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

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BACKGROUND	OBJECTIVES				
 Diabetes has increased prevalence in childhood cancer survivors, particularly following bone marrow transplantation with total body irradiation (BMT/TBI). 	 This case series aims to characterise presentation, treatment and clinical course of diabetes in childhood BMT survivors 				
 Previous audits from our centre showed prevalence of impaired glucose tolerance 43%, DM 17% post 	METHODS				
BMT/TBI in patients with ALL (acute lymphoblastic leukaemia) Auto-immune conditions have been described post-	 A single centre retrospective case notes review using departmental database at Bristol Royal Hospital for Children, UK. 				

- BMT/TBI, including type 1 diabetes (T1DM)
 Diabetes due to a combination of insulin resistance
 Instal Bistor 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

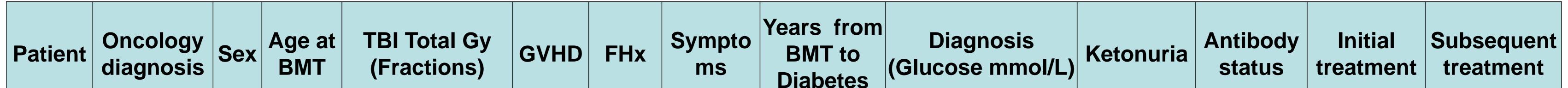
and deficiency (reduction in beta cell reserve) has also been described post BMT/TBI¹

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
 Disperse diagnosed at 15 5(11.26) years, and 12 5 (2.5.18.2) years next BMT
- 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).



								Diabeles					
		R 4	0 5			T2DM and Thyroid	V		Random glucose		Positive ZnT8, Negative		
1	Pre B ALL	M	8.5	14.4(8)	N	disease	Y	3.5	27.5	DKA	GAD&IA2	MDI	Same
		R A										Mixed insulin	
2	HLH	M	1	No TBI	Y	No	Y	14.5	Random glucose 42	DKA	Positive ICA	BD	MDI
3	ALL	F	3.3	10(1)	Y	No	Y	7.8	Random glucose 31.5	Ν	Negative IA2&GAD	MDI	Metformin & Gliclazide, off insulin
4	ALL	M	4.9	14.4(4)	N	No	Ν	9	Random glucose 'high'	Ν	Not taken	MDI	Same
5	ALL	Μ	3	10(1)	N	Father T2DM	Ν	12.5	OGTT (oral glucose tolerance test) 0'=4.5, 120'=13.5	Ν	Not taken	Diet, lifestyle	Same
6	ALL	F	6	14.4(8)	N	Father T2DM	Ν	7.9	OGTT 0'=4.5, 120'=11.6	Ν	Negative GAD & ICA	Diet, lifestyle	Same
7	AML	F	2.4	12(6)	N	No	Ν	16.4	OGTT 0'=7.5, 120'=23.9	Ν	Not taken	Diet, lifestyle, OD long acting insulin	sitagliptine/glic
8	ALL	M	5.8	14.4(8)	N	Father T2DM	Y	18.2	OGTT 0'=8.9, 120'=16.9	Ν	Not taken	Diet, lifestyle, metformin	Same
9	ALL	F	10	14.4(8)	Y	No	Ν	15.9	OGTT 0'=6.6, 120'=11.2	N	Negative GAD, ICA	Diet, lifestyle, metformin	Same
10	ALL	M	95	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.

