Genetic testing for Adult Refsum’s disease should be strongly considered in all cases of Idiopathic Retinitis pigmentosa

Authors: Raphael Buttigieg¹, Anthony Wierzbicki² and Radha Ramachandran¹
1 NHS Guys and St Thomas NHS Foundation Trust, London, United Kingdom

Contact for correspondence: raphael.buttigieg1@nhs.net

Background and Introduction:

Adult Refsum Disease (ARD: OMIM # 266500) occurs due to Phytanoyl-CoA hydroxylase deficiency (a peroxisomal VLCFA metabolism defect).

This results in high plasma Phytanic acid (PA) levels.

Individuals with ARD develop normally as infants, and the onset of symptoms varies between childhood to the fifth decade.

Diagnosis based on the identification of highly raised (often > 200 umol /L) plasma PA. A diagnostic delay of up to 14 years has previously been reported.

Disease manifestations:
- Retinitis pigmentosa (RP) is often the first and only presenting symptom of ARD. Possible cataracts and optic atrophy
- Anosmia
- Sensorineural deafness
- Polyneuropathy
- Ataxia and ichthyosis

Acute/subacute ARD:

Presents with polyneuropathy, weakness, ataxia, visual and often auditory deterioration. May be accompanied by ichthyosis, cardiac arrhythmias, and elevated liver transaminases

Triggers for acute ARD include weight loss, stress, trauma, and infections
Case studies:

Patient 1: 48 year old male.
Diagnosed in early 20s with Retinitis pigmentosa. Previous history of night blindness and deteriorating vision. Recently had cataract extraction
Patient asked for referral for genetic screening in view of uncertainty of diagnosis
Genetics: compound heterozygous for intronic abnormalities in PHYH gene
Bloods: Phytanic acid level 22.5umol/L (Ref: 0-15umol/L) (standard western diet)
Treated with dietary modification
6 months after dietary modification – Phytanic acid within reference range

Patient 2: 30 year old male.
Diagnosed at 18 years with Retinitis Pigmentosa, after few years background of deteriorating vision and night blindness. Previous cataract operation and anosmia noted.
Genetic screening as part of clinical trial
Genetics: compound heterozygous PHYH gene:
Phytanic acid level 17.56 umol/L (Ref: 0-15umol/L) (standard western diet)
Fibroblast studies: Phytanic acid oxidation 7pmol/hr:mg protein (28-95).
8 months after dietary modification – Phytanic acid within reference range
Conclusion and take away points

1) Increased recognition of milder spectrum of patients with IEM across the board

2) Increased adoption of plant based diets in the Western World increases the chance of false negative biochemistry for diagnosis of Adult Refsum disease

3) Patients with a diagnosis of Idiopathic Retinitis Pigmentosa, even in absence of other clinical features or suggestive biochemistry should be considered for genetic testing for ARD