Metals in cerebrospinal fluid - a diagnostic tool

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Environmental toxicants accumulate in food chains. Metal exposure from marine sources add to toxic burdens of the developing foetus. Metal accumulation over lifetime may contribute to **neurodegenerative disorders** in advanced age. Multisystem effects are sometimes noted. In Parkinson's disease (PD) an increased frequency of scoliosis has been described. Its aetiology is unknown. Exposure to metal has been proposed to contribute to PD. Sampling of cerebrospinal fluid (CSF) and muscle tissue may display metal distribution. Also in other neuro-degenerative disorders such as amyotrophic lateral sclerosis (ALS) and Alzheimer dementia (AD) metal exposure over the entire life span may need attention. CSF concentrations of toxicants reflect accumulation in brain and spinal cord.

Hypothesis

Metals in CSF and tissue are potential biomarkers of exposure.

Methods

1. Electromyography (EMG) and muscle biopsy was performed in paravertebral muscles from a patient with rapidly progressing scoliosis in recently diagnosed PD (fig 1).

2. Detailed interviews concerning significant metal exposure were compilated from ALS patients (fig.2). A well defined cohort using standardised Arlie House criteria was studied. Outpatients under investigation served as controls.

3. Concentrations of Al, P, Ti, V, Cr, Mn, Co, Ni and Sr in CSF were analysed by ICP-SFMS in subjects (age >63y.) undergoing dementia investigation. Patients under investigation for AD but scoring as subjective cognitive impairment (SCI) served as controls. Data for Al are shown (fig 3).

Results

In a PD patient low amplitude short duration polyphasic motorunitpotentials with early recruitment, consistent with myopathy, were detected with EMG. Muscle biopsy revealed atrophy and fibre type grouping and ragged red fibres indicating mitochondrial dysfunction. Electron microscopy showed accumulations of abnormal mitochondria with rounded intra-mitochondrial electron dense bodies indicating metal accumulation. The precise chemical nature of these bodies (blue arrows) is however not known.

In ALS anamnestic data indicate elevated metal exposure.

In AD increased metal concentrations have been noted in CSF.

Implications

Sampling of urine, hair, nails and umbilical cord blood have limitations as metal concentrations therein reflect conditions remote from the neuronal activity of interest. CSF surrounds the brain and spinal cord and is an extension of the extracellular fluid of nerve cells. Samples from inside the blood-liquor barriers can be anticipated to reflect the true metal concentrations affecting the cerebral cortex and spinal cord. Synergistic effects from multiple metal exposure can be evaluated. Tissue sampling and electrophysiological methods are also useful. These techniques may be relevant in studies of the recently noted doubling in PD incidence in the Faroe Islands.

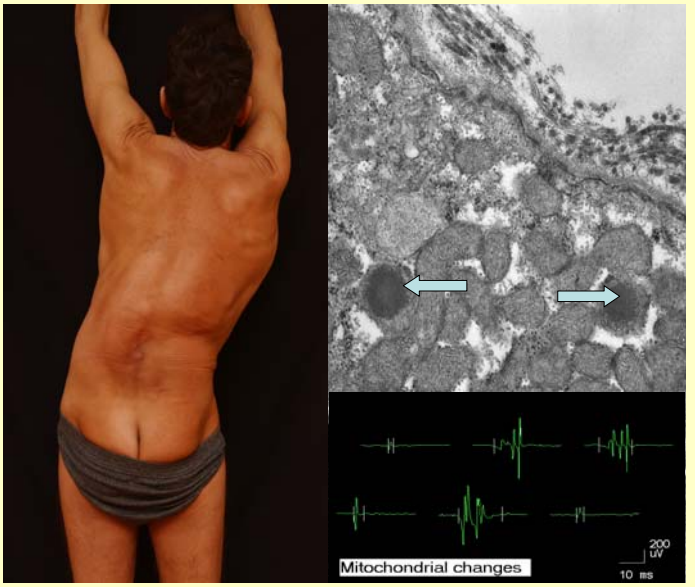

Fig.1 Scoliosis in PD. Myopathic EMG findings. Dense bodies in muscle mitochondria.Electron microscopy by neuropathologist Sigurd Lindal,university of Tromsø. Rear view of patient by medical photografpher Finn Stokke.

	Born	A	Sm	Ag	Al	Au	C	Cd	Cr	Cu	Fe	Hg	Mg	Na	Pb	Si	Sn	Zn
ALS CASES																		
1	1952	51	Y	•		•				•		•					•	•
2	1950	52	N								•							
3	1919	83	N	•		•				•		•					•	•
4	1954	49	Y	•		•	•			•		•					•	•
5	1926	75	N	•		•				•		•					•	•
6	1938	64	Y															
7	1932	61	N															
8	1942	52	N		•				•		•		•	•		•		
9	1936	67	Y	•	•					•	•	•	•	•	•	•	•	•
10	1948	56	Y			•												
11	1959	45	N	•						•		•					•	•
12	1953	51	N	•	•					•	•	•	•	•	•	•	•	•
13	1931	62	Y		•			•							•			•
14	1928	77	N	•		•				•		•					•	•
CONTROLS																		
1	1947		Y	•						•		•					•	•
2	1979		N															
3	1962		N								•							
4	1962		Y															
5	1927		N															
6	1941		N	•						•		•					•	•
7	1975		Y															
8	1974		N							•								
9	1957		Y															
10	1921		N	•		•				•		•					•	•
11	1981		N															
12	1964		N								•						•	

Fig 2 Metal exposure in ALS patients compared to controls. Sm indicates smoker Yes/No

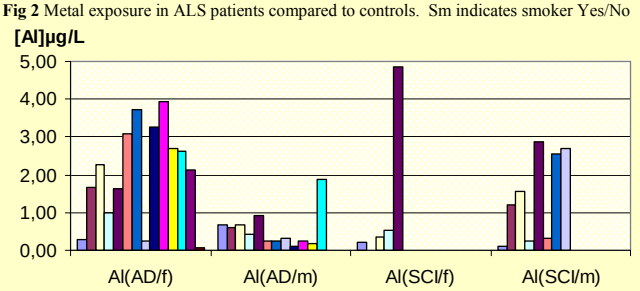

Fig 3. Concentrations of Aluminium in CSF from female (f) and male (m) AD patients compared to SCI. Data from Johansson N, Nordberg M, et al (2004) Journal Trace Elements in Experimental Medicine, 17,4,213.

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