ABSTRACT

Introduction: Uterine fibroids are the most common benign tumours of female genital tract with the peak incidence in the 4th and 5th decennium. The aetiology of uterine fibroids still remains poorly understood. Genetic factors play undisputed role in the onset of uterine fibroids. Up to date numerous gene mutations were identified in certain percentage of patients with uterine fibroids. One of the candidate genes is Fumarate hydratase gene (FH). Heterozygous germiline mutations of FH cause two hereditary syndromes: Multiple smooth muscle tumours of the skin and uterus (MCUL1)/ Hereditary leiomyomatosis and renal cell cancer syndrome (HLRCC) characterised by leiomyomata of the skin, early onset uterine fibroids between 20-30 years of age and renal papillary carcinoma. The aim of our thesis was to identify the frequency of FH mutations in patients with early onset sporadic uterine fibroids.

Methods: Patients with the diagnosis of uterine fibroids up to the age of 30 years were enrolled in the study. Control group consisted of patients with absence of uterine fibroids. Activities of Fumarate hydratase and control protein Citrate synthase were measured in lymphocytes and compared to the results obtained from the healthy controls. Mutation analysis of FH gene was performed. Activity of Fumarate hydratase and its amount was determined also in the leiomyomata tissue.

Results: 14 patients out of 41 (34.1 %) showed reduced activity of Fumarate hydratase to 2-50 % measured in the control group. Heterozygous mutations in the FH were, however, identified only in two patients (4.9 %). In one case the mutation c.584T>C was previously described and in the other case the mutation c.892G>C was newly identified. Both the patients inherited the mutations from their mothers who also developed uterine fibroids around 30 years of age. In the leiomyoma tissue samples (n=22) one case of reduced activity and amount of Fumarate hydratase was recorded. This patient was not identified as FH mutation carrier.

Conclusion: Our data show that the frequency of FH mutations in patients with sporadic fibroids is relatively low.

Key words: uterine fibroid, leiomyoma, Fumarate hydratase, Fumarase, FH gene