INTRODUCTION

Carriers of germline DICER1 mutations are predisposed to a rare cancer syndrome, the DICER1 syndrome, associated with tumors such as pleuropulmonary blastoma (PPB), ovarian Sertoli-Leydig cell tumors (SLCT), cystic nephroma (CN), embryonal rhabdomyosarcoma (ERMS) or primary neuroectodermal tumor.

DICER1 is involved in the generation of microRNAs (miRNAs), short, double-stranded, non-coding RNAs that modulate gene expression at the posttranscriptional level. Germline mutations in DICER1 would cause an alteration in miRNAs processing deregulating target oncogenes and leading to elevated risk of tumorigenesis.

AIM

To analyze the presence of DICER1 germline gene alterations in 4 patients with paediatric tumors associated with DICER1 spectrum. To investigate the presence of somatic DICER1 mutations when a sample tissue is available.

METHODS

Automated sequencing of DICER1 gene from gDNA extracted from blood of affected subjects and relatives. (ABI PRISM 3130 Genetic Analyzer capillary DNA Sequencer, Applied Biosystems)

RESULTS

A novel heterozygous nonsense mutation in exon 21 (p.Trp1098*) was found.

A novel heterozygous deletion in exon 8 that causes a frameshift and a premature stop codon (p.Phe351fs*) was found.

A novel heterozygous deletion in exon 6 that causes a frameshift and a premature stop codon (p.Asp244Glyfs*27) was found.

A previously described heterozygous deletion in exon 23 that causes a frameshift and a premature stop codon (p.Asp1437Metfs*16) was found.

CONCLUSIONS

In this study we report three novel heterozygous frameshift mutations in the DICER1 gene. We also found two somatic RNase IIIb mutations in two MNG tissue samples. This findings confirm that a second hit event is involved in the mechanism of MNG development, as it was very recently described. MNG is a benign condition in which DICER1 germline and somatic RNase IIIb mutations coexist. Molecular analysis of DICER1 gene allows identification of high-risk families, to perform an early diagnosis and to offer a genetic counselling about familial recurrence risk.

REFERENCES