

## BACKGROUND

- X-linked adrenoleukodystrophy (ALD) is a single gene disorder caused by mutations in the *ABCD1* gene, leading to a progressive myelopathy in adults
- While clinical presentation has been well-studied in males, less information is available on symptom prevalence in females
- Previous reports estimate that roughly one half of females develop myelopathy in adulthood
- We highlight this as an area of unmet need and aim to evaluate disease burden among female patients and add to the literature in the largest cohort of females to date

## METHODS

- We performed a retrospective medical chart review of all female patients with ALD seen in the MGH Leukodystrophy Clinic from September 2007 through March 2022
- We extracted data on presence of neurological signs and symptoms, age of symptom onset, what led to ALD diagnosis, and medication history
- For comparison, we gathered age of symptom onset and data from ALD diagnosis for all male patients seen in the same study period

## RESULTS

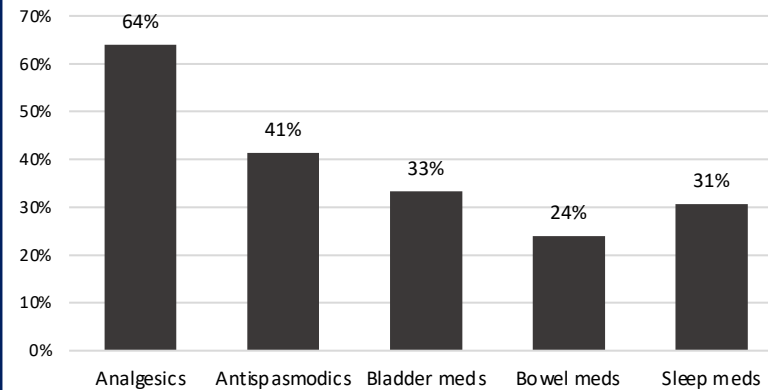
- We identified 75 female patients with ALD, ranging in age from 28-86 years (median = 48.9 years) at last visit
- 93.3% of patients had at least one neurological sign or symptom
- The most common neurological sign was impaired sensation in lower extremities (81.3%)
- The most common neurological symptom was neuropathic pain (76.0%)

Signs	n	%	Symptoms	n	%
Impaired Sensation	61	81.3%	Neuropathic pain	57	76.0%
Hyperreflexia	55	73.3%	Bladder dysfunction	54	72.0%
Romberg +	44	58.7%	Gait/walking difficulty	52	69.3%
Gait abnormality	40	53.3%	Balance difficulty	42	56.0%
Weakness	31	41.3%	Bowel dysfunction	38	50.7%
Hypertonia	20	26.7%	Spasticity	37	49.3%
Coordination	16	21.3%	Numbness	34	45.3%
			Paresthesia	33	44.0%

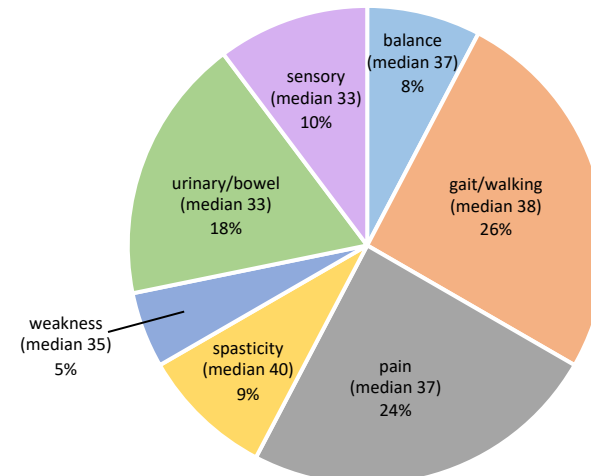
**Table 1. Prevalence of neurological signs and symptoms in women with ALD (N=75)**

## RESULTS

- 24 (32.0%) patients used walking aid for ambulation
- 23 (30.7%) patients had a history of fractures
- 52 (69.3%) patients reported sleep disturbances, most commonly due to spasms and/or pain
- Analgesics were the most commonly used medication
- The most frequent first symptom was gait changes and/or walking difficulty



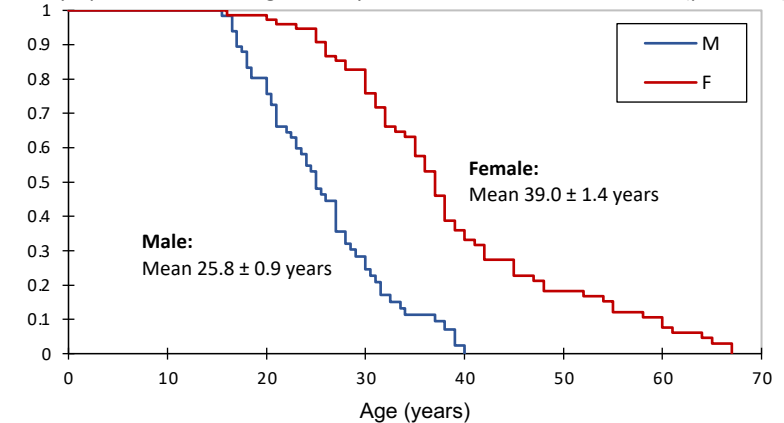
**Figure 1. Classes of medications used by women in our cohort and percentage of women who have tried each medication type for symptom relief (N=75)**



**Figure 2. Frequency of first symptoms in women with ALD and median age of onset (years)**

## RESULTS

- Comparator:** 66 ALD men were disease controls (median = 36.1 years)
- Men were more likely to be diagnosed by symptoms than by family history ( $p < 0.0001$ ) – 56% were diagnosed due to symptoms
- Although 55% of women experienced symptoms prior to diagnosis, only 15% were diagnosed due to symptoms
- Symptom onset was significantly earlier in males than in females ( $p < 0.0001$ )



**Figure 3. Time to onset of myelopathy symptoms in adults with ALD**

## CONCLUSIONS

- Despite a later onset of symptoms than in males, most females with ALD develop neurological deficits in adulthood severe enough to have a negative functional impact
- Understanding the disease course in females will help inform the pathophysiology and appropriate treatment for this disorder

## DISCLOSURES

We thank the GLIA-CTN consortium (1U54NS115052), the Arrivederci ALD Foundation, and the Hammer Family Fund for ALD Research and Therapies in Women for their support. No other disclosures.

## REFERENCES

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