



Hereditary Thrombophilia Cases



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Abstract

Aim: The aim of this study to determine inherited thrombophilia mutations in venous thromboembolic cases.

Method: The study includes 30 patients presented with thromboembolic events due to hereditary thrombophilia. 21 (70%) of cases were female and 9 (30%) were male. The mutations including MTHFR C677T, MTHFR A1298, factor V G1691A, factor V 1299, factor II G20210A investigated.

Results: There were total 45 thromboembolic events in 30 patients including 25 pulmonary thromboembolism, eight deep vein thrombosis, seven cerebrovascular accident, two portal vein thrombosis, two recurrent abortion and one retinal vein thrombosis. Majority of patients had more than one thromboembolic event at the same time. While 90% of cases has been found positive for MTHFR mutation, 57% was positive for Factor V Leiden and 10% was positive for Factor II (prothrombin gene). 16,6% of the patients has three different mutations at the same time and 30% of them has two mutations.

Keywords: Hereditary; Trombophilia; MTHFR; Factor V, Prothrombin gene

Introduction

Thromboembolic events complication is one the most frequent reason of mortality worldwide. Hereditary thrombophilia plays a common role in etiology of thromboembolic events along with many other reasons. The ratio of hereditary thrombosis is 1% to 25% in thrombotic cases while 0,02% to 10% in normal population. Factor V Leiden (40-50%) mutation is the most common cause of cases [1-3]. This study intended to investigate hereditary thrombophilia mutations in patients with thromboembolic events.

Method

This study includes 30 cases with inherited thrombophilia mutations who presented to hematology outpatient clinic between 2009-2010. 70% of cases were female and 30% were male. The cases were investigated retrospectively for thromboembolism locations and type of mutations. The thrombophilia markers including MTHFR C677T, MTHFR A1298,

factor V G1691A, factor V 1299, factor II G20210A mutations noted.

Results

The age of study population was between 18-66 and mean age was 41.96±14.62. There were total 45 thromboembolic events in 30 patients including 25(55,5%) pulmonary thromboembolism, 8(17,7%) deep vein thrombosis, 7(15,5%) cerebrovascular accident, 2(4,4%) portal vein thrombosis, 2(6,7%) recurrent abortion, 1(2,2%) retinal vein thrombosis. Majority of patients had more than one thromboembolic event at the same time. 27(90%) of cases is positive for MTHFR mutation while 17(57%) is positive for Factor V Leiden and 3(10%) is positive for Factor II (prothrombin gene). 5(16,6%) of the patients has three different mutations at the same time and 9(30%) of them has two mutations. The distribution of thrombophilia mutation of cases is given in Table 1.

Table 1: The distribution of thrombophilia mutation of cases.

Thrombophilia Mutation		Heterozygous	Homozygous	No Mutation
MTHFR	MTHFRC	10(33.3%)	4(13.3%)	16(53.3%)
	MTHFRA	7(23.3%)	10(33.3%)	13(43.3%)

FV leiden	FV1299	4(13.3%)	0	26(86.7%)
	FVg	10(33.3%)	3(10%)	17(56.7%)
FII	3(10%)	0	27(90%)	

Discussion

Inherited thrombophilia is a genetic tendency to venous thromboembolism. It usually occurs before age of 40-45 and should be considered in patients with unclear etiology of thromboembolic attacks, development of thrombosis in unusual location (cerebral, upper extremity, abdominal vessels), history of recurrent, mobile or massive thrombosis, family history of thromboembolism, skin necrosis due to warfarin. Venous thrombosis risk may increase 3-5 fold when factor V leiden mutation activates factor V, and resist to destruction with protein C. Protein gene mutation increases venous thromboembolic risk 3 fold by increasing protein gene levels. The catalytic activity of MTHFR enzyme decrease by MTHFR gene mutation. The people with this mutation has 2,3 fold increase of venous thrombosis risk due to hyperhomocysteinemia [4,5].

Factor V leiden, prothrombin gene (Factor II) and MTHFR mutations are three important markers for evaluating venous thrombosis tendency. MTHFR mutation is the most common reason of hereditary thrombosis (90%) in our study. Factor V leiden (56.7%) and prothrombin gene (10%) mutations follows this respectively.

MTHFR gene mutation frequency is 2-15% in healthy subjects and 10-25% in patients with first venous thromboembolus attack [6]. In our study the frequency of MTHFR mutation is 90%, MTHFR C677T mutation is 46,6% and MTHFR A1299 mutation is 56,6%.

Factor V Leiden mutation is seen 3-12% in white race. During first venous thromboembolic attack factor V Leiden homozygosity is 1,5% and heterozygosity is 7-20%. In hereditary thrombophilia cases Factor V Leiden mutation is as high as 50%. In our study Factor V mutation is 57%, Factor V G1691A frequency is 43,3% and factor V 1299 mutation frequency is 10% [7,8]. The frequency of Factor II G20210A mutation is 0, 06-2% in healthy subjects, 6-7,1% in patients with first venous thromboembolus attack and 20% in hereditary thrombophilia cases [9-11]. In our case Factor II G20210A frequency has been found 10%.

Even though there is an increase risk of thrombosis in hereditary thrombophilia cases, there is no evidence of definite thrombosis development. Presence of more than one mutation increases the risk of recurrent thromboembolic attacks [9].

Carrying Factor V Leiden and prothrombin gene mutation at the same time increase risk of thrombosis 3-5 fold [10]. In our study the rate of mutations is higher than the literature, the reason of this might be due to carrying more than one mutation at the same time Despite a small sample size, in contrast to the literature the increase frequency of MTHFR mutation has been found as an interesting point. To make a definite conclusion carefully designed studies with larger sample size is needed.

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