Congenital hypothyroidism and tuberous sclerosis: an association or a coincidence?

Francesco Gallo[1], Francesco La Torre[1], Pietro Conte[1], Rosa Maria Alfano[2], Gaetano Bulfamante[2], Fulvio Moramarco[1]

1: Pediatric Unit, Perrino Hospital, Brindisi, ASL BR, Italy; 2: Department of Human Pathology,Cytogenetic and Molecular Pathology, San Paolo Hospital Medical School, University of Milan, Milan

Background

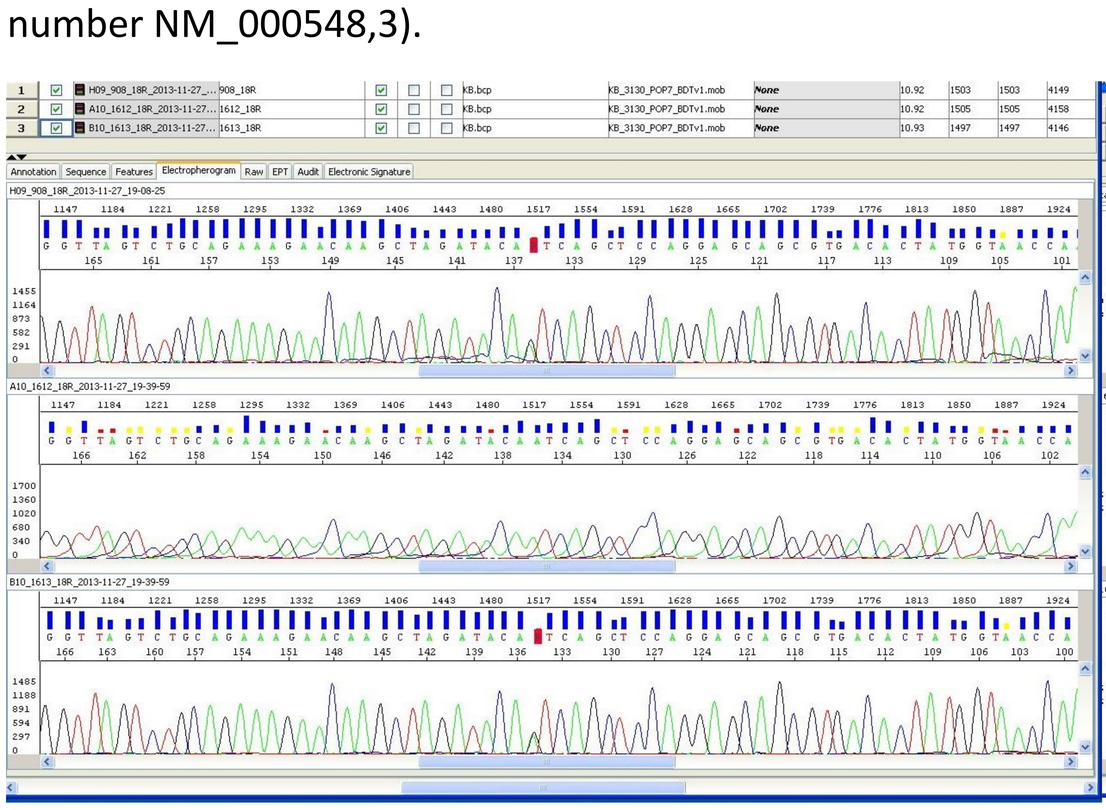
Tuberous sclerosis (TS) is a polymorphic, dominantly inherited syndrome caused by an inactivating mutation in tumor suppressor genes, TSC1 or TSC2; they regulate a key player in control of cellular growth and protein synthesis: mammalian target of rapamycin (mTOR), . The disease involves benign tumors in several distinct organs (such as the skin, kidneys, heart and central nervous system), that can interfere with organ function. Rarely TS is associated with endocrine abnormalities, but the association with congenital hypothyroidism has been published only in another case report.

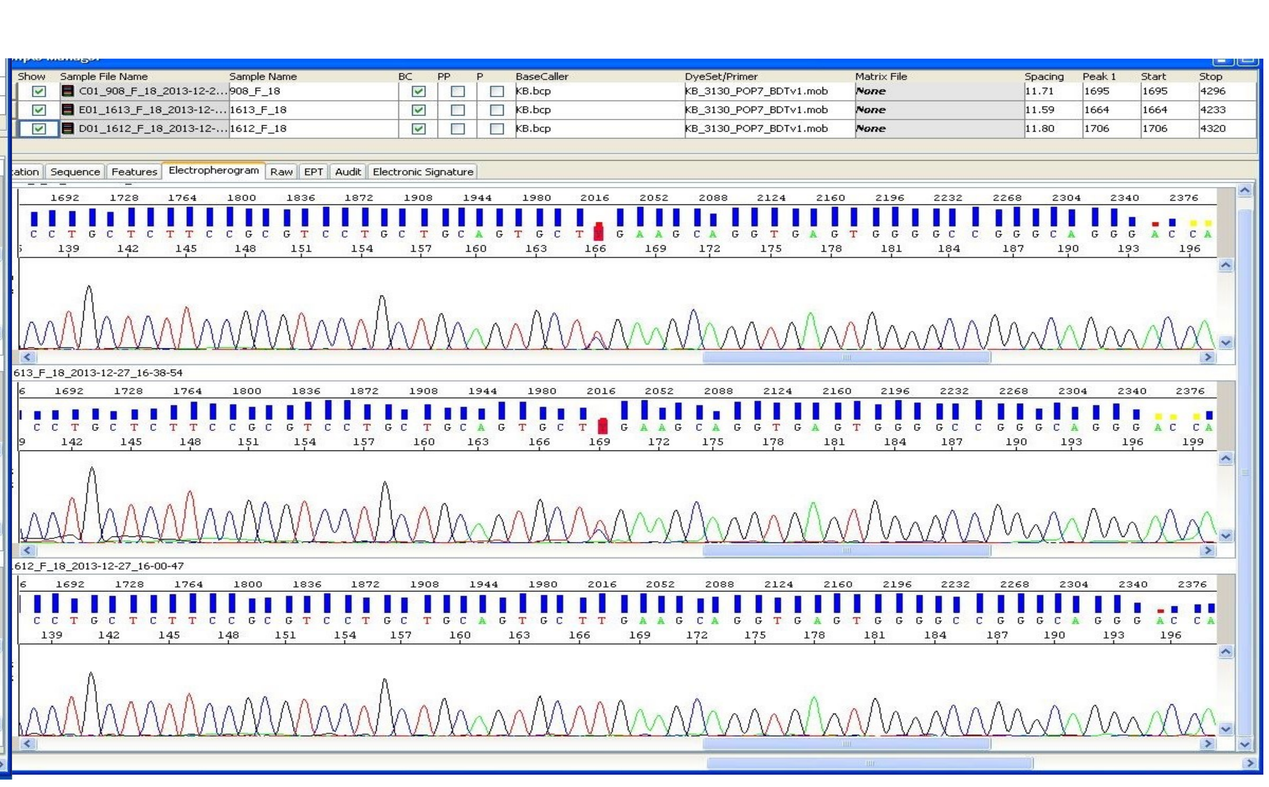
Objective and hypotheses

EG was a female newborn, positive at neonatal screening for congenital hypothyroidism (CH) (confirmed with venous sample). USgraphy and scintigraphy showed hypo-dysplasia of her thyroid (treated with L-tiroxine). As a part of diagnostic approach, we made echocardiography, founding several rabdomiomas. These benign tumors are frequently associated with TS, so we searched for mutations of TSC1 and TSC2 genes. No skin lesions were found. EG had also abdominal organs echography (normal) and brain magnetic resonance imaging (MRI).

Method

DNA was extracted from peripheral blood using standard techniques. Mutation analysis was performed on all TSC1 and TSC2 exon and exon boundery with DHPLC methods and direct sequencing. The mutation is described according to HGVS nomenclature (Accession number NM_000548,3).





Results

EG had heterozygosis in pLeu697Ser^ of TSC2 exon 18 and p.Asn762Ser mutation of TSC1 exon 18. The same abnormalities were found in her father. The brain MRI showed a small altered signal in left front-insular white substance. Afterwards EG had to start valproic acid therapy because of seizures.

Conclusions

Although the association of CH and TS in one patient may be merely coincidence, we speculate that the dysgenetic thyroid gland in this baby could be a "hamartia" as a consequence of the tuberous sclerosis gene mutation.

References

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