Diabetes Mellitus caused by bone marrow transplantation – experience from a single regional centre

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**BACKGROUND**

- Diabetes has increased prevalence in childhood cancer survivors, particularly following bone marrow transplantation with total body irradiation (BMT/TBI).
- Previous audits from our centre showed prevalence of impaired glucose tolerance 43%, DM 17% post BMT/TBI in patients with ALL (acute lymphoblastic leukaemia).
- Auto-immune conditions have been described post-BMT/TBI, including type 1 diabetes (T1DM).
- Diabetes due to a combination of insulin resistance and deficiency (reduction in beta cell reserve) has also been described post BMT/TBI.

**OBJECTIVES**

- This case series aims to characterise presentation, treatment and clinical course of diabetes in childhood BMT survivors

**METHODS**

- A single centre retrospective case notes review using departmental database at Bristol Royal Hospital for Children, UK.
- 13 cases (M=9) were identified with diabetes from 40 BMT patients (33% prevalence).
- 10 cases were fully reviewed, 3 cases had follow up elsewhere with limited access to clinical data therefore are not included in this case series

**RESULTS - results expressed as Median (range)**

- Primary leukaemia diagnosis at: 2.3(0.5-9.7) years, BMT/TBI: 14.4 (10-14.4) Gy in 7 (1-8) fractions, N=2 had additional cranial irradiation
- Diabetes diagnosed at 15.5(11-26) years, and 12.5 (3.5-18.2) years post BMT.

**Diagnosis:**

- 6 were diagnosed by routine oral glucose tolerance test (OGTT): 4 with raised 120 min glucose only and 2 with both raised fasting and 120 minute glucose
- At presentation, 6/10 were asymptomatic, 3/10 had polyuria/polydipsia/weight loss, 1/10 had significant lethargy

**Management:**

- 5 were commenced on insulin, 2 on metformin with lifestyle interventions and 2 lifestyle interventions alone. One patient had improvement of glycaemic control after dietary and lifestyle/exercise interventions with subsequent OGTT demonstrating impaired glucose tolerance.
- Complications included dyslipidaemia (n=4), microalbuminuria (n=2) and hypertension (n=1).

**CONCLUSIONS**

- Survivors of BMT +/- TBI for childhood leukaemia may present with either T1 DM or non autoimmune diabetes and therefore need full assessment including diabetes related antibodies to identify the underlying aetiology.
- BMT +/- TBI survivors with diabetes may be asymptomatic, demonstrating the need for screening with regular OGTTs.
- Patient management is currently individualised and quite variable. 4/10 patients do not currently need insulin for treatment with another patient successfully switching from insulin to oral medication.
- There is need for further studies to identify optimum management plans to improve outcomes and reduce metabolic risk.

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**Patient** | **Oncology diagnosis** | **Sex** | **Age at BMT** | **TBI Total Gy (Fractions)** | **GVHD** | **Fhx** | **Symptoms** | **Years from BMT to Diabetes** | **Diagnosis (Glucose mmol/L)** | **Ketonuria** | **Antibody status** | **Initial treatment** | **Subsequent treatment**
---|---|---|---|---|---|---|---|---|---|---|---|---|---|---
1 | Pre B ALL | M | 8.5 | 14.4(8) | N | T2DM and Thyroid disease | Y | 3.5 | Random glucose 27.5 | DKA | Positive ZnT8, Negative GAD&IA2 | MDI | Same
2 | HLH | M | 1 | No TBI | Y | No | Y | 14.5 | Random glucose 42 | DKA | Positive ICA | Mixed insulin | BD | MDI
3 | ALL | F | 3.3 | 10(1) | Y | No | Y | 7.8 | Random glucose 31.5 | N | Negative IA2&GAD | MDI | Metformin & Gliclazide, off insulin
4 | ALL | M | 4.9 | 14.4(4) | N | No | N | 9 | Random glucose ‘high’ | N | Not taken | MDI | Same
5 | ALL | M | 3 | 10(1) | N | Father T2DM | N | 12.5 | OGTT (oral glucose tolerance test) 0’=4.5, 120’=13.5 | N | Not taken | Diet, lifestyle | Same
6 | ALL | F | 6 | 14.4(8) | N | Father T2DM | N | 7.9 | OGTT 0’=4.5, 120’=11.6 | N | Negative GAD & ICA | Diet, lifestyle | Same
7 | AML | F | 2.4 | 12(6) | N | No | N | 16.4 | OGTT 0’=7.5, 120’=23.9 | N | Not taken | Diet, lifestyle, OD long acting insulin | Long acting insulin & sitagliptine/glicazide
8 | ALL | M | 5.8 | 14.4(8) | N | Father T2DM | Y | 18.2 | OGTT 0’=8.9, 120’=16.9 | N | Not taken | Diet, lifestyle, metformin | Same
9 | ALL | F | 10 | 14.4(8) | Y | No | N | 15.9 | OGTT 0’=6.6, 120’=11.2 | N | Negative GAD, ICA | Diet, lifestyle, metformin | Same
10 | ALL | M | 9.5 | 14.4(8) | N | n/k | N | 12.6 | OGTT 0’=5.1, 120’=13.4 | N | n/k | n/k | Died

**Notes: OGD= once daily, BD= twice daily, MDI= multiple daily injections, IA2= Islet antigen 2, ICA= Islet cell antibodies, GAD = glutamic acid decarboxylase. References: 1. Wei C, Clin Endo 2015**

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**Table:**

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<tr>
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