Metachromatic leukodystrophy burden of disease: patient and caregiver experience

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Introduction

Metachromatic Leukodystrophy (MLD) is a rare, autosomal recessive lysosomal storage disease caused by a deficiency in the enzyme arylsulfatase A, which leads to the accumulation of sulfatides in the nervous system. This causes a progressive loss of gross motor function and severe decline in cognitive function, ultimately leading to premature death.

Aim

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 semi-structured interviews. The study was open to patients or caregivers aged ≥18 years, resident in the UK or Republic or Ireland, able to provide informed consent.

Responses

Responses were received for 24 patients (58% female), including three deceased patients: two late infantile, one adult onset MLD. All deceased patients had received no disease modifying treatment. Six patients had taken part in gene therapy clinical trials and one had received a hematopoietic stem cell transplant (HSCT).

Table 1. Patient demographics	Untreated		Gene therapy		HSCT	
Age at symptom onset	**n**	**Mean age, years***	**n**	**Mean age, years**	**n**	**Age, years**
Late infantile (LI), <30 months	10	5.7	3	4.7	–	–
Early juvenile (EJ), 30 months–6 years	3	13.3	3	11.3	–	–
Late juvenile (LJ), 7–16 years	2	24.0	–	–	–	–
Adult onset (AO), ≥ 17 years	2	34.5	–	–	1	48

*age at time of survey or death

Results

Patient burden

No disease modifying treatment

Most of the untreated patients had lost all speech (Figure 1). All had difficulty swallowing or severe swallowing difficulties necessitating tube feeding (Figure 2).

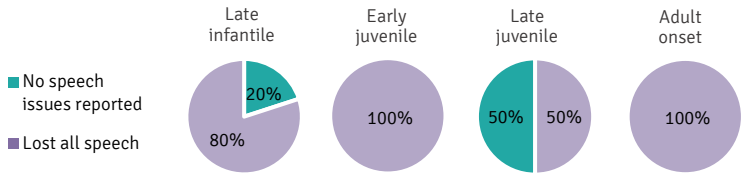

Figure 1. Speech status of untreated patients

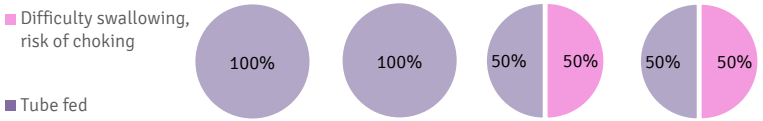

Figure 2. Swallowing status of untreated patients

Childhood onset patients were all wheelchair dependent or immobile (AO 50%) (Figure 3) and needed specialist education or were not well enough to attend school (Figure 6). All AO patients had dementia.

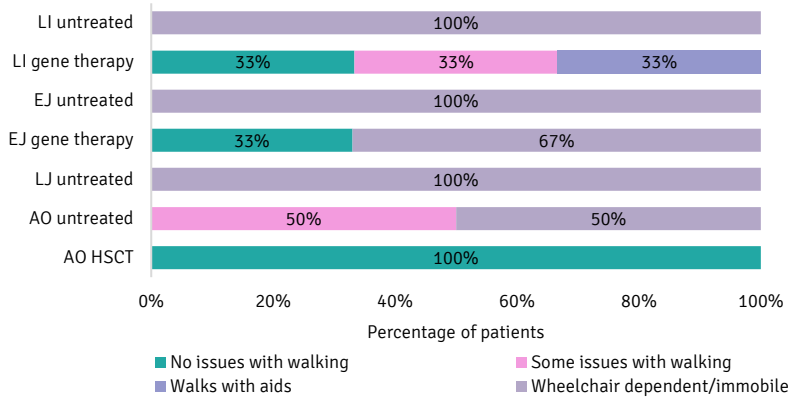

Figure 3. Patients' walking status

Other burdens on patients and families

Financial constraints often brought about by inability to work, required families to rely on pensions and benefits to make home adaptations and provide care for their child (Figure 5). Additional burdens on both the patient and the family included hospital visits, medication, and surgery to manage symptoms (Figure 5).

Gene therapy and HSCT

All treated patients had retained their speech, although for some EJ patients, their speech was deteriorating (Figure 4).

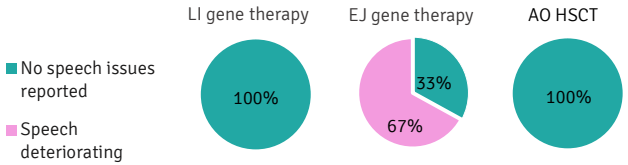

Figure 4. Speech status of treated patients

Patients treated with gene therapy or HSCT had no issues with swallowing (Figure 5), were more mobile (Figure 3), and most children were able to attend mainstream school (Figure 6).

Figure 5. Swallowing status of treated patients

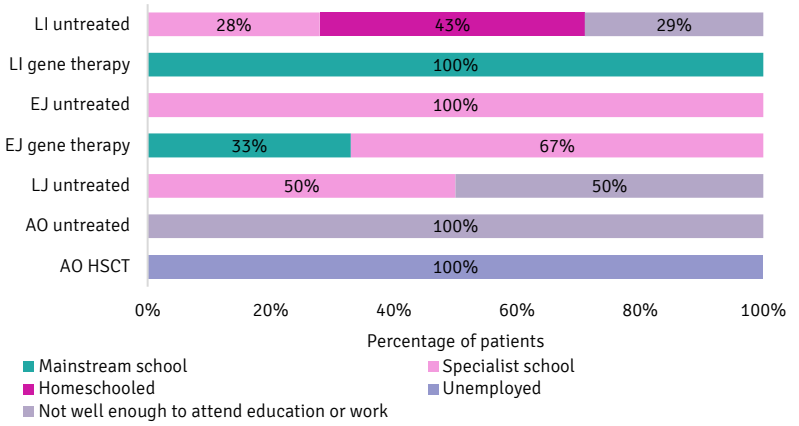

Figure 6. Patients' education / employment status

Conclusion

Patients who received no disease modifying treatment followed a relentlessly progressive disease course with many having lost the ability to walk, speak and swallow. The impact of illness upon patients, parents and siblings was extensive, with many physical, mental, and social issues described.

Acknowledgements

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