Pulmonary Hypertension in Chuvash Polycythemia

Student Researcher: Raha Dastgheyb
Mentor: Victor Gordeuk, MD

The objective of our study was to compare clinical manifestations and Doppler echocardiography for patients with Chuvash polycythemia. Data was collected on 30 patients: 15 with Chuvash polycythemia and 12 control patients. We hypothesized that the upregulation of the hypoxic response in Chuvash polycythemia would be associated with a risk for the development of pulmonary hypertension. We found that, although the patients with Chuvash polycythemia had lower systemic blood pressures than controls, their pulmonary artery pressures were significantly higher than controls. We conclude that pulmonary hypertension may be a previously unrecognized complication of Chuvash polycythemia.

From Howard University; McLean, Virginia.

Introduction

Chuvash polycythemia is a congenital disorder in which an excessive number of red blood cells are produced by the bone marrow. A more commonly known myeloproliferative disorder, polycythemia vera, also has excess red blood cell production and clinical symptoms and signs of headaches, dizziness, shortness of breath, bleeding, red coloration, and hypertension. Patients with polycythemia vera have elevated hematocrit levels and often-elevated white blood cell and platelet counts. Its cause is not known, but it has been known to lead to acute myelogenous leukemia.

Like polycythemia vera, Chuvash polycythemia is characterized by an increase in the red blood cell mass. However, it does have some noted differences. Chuvash polycythemia is an autosomal recessive disease endemic to the mid-Volga River region of Russia. In addition, it is a genetic disorder, unlike polycythemia vera, and is found in younger patients.

The VHL genetic lesion in Chuvash polycythemia leads to a generalized increase in the hypoxic response at normal oxygen levels. Chronic hypoxic disorders are often complicated by pulmonary hypertension, a condition that leads to shortness of breath and early mortality. The purpose of this study was to determine if pulmonary hypertension is a complication of Chuvash polycythemia.

Methods

Routine laboratory tests and non-invasive Doppler echocardiography were conducted on 15 patients with Chuvash polycythemia and 12 control patients. The results produced a data set that could be used to statistically compare the two groups.

Data Analysis

Mean values were compared between cases and controls using the student *t* test, while proportions were compared with the Fisher exact test.

Results

Table 1 shows that the control patients and the patients with Chuvash polycythemia were similar in age and sex. Patients with Chuvash polycythemia reported dizziness, headaches and shortness of breath on exertion significantly more often than controls. On physical examination, the patients with Chuvash polycythemia had significantly lower systolic blood pressure than the control patients and, they more often had plethora or injected sclera. Although the difference was not statistically significant, four of the patients with Chuvash polycythemia had clubbing, a finding that can be associated with pulmonary hypertension. As expected, hemoglobin, hematocrit and red blood cell counts were significantly higher in patients with Chuvash polycythemia than in controls.

The results of the Doppler echocardiography in Table 2 show that the tricuspid regurgitation velocity, which reflects the mean pulmonary artery pressure, was significantly higher in patients with Chuvash polycythemia compared to the control group. Similarly, three of the patients with Chuvash polycythemia had a tricuspid regurgitation velocity of at least 2.5 m/s, which indicates an elevated mean pulmonary artery pressure.

Conclusion

Patients with Chuvash polycythemia have remarkably higher hemoglobin and

Table 1. Baseline characteristics of the study participants

Variable	Chuvash Polycythemia	Controls	*P*-Value
Demographics			
Age in years; mean (SD)	35 (17)	35 (17)	1.000
Female sex; no. (%)	7 (46.7%)	7 (46.7%)	1.000
Medical history			
Cancer	0 (0%)	0 (0%)	1.000
Peptic ulcer disease	4 (47%)	0 (0%)	.100
Loss of consciousness	1 (7%)	0 (0%)	1.000
Dizziness	7 (47%)	1 (7%)	.035
Headaches	13 (87%)	6 (40%)	.021
Dyspnea, rest	2 (13%)	0 (0%)	.483
Dyspnea, exertion	5 (33%)	0 (0%)	.042
Surgery	5 (33.3%)	6 (40%)	1.000
Smoking	5 (33%)	5 (33%)	1.000
Alcohol use	3 (20%)	1 (7%)	.598
Other medical problems	11 (73.3%)	5 (33.3%)	.066
Medications	9 (60%)	5 (33%)	.272
Physical examination			
Height in centimeters; mean (SD)	157 (15)	165 (16)	.151
Weight in kilograms; mean (SD)	50 (12.1)	61 (18.5)	.079
Body mass index in kg/m^3; mean (SD)	20.2 (3.6)	21.7 (4.6)	.321
Hepatomegaly	3 (20%)	0 (0%)	.224
Splenomegaly	0 (0%)	0 (0%)	1.000
Systolic blood pressure in mm Hg; mean (SD)	103 (15.7)	114 (12.3)	.043
Diastolic blood pressure in mm Hg; mean (SD)	74 (11.8)	78 (12.1)	.376
Pulse in beats/minute; mean (SD)	72 (8.7)	73 (6)	.809
Plethora	10 (67%)	0 (0%)	<.0005
Injected sclera	11 (73%)	2 (13%)	.003
Varicose veins	7 (47%)	4 (27%)	.450
Edema	1 (7%)	0 (0%)	1.000
Clubbing	4 (27%)	0 (0%)	.100
Systolic murmur	5 (33%)	3 (20%)	.682
Diastolic murmur	3 (20%)	0 (0%)	.224
Laboratory data			
Hemoglobin in g/l; mean (SD)	167 (23.3)	133 (1.9)	<.0005
Hematocrit l/l; mean (SD)	0.536 (0.062)	0.402 (0.032)	<.0005
Red blood cells; mean (SD)	6.532 (0.701)	4.641 (0.358)	<.0005
Platelets $\times$ 10^3/μl; mean (SD)	187 (56.4)	236 (54.6)	.021
White blood cells $\times$ 10^3/μl; mean (SD)	6.1 (1.5)	6.6 (1.7)	.380
Lymphocytes $\times$ 10^3/μl mm Hg; mean (SD)	1.9 (0.6)	2.2 (0.7)	.317

hematocrit levels and more commonly have symptoms and signs that could be associated with pulmonary hypertension (eg, shortness of breath on exertion and clubbing).

Despite having significantly lower systemic blood pressures than controls, patients with Chuvash polycythemia have significantly higher pulmonary artery pressures as measured by the Doppler echocardiography. These findings are consistent with the hypothesis that the upregulation of the hypoxic response with Chuvash polycythemia is associated with a risk for the development of pulmonary hypertension even though the actual oxygen levels are normal.

Table 2. Results of Doppler echocardiography

Variable	Chuvash Polycythemia	Controls	*P*-Value
Tricuspid regurgitation velocity in m/s; mean (SD)	2.2 (0.6)	1.2 (0.6)	.001
Systolic pulmonary artery pressure; mean (SD)	20.3 (8.9)	10.1 (4.9)	.001
Right ventricular systolic pressure	30.3 (8.9)	20.1 (4.9)	.001
Tricuspid regurgitation velocity > 2.5 m/s; No (%)	3 (33.3%)	0 (0%)	.224

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