Hyperviscosity syndrome
Recent advances

An Essay

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List of abbreviations

AF	Atrial fibrillation.
ALL	Acute lymphoblastic leukemia.
AML	Acute myeloid leukemia.
APCr	activated protein C resistance
CAP	College of American Pathologists
CBC	Complete blood count.
CNS	Central nervous system
cP	Centipoise
ED	Emergency department
ET	Essential thrombocythemia.
HVS	Hyperviscosity syndrome.
ICAM-1	Intercellular adhesion molecule-1.
IEP	immunoelectrophoresis
IFE	immunofixation electrophoresis
Ig	Immunoglobulin.
IL-6	Interleukin-6.
IV	Intravenous
MGUS	Monoclonal gamopathy of unknown significance.
MKS	Meter-kilogram-second system
MM	Multiple myeloma.

mPa•s	Milli-Pascal-second
OC	Oral contraceptive
PAS	Periodic acid-Schiff
PV	Polycythemia vera.
RBC	Red blood cells
TA	Therapeutic apheresis
TPE	Therapeutic plasma exchange
VCAM	Vascular cell adhesion molecule.
VTE	Venous thrombo-embolism
VWF	Von willebrand's factor.
WBCs	White blood cells
WBV	Whole blood viscosity
WM	Waldenström's macroglobulinemia.

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Introduction

The rheological properties of blood depend on several of its constituents, such as proteins, red cells, leukocytes, platelets, lipids, and cholesterol. Qualitative or quantitative changes in any of these can influence blood viscosity. If there is sufficient impairment of blood flow, a combination of clinical signs and symptoms known as hyperviscosity syndrome develops **(Mehta and Singhal, 2003).**

Normally, the main contributor to the viscosity of whole blood is the erythrocyte compartment. The reasons are their large concentrations in a normal blood sample and the very high internal protein concentration. Nevertheless, the red cell is extremely flexible because of its lack of internal organelles, its highly deformable membrane, and its biconcave shape. The result is that blood has a viscosity that is much reduced compared with that obtained when the red cells are stiff. In principle, the leukocytes should have much more influence on blood viscosity because of their complex internal organization, the presence of organelles, and the greater viscoelasticity of their membranes. Nevertheless, in the healthy subject this is of no significance because the leukocyte number concentration is so small by comparison with that of the red cell. But large

leukocyte concentrations as in leukemias can be expected to influence whole-blood viscosity **(Rampling, 2003).**

Viscosity is a property of liquid and is described as the resistance that a liquid exhibits to the flow of one layer over another. As serum proteins or cellular components increase, the blood becomes more viscous, leading to the clinical symptoms of hyperviscosity syndrome secondary to the vascular stasis and resultant hypoperfusion **(Hemingway et al., 2006).**

One of the most striking complications in hematologic disease is the development of blood hyperviscosity. Classically, hyperviscosity presents with the triad of bleeding, visual disturbances, and focal neurologic signs. Hyperviscosity occurs from pathologic elevation of either the cellular or a-cellular (protein) fractions of the circulating blood. In cellular fractions, significant elevation of any of the three primary blood cell lines may lead to clinical manifestations: erythrocytosis, leukocytosis and thrombocytosis. The term ‘‘hyperviscosity syndrome’’ (HVS) is best reserved for pathologic increases in circulating serum proteins, which also manifest with emergency signs and symptoms **(Adams et al., 2009).**

Acute hyperviscosity syndrome (HVS) can occur when the normal plasma viscosity of 1.4 cp (centipoises) increase up to 4-5 cp and it is more common in Waldenström's macroglobulinemia, than multiple myeloma or cryoglobulins **(Ballestri et al., 2007).**

Aim of work

To review etiology, pathogenesis, and proper management of HVS.

Particular attention will be paid to the recent insight into the pathogenesis of HVS, that may lead to new diagnostic tests and novel therapeutic strategies.

Definition and incidence

Hyperviscosity syndrome classically refers to a combination of clinical symptoms and physical findings, with laboratory documentation of an increased serum viscosity. Symptoms are often related to an impairment of blood flow in the microcirculation of the central and peripheral nervous system **(Blum and Porcu, 2007).**

Physical findings are related to the major organ systems involved. Bruises, epistaxis, or gum bleeding may be noted. Neurologic examination may reveal various findings, including diminished mental status, confusion, ataxia, or nystagmus **(Hemingway et al., 2006).**

However, **Pappas and Delaney-Black (2004)** defined hyperviscosity as an increase in the internal friction of blood or the force required to achieve flow. The viscosity of whole blood is affected by numerous factors, including the red cell mass, the platelets, the plasma components, and the interaction of cellular elements with the vessel wall**.**

Usually HVS is the result of increased circulating serum Igs and can be seen in Waldenström macroglobulinemia and

multiple myeloma **(Kupas et al., 2005).** It can also result from increased cellular blood components (typically white or red blood cells) in hyperproliferative states such as the leukemias, polycythemia, and the myeloproliferative disorders **(Hemingway et al., 2006).**

No information is available regarding the incidence of hyperviscosity syndrome, little information is available regarding the age of patients with hyperviscosity syndrome. Most cases of hyperviscosity syndrome are not diagnosed until the seventh decade of life **(Kupas et al, 2005)** and its incidence ranges from 5% to 13% in adult acute myeloid leukemia (AML) and from 10% to 30% in adult acute lymphoblastic leukemia (ALL) **(Adams et al., 2009).** Hyperviscosity syndrome may complicate about 8% of all cases of chronic myeloid leukemia **(Shepherd and Farquharson, 2007).**

In patients with a symptomatic hyperviscosity linked to monoclonal immunoglobulin, Waldenstrom's disease accounts for up to 90% of cases **(Decaux et al., 2009).** Symptomatic hyperviscosity is much more common in Waldenström's macroglobulinemia (10 to 30%) than it is in myelomas (2 to 6%) but still they are the second leading cause. Symptoms of hyperviscosity usually appear when the normal serum viscosity