Hyperhomocysteinemia-associated Thrombosis in Patients With Pernicious Anemia

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INTRODUCTION

- Pernicious anemia (PA) is due to cobalamin deficiency (CD) resulting from cobalamin malabsorption in the ileum, secondary to autoimmune chronic atrophic gastritis (CAG).
- CD leads to hyperhomocystinemia, a risk factor for thrombosis.
- However, the clinical presentation and outcomes of PA-related hyperhomocystinemia-associated thrombosis are not fully understood.

AIM

- Our main aim was to illustrate the clinical features and outcomes of PA-related hyperhomocysteinemia-associated thrombosis by descriptive statistics.

METHOD

- We undertook a literature search using PUBMED and SCOPUS databases using the terms “pernicious anemia AND thrombosis”, “pernicious anemia AND embolism”, “pernicious anemia AND thromboembolism”, “autoimmune gastritis AND thrombosis”, “autoimmune gastritis AND embolism”, “autoimmune gastritis AND thromboembolism” from inception through July 2023 and reviewed the published literature.
- We collected data on age/sex, homocysteine and cobalamin levels, types of thrombosis (initial vs late presentation of PA, thromboses at usual sites vs unusual sites, arterial vs venous), positive anti-intrinsic factor (anti-IF) and anti-parietal cell (anti-PC) antibodies, presence of bone marrow (BM) megaloblastosis, and chronic atrophic gastritis and overall survival (OS).

RESULTS

- Of 19 patients, the median age was 53 years with 58% males.
- The median serum homocysteine level was 70 umol/L.
- 25% of patients developed thromboses at multiple locations while 21% had thromboses at unusual sites.
- 95% of cases presented with thrombosis before the diagnosis of PA was established.
- 42% of patients had co-existing neuropsychiatric symptoms.
- 78% of patients were positive for anti-intrinsic factor (anti-IF) antibodies.
- All patients received antithrombotics with a median duration of 6.5 months, and cobalamin replacement.
- None developed recurrent thromboembolism.
- BM megaloblastosis was present in those who underwent BM biopsy.
- 15 patients (79%) had macrocytic anemia while one each presented with normocytic anemia (5%), and microcytic anemia (5%).
- Hemoglobin was normal in 2 patients (11%).
- Chronic atrophic gastritis was present in 85% of patients who underwent gastric biopsies
- One died of liver failure following intestinal resection and the OS rate was 95%.

Median Age	**53 years**		
Median Serum Homocysteine Level	70 umol/L		
Sex	Male	Female	
	11 (58%)	8 (42%)	
Type of thrombosis	Venous	Arterial	Both
	15 (79%)	3 (16%)	1 (5%)
Number of thromboses at presentation	Multiple	Single	
	5 (25%)	14 (75%)	
Unusual site thrombosis	CVST	Splanchnic	
	2 (10%)	2 (10%)	
Recurrent Thrombosis	None		
Auto antibody	Anti IF antibody	Anti PC antibody	
	15 (78%)	2 (10%)	
Neuropsychiatric symptoms	Present	Absent	
	8 (42%)	11 (58%)	
Median Duration of antithrombotics and cobalamin replacement	6.5 months		

Table 1 Characteristics of cases in the cohort

CONCLUSIONS

- This condition, although rare, is associated with high incidence of thromboses at unusual sites, multiple-site thromboses, co-existing neuropsychiatric symptoms and high rate of positive anti-IF antibodies, and very low recurrent thrombosis rate and low mortality rate.

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CONTACT INFORMATION

I have no potential conflicts of interest

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