

'Vampire Syndrome': Serum Protein and Lipid Abnormalities Related to Frequent Sale of Plasma

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The sale of plasma for profit has become a common occurrence. In the United States, a healthy individual can donate as frequently as six times per month and up to 60 L of plasma per year. Although plasma donors are generally healthy, intervening conditions can increase the catabolism or decrease the synthesis of certain serum constituents and thereby produce a confusing clinical picture. In 1 month, we encoun-

tered two patients who presented with hypoalbuminemia and hypocholesterolemia for which there was no obvious cause except a history of frequent plasma sales.

Key words. Plasmapheresis; hypoalbuminemia; hypocholesterolemia; plasma; blood donors.

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The term *plasmapheresis* was first used by Abel¹ in 1914 to describe the removal of whole blood for the collection of the plasma fraction with the subsequent replacement of the cellular elements. Since that time, plasmapheresis has become a method of treatment for many diseases, such as systemic lupus erythematosus,² Goodpasture's syndrome,³ thrombotic thrombocytopenic purpura,⁴ and homozygous familial hypercholesterolemia.⁵ It is also a valuable tool for obtaining normal plasma and plasma products for use in the treatment of diseases, such as hemophilia,⁶ and for plasma replacement in some critically ill patients.

The demand for plasma and plasma products has resulted in the development of entrepreneurial plasmapheresis centers that remunerate donors. In the United States, an individual may donate up to 60 L of plasma per year.⁷ Although many studies have shown no deleterious effect,^{8,9} frequent plasma donation may result in changes in plasma constituents that can complicate the evaluation of a donor who develops medical problems. The prevalence of this disorder has not been documented but is probably low because few donors sell at a high rate.

Other than the hypoalbuminemia and hypocholesterolemia, we are not aware of any other markers for this disorder. Since the blood is collected and replaced using the antecubital vein, there are no appreciable needle tracks or other external markers to alert the examining physician that plasmapheresis has occurred.

Case Reports

Case 1

The first patient was a 33-year-old black housewife who presented with complaints of fever, chills, and body aches of approximately 1 week's duration. On the morning of admission, she began experiencing dizziness upon standing, fever to 101°F, and emesis. Her medical history was significant for endometriosis. She denied any drug allergies and reported only occasional use of ibuprofen, which she took two to four times daily for the relief of menstrual pain.

The patient was married and had three healthy children. She smoked six to eight cigarettes per day and drank one to two beers per week. On physical examination, the patient had a temperature of 38.5°C; pulse of 100 beats per minute; regular, supine blood pressure of 108/68 mm Hg; and no orthostatic changes. Her examination was normal except for costovertebral angle tenderness

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bilaterally. All values on her initial laboratory evaluation were within reference limits except for an albumin level of 2.3 g/dL (23 g/L) and a cholesterol level of 58 mg/dL (1.50 mmol/L). Urinalysis was nitrite positive and revealed bacteria and 4+ white blood cells.

The patient was admitted with an initial diagnosis of pyelonephritis and was started on intravenous piperacillin. A computed tomography scan of the abdomen obtained after she showed a slow clinical response to antibiotics supported the diagnosis of acute focal bacterial nephritis. She received 10 days of intravenous antibiotics, which resulted in the complete clinical resolution of her illness.

The markedly low albumin and cholesterol levels could not initially be explained. Repeated questioning finally revealed that the patient had been selling plasma at a local center one to two times per week (averaging approximately five times per month) for the previous 12 months. Her most recent donation had been 5 days before admission.

Case 2

The second patient was a 39-year-old black man who was brought to the hospital emergency department by ambulance after arriving at work disoriented and reporting a history of physical assault. He complained of a diffuse headache and sharp epigastric abdominal pain. He also reported a history of hematemesis on two occasions in the past 3 weeks. Medical history was significant for peptic ulcer disease, which had been diagnosed in 1982 by means of esophagogastroduodenoscopy and treated with cimetidine for 1 year. At the time of the examination, he reported taking no medications and denied drug allergies. Social history was significant for cigarette smoking (10 pack-years) and alcohol use (one to three cans of beer daily). Physical examination was entirely within normal limits. All admission laboratory values were normal except for an albumin level of 2.5 g/dL (25 g/L) and a cholesterol level of 90 mg/dL (2.33 mmol/L).

The patient refused further workup and was treated empirically with ranitidine for peptic ulcer disease. When low albumin and cholesterol levels were identified, the patient was asked if he had a history of selling plasma. He reported that he had been doing so one to two times per week for approximately 3 months.

Discussion

The rate of albumin synthesis is about 14 g per day in a normal 70-kg man.¹⁰ At each plasma collection, approximately 835 mL of plasma is removed. This corresponds to 35 g of albumin removed per collection. Therefore, in

a "normal" donor, it would take 2.5 days to regenerate the amount of albumin removed. During acute inflammatory processes, albumin acts as a negative acute-phase protein, and plasma concentrations can decrease by a factor of 0.6 to 0.7.¹¹ Among factors controlling albumin synthesis, amino acid supply to the liver appears to be the most important. In protein depletion, with adequate caloric intake, albumin synthesis is depressed by 60% or more. Therefore, donors who have an acute infection or are nutritionally deprived of amino acids could have a decrease in production or increase in catabolism sufficient to cause a significant decrease in serum albumin concentration.

The normal level of cholesterol is 140 to 200 mg/dL (3.62 to 5.17 mmol/L). Severe hypocholesterolemia has been shown to have prognostic significance and has been regarded as indicative of life-threatening conditions.^{12,13} There are few existing data regarding the effect plasma donation has on cholesterol; however, plasmapheresis has been used to lower cholesterol in patients with severe hypercholesterolemia, indicating that this process is capable of reducing serum cholesterol.¹⁴⁻¹⁶ Cholesterol, like albumin, may be further reduced by acute infections.¹⁷

There is controversy regarding the amount of plasma each individual can donate over a given time without developing a reduction in the serum level of plasma constituents. The World Health Organization recognizes three levels of plasmapheresis intensity.¹⁸ Level 1 allows a donor to participate in a plasmapheresis program one to two times per year. At the second level, a donor participates in a plasmapheresis program in which the quantity and the frequency of sessions are planned so that both the serum level and the synthesis rate of the serum proteins return to normal before a subsequent collection. At this level, which has been adopted by the International Society of Blood Transfusion,¹⁸ 2 to 4 weeks are allowed to pass between plasma collections. The third level is the program permitted in the United States. It allows the removal of 1000 to 1200 mL of plasma per week and 50 to 60 L per year for each donor. It has been argued that at this level of intensity, the liver may be unable to maintain normal levels of serum constituents in the event of an illness or calamity that would cause decreased synthesis or increased catabolism.¹⁹

Some conditions, eg, malnutrition, alcoholism, and infections, frequently prompt patients to seek medical evaluation. If either hypoalbuminemia or hypocholesterolemia is present, it is important to specifically inquire about a history of plasmapheresis. Without inquiry about plasmapheresis, an extensive and expensive diagnostic evaluation may ensue, including a search for such conditions as cancer, amyloid disease, parenchymal renal disease, and spruce.

The hypoalbuminemia and hypocholesterolemia associated with plasmapheresis are probably not of clinical significance since the albumin and cholesterol are rapidly replenished after cessation of plasmapheresis. There is no indication that either healing or metabolism is impaired. In the first patient, immunoglobulins and cholesterol-dependent hormones were all present in normal quantities. It is unclear how a low albumin level affects drug metabolism for medications that routinely bind to serum proteins.

At present, the main significance of this disorder is that plasmapheresis can cause a decrease in serum cholesterol and albumin, which may be interpreted as a marker of more serious disease. Careful inquiry into the patient's history with regard to plasmapheresis may prevent an unnecessary and expensive medical evaluation.

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