The importance of early diagnosis and views on newborn screening in Metachromatic Leukodystrophy

Results of a caregiver survey in the UK and Republic of Ireland

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Background

Metachromatic Leukodystrophy (MLD) is a rare, autosomal recessive lysosomal storage disease caused by a deficiency of arysulfatase A enzyme. MLD causes progressive loss of motor function and severe decline in cognitive function, leading to premature death. MLD is not included in newborn screening in the UK, and diagnosis is often delayed.

Aims

To increase understanding of the natural history of MLD, its impact and burden on patients and their families, the effects of gene therapy and views on newborn screening.

Methods

The study consisted of an online survey, and follow-up interviews. It was open to MLD patients or caregivers, aged 18 years and over resident in the UK or Republic or Ireland, able to provide informed consent. .Results relating to diagnosis and newborn screening from the survey only are presented here.

Patient demographics

24 Responses for 24 patients were received

Mean age of patients was 12.3 years, range 2—48

3 Three patients were deceased, age at death ranged from 5—39 years

58% female, 42% male

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Results

Diagnostic delay

Four patients were diagnosed before symptoms appeared (3 late infantile, 1 early juvenile), due to diagnosis of an older sibling.

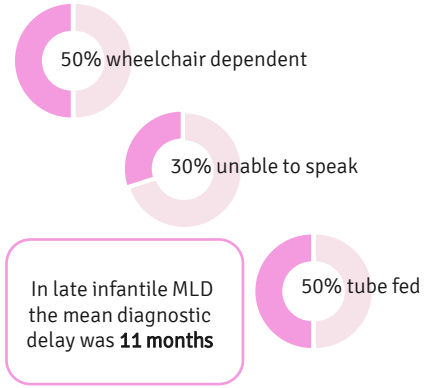
Diagnostic delay from first symptoms was between 0—3 years for the remaining patients.

MLD subtype (by age of symptom onset)	Number of patients	Age symptoms first appeared	Age at diagnosis	Diagnostic delay
		Mean (range) years		
Late infantile, <30 months	10	1.5 (0.3—2.5)	2.4 (1.5—3.0)	0.9 (0—2.3)
Early juvenile, 30 months—6 years	5	4.6 (3—6)	5.9 (5.5—6.2)	1.3 (0—3)
Late juvenile, 7—16 years	2	10.5 (7—14)	11.5 (8—15)	1
Adult onset, ≥17 years	3	22.5 (20—25)*	24.7 (23—26)	2.0 (1—3)*

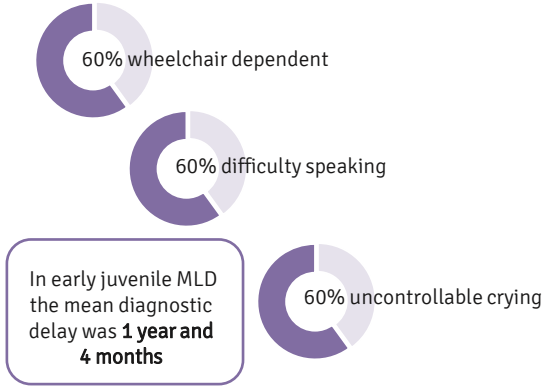
**age at first symptoms not recorded for one patient*

During the period from first symptoms to a confirmed diagnosis, deterioration was rapid, especially in earlier onset MLD.

Late infantile patients at diagnosis



Early juvenile patients at diagnosis



Views on newborn screening

There was a high degree of support for newborn screening among caregivers, with 95% describing it as very or extremely important (Figure 1).

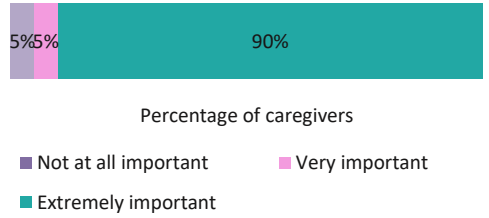


Figure 1. Caregiver opinion on newborn screening

Most considered an undetected case of MLD at birth as more harmful than a false positive screening result (Figure 2).

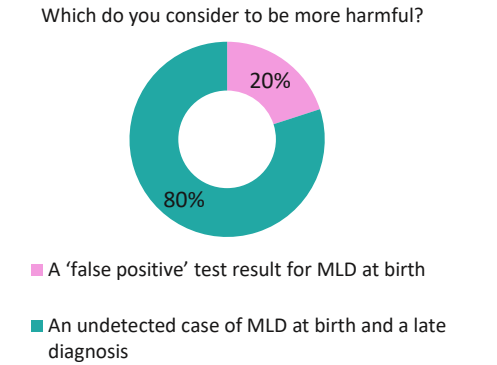


Figure 2. Caregiver opinion on false positive screening results

86% of respondents believed detection of MLD at birth would have changed their child's future.

Conclusion

It can take up to three years from the appearance of first symptoms of MLD to a confirmed diagnosis. During this period deterioration is rapid, particularly in the earlier onset forms of MLD. Children often lose their mobility and speech during this time. For the majority, early diagnosis was only achieved due to the diagnosis of MLD in an older sibling. The rapid rate of deterioration in MLD makes it an essential candidate for newborn screening, particularly now as the first disease modifying treatment has been approved by the European Medicines Agency.