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Monosomy 7 in childhood Acute Lymphoblastic Leukaemia (ALL)

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Introduction

Monosomy 7 is a rare cytogenetic abnormality in paediatric patients with ALL[1]. It has unclear prognostic significance for children treated on UK ALL protocols.

Traditionally monosomy 7 has been identified by karyotype as it is too rare to justify routine screening by Fluorescence In Situ Hybridisation (FISH). However, chromosome 7 material may be located in 'markers', i.e. abnormal chromosomes that cannot be recognised by karyotype analysis alone. Additional FISH studies can be performed with probes specific to chromosome 7 loci to enhance the cytogenetic description.

This study describes the 16 year experience at a large UK paediatric oncology centre of outcomes for patients with monosomy 7 karyotype, and the subset with 'secure' monosomy 7 where the karyotype abnormality was confirmed with additional FISH probes, or where no 'marker' chromosomes were present.

Methods

Demographics, relapse and survival outcomes were obtained for all patients age < 19 years with ALL, diagnosed at the Royal Marsden Hospital, London, England from March 2000 – March 2016.

Monosomy 7 was identified by karyotype G-banded chromosome analysis. FISH using Vysis probes D7S486 (at 7q31) and CEP7 (at 7 centromere) was performed when possible.

	Monosomy 7 on karyotype analysis		FISH analysis support monosomy 7	Number of cases
	With markers	Without markers		
'Secure' Monosomy 7	✖	✔	NA	2
	✔	✖	✔	2
Karyotype Monosomy 7	✔	✖	-	9
No Monosomy 7	✖	✖	-	727

Figure 1. Division of patients with ALL between those with 'secure' monosomy 7, with karyotype monosomy 7 and no monosomy 7.

Reference: 1. Heerema, N. A., et al. "Deletion of 7p or monosomy 7 in pediatric acute lymphoblastic leukemia is an adverse prognostic factor: a report from the Children's Cancer Group." *Leukemia* 18.5 (2004): 939-947.

Results

Of 744 patients with ALL, 17 (2.3%) patients had monosomy 7 on karyotype. Four patients with concomitant, recognised, high-risk cytogenetic abnormalities were excluded.

FISH data were available for 8/13 cases. True monosomy 7 was confirmed in two cases, five cases found chromosome 7 material on marker or ring chromosomes and hybridisation failed in one case. From the five cases without FISH, two had simple monosomy 7 karyotype with no unidentifiable material in the clone. Thus 4/13 had 'secure' monosomy 7 (Figure 1).

Event free survival (EFS) was significantly worse for patients with monosomy 7 by karyotype versus patients without monosomy 7 by karyotype (Figure 2a), (Logrank Hazard ratio 3.91 (3.44-78.1 95% CI.) Event free survival at 5 year was 2/8 (25%) versus 387/493 (80.2%) for patients with and without monosomy 7 by karyotype respectively, p=0.0003 (X2). No significant difference was found in overall survival (Figure 2b).

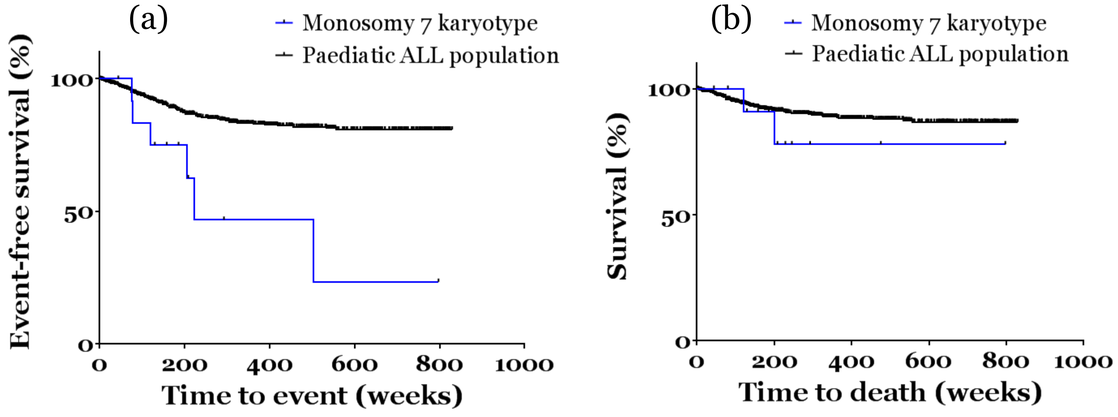

Figure 2. (a) Kaplan Meier curve for EFS at 5 years and (b) Kaplan Meier survival curve for patients with monosomy 7 karyotype.

Of the 4 patients with secure monosomy 7, 3 patients have relapsed including one death from secondary Acute Myeloid Leukaemia.

Conclusions

1.True monosomy 7 in ALL may be more rare than previously supposed based on karyotype alone. It is important to confirm full loss of chromosome 7 by FISH if there is unidentified material in the clone.

2. In this small series, event-free survival was significantly worse for the patients with apparent monosomy 7, and particularly poor if true monosomy 7 is confirmed.

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