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[1]

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).

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

CONCLUSIONS

Topic: *Diabetes, late effects.* ***Table:*** *HLH*=Hemophagocytic Lymphohistiocytosis, *n/k=not known, OD= 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

- 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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