# Familial Partial Lipodystrophy

## Importance of family history - a case report

Dr C Stockley (Paediatric SpR)
Dr S Holder (Consultant Geneticist)
Dr J J Rangasami (Consultant Paediatrician)

West Middlesex University Hospital
Paediatric Department

***Background:***

TN presented due to increasing belly fat and tall stature in India. The family moved to the UK shortly after.

TN was referred to the paediatric endocrinology clinic due to blood results showing high triglycerides and high insulin, as well as strong family history.

Age 7.7yrs, Ht 133.3cm (91st), Wt 31.95kg (91st), BMI 18 (91st)

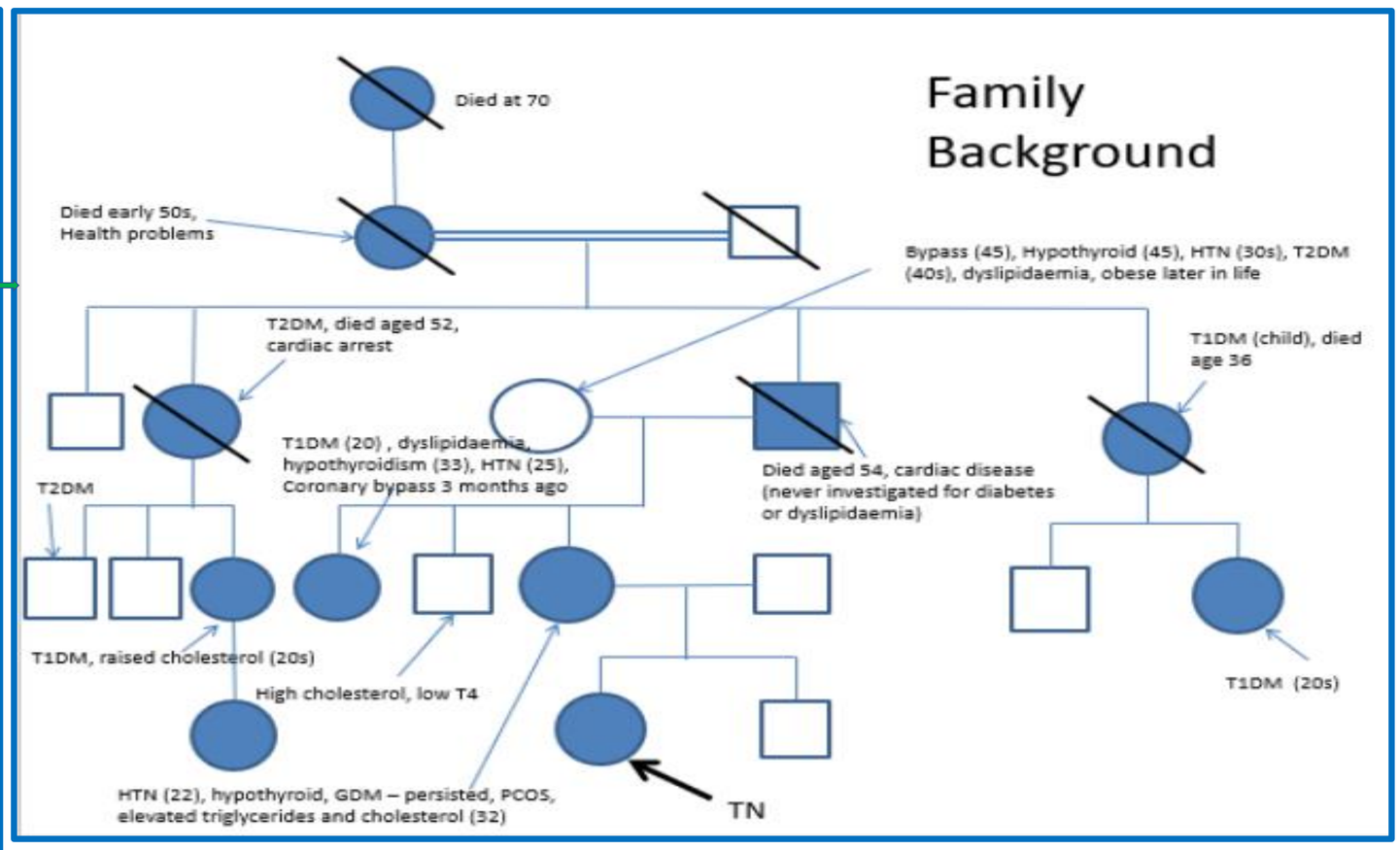
Born at 36 weeks by elective CS- due to maternal GDM on insulin (Birth Wt 2.69kg 50-75th)

No significant past medical history. Family of Indian origin.

TN was generally well. Her blood tests had normalised with dietary management.

O/E: acanthosis nigricans on neck, axilla and groin, protuberant abdomen, no organomegally, did not appear lipodystrophic

*Main feature: 5 generation family history of lipodystrophic build, early cardiovascular deaths, diabetes and dyslipidaemia.*

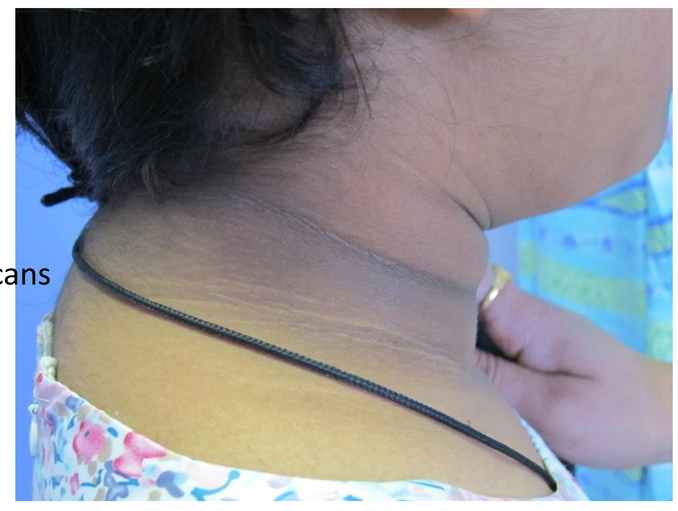



***TN was referred to a Geneticist who saw the whole family and tested TN's mother as she was pregnant:***

Heterozygous mutation identified

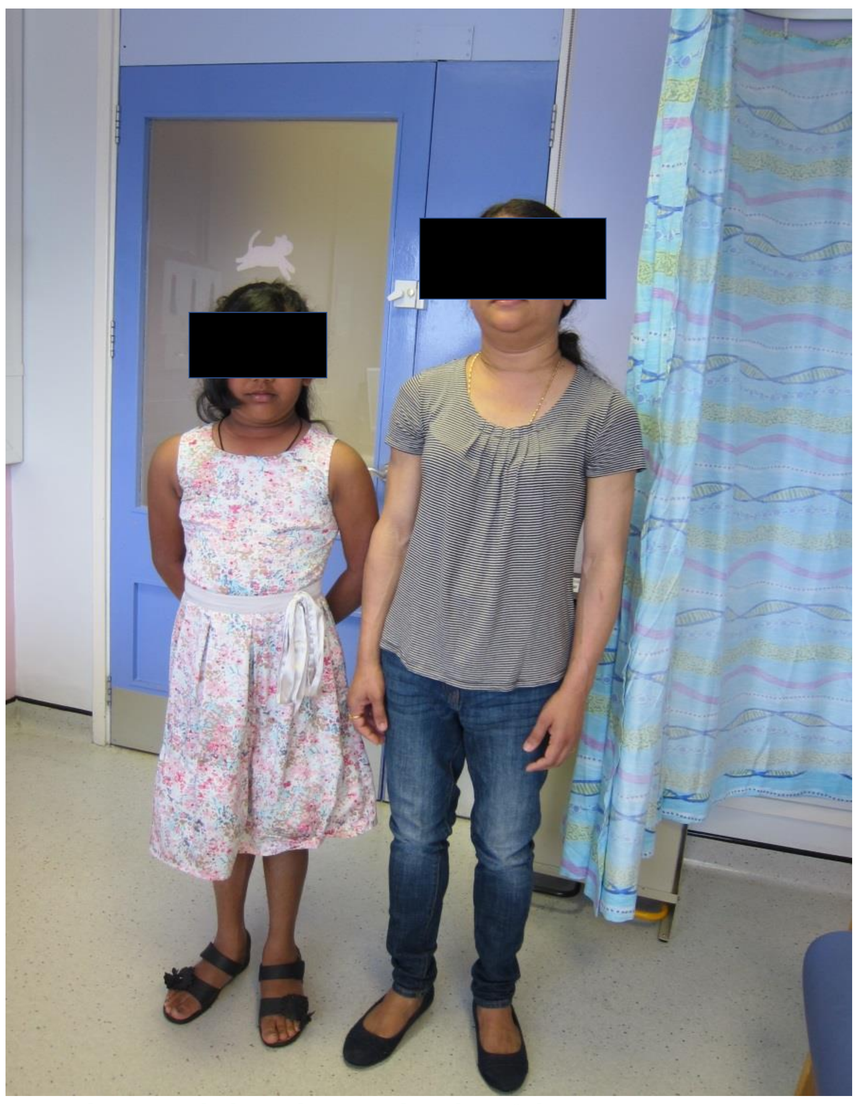
- Gene: LMNA
- Location: Exon 8
- DNA description: c.14444C>T
- Protein Description: p.Arg482Trp (p.R482W)
- Consequence: Missense

Acanthosis Nigricans



***Gene predicted to be pathogenic: confirmed LMNA related familial partial lipodystrophy***

TN and sibling tested: TN also positive for autosomal dominant gene



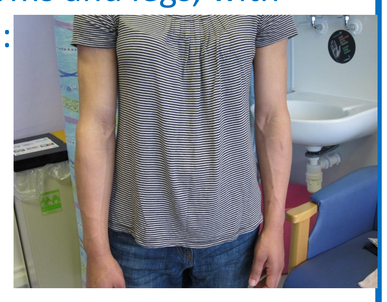
**Mother and daughter – both with proven LMNA related autosomal dominant Familial Partial Lipodystrophy.** **With thanks for their permission to publish these photos.**

***Partial Lipodystrophy – brief overview***

**Lipodystrophy is a rare group of conditions in which there is abnormal amount and distribution of subcutaneous fat.** It is split into Total/Generalised and Partial Lipodystrophy; it is further subcategorised into congenital and acquired. There are several forms of each. Estimated prevalence of <1/million.

**Familial Partial Lipodystrophy**: Usually Autosomal Dominant

The lipodystrophic build is due to abnormal distribution of fat – fat loss from arms and legs, with sparing of the face and abdomen. Note the very muscular arms:



Currently classified into 5 main types depending on genetic cause.

The fat loss pattern can vary with the genetic diagnosis. It is this that causes changes to appearance. This is usually the first noted sign, often picked up around puberty. Due to fat distribution this is easier to recognise in females. One systematic review found a female preponderance of 83%.

Patients can have central obesity with a normal BMI.

Metabolic: Patients can have difficulties fasting and exercising due to reduced triglyceride stores in fat cells. As there is reduced fat to store the triglycerides they can build up in the blood, this can lead to eruptive xanthoma or acute pancreatitis.

Low leptin can abnormally stimulate appetite leading to weight gain and increased metabolic complications.

Fat is deposited in muscles, liver and pancreas as there is reduced subcutaneous fat. This can lead to severe insulin resistance which can be difficult to control.

Liver: excess fat deposits in the lever can lead to non-alcoholic fatty liver disease and cirrhosis.

Cardiovascular: Patients are at higher risk of coronary heart disease, cardiomyopathy, arrhythmia and stroke.

Fertility: High insulin levels can disrupt the balance of sex-hormones resulting in irregular periods and can lead to hirsutism and acne. High insulin can also impair ovulation. The combination of problems can mimic PCOS. There is no evidence of any impact on fertility in men.

There is currently no cure for lipodystrophy. Treatment aims at reducing the daily and long term impacts by correcting the associated metabolic abnormalities. Management includes regular screening for known complications.

Low fat diet is the mainstay to manage blood glucose and lipid control. This needs to be carefully monitored in children to balance with energy requirements for growth. Physical activity is also important. Specific aspects need treatment eg metformin/insulin for diabetes. Psychological support can be needed especially for the cosmetic impact. Leptin is being looked at as a treatment for hypertriglyceridaemia, diabetes and liver problems.

Management should be by a specialist multi-disciplinary team. Difficulty in children due to lack of long term outcome studies.

Bibliography/references: 1. Diagnosis and management of lipodystrophy: a practical update; Stears, A, Hames, C. Clin. Lipidol. (2014)9(2), 235-259. 2.Clinical features and management of non-HIV related lipodystrophy in children: a systematic review. Gupta et al. J Clin Endocrinol Metab, February 2017, 102(2):363–374. 3. Royal Exeter and Devon NHS Foundation Trust Genetics Patient information leaflet. 4. Nelson Textbook of Pediatrics, 19th Edition. Kliegman, Stanton, St. Geme, Schor, Behrman. Elsevier Saunders 2011. 5. Diagnosis and Management of Lipodystrophy. Brown et al. J Clin Endocrinol Metab, December 2016, 101(12):4500 – 4511

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