis

- Abnormal liver glucose-6-phosphatase enzyme activity only in intact microsomes
- GSD type 1b diagnosis given
- Genetic mutation identified in the gene encoding Glucose-6-phosphate translocase

Initial Management

- 2-hourly day-time feeds and overnight continuous feed
- Chlorthiazide and Diazoxide
- Uncooked cornstarch introduced at the age of 21 months: fasting tolerance improved to 4 hours

Age 3

- Worsening diarrhoea (up to 20 movements per day)
- Abdominal pain
- Bleeding
- Also decreasing fasting tolerance
- Gut lining had changes of Inflammatory Bowel Disease
- Raised uric acid in the blood

To control disease

- Continuous feed was introduced
- Cornstarch was stopped
- Allopurinol was started to prevent formation of the kidney stones

Age 3.5

- Developed breathing difficulties
- Was found to have a mass obstructing the airway
- Investigations of the mass revealed similar pathology to inflammatory bowel disease
- Requires tracheostomy to avoid upper airway obstruction

Age 5

- Frequent admissions with chest infections requiring intravenous antibiotics
- Continuously low neutrophil counts
- Granulocyte colony stimulating factor introduced three times per week to improve immune status

Age 6

- Frequent chest infections despite treatment
- Low platelet count
- Now developed enlarged spleen and severe intra-lung bleeding
- Admitted to PICU for intensive ventilation (oscillation)
- Bone marrow shows increased number of cells and some abnormal blood cells but not malignant
- Osteoporosis

Age 6.5

- Monthly admissions
- 270 days (74%) spent in hospital per year
- Decision to carry out a bone marrow transplant due to poor quality of life
- Family counselled that liver transplant may be required in the future

BMTx

- Pre-treatment with chemotherapy
- Donor-mum
- 3 doses of donor blood cells given in 3 months
- Complications included severe central line infection and immune reaction of the donor blood cells against JH (GVHD)

18 months follow-up after transplant

- GCSF was stopped
- Continues to be mildly neutropenic but normal platelet numbers
- Decreased number of infections
- Only 2 hospitalisations in 18 months
- Improved bowel symptoms
- Fed 4-hourly in the day
- Continuous feed overnight
- Cornstarch re-introduced

Rationale for BMTx

- Neutrophils apoptotic (have tendency to self-destruct)
- This is probably not corrected by GCSF
- In addition IBD is associated with abnormal neutrophil function Kujpers et al, 2003
- Donor blood cells may not have the same self-destructive behaviour
- Continuous administration of GCSF carries risks of malignancy