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Review of Eisenmenger syndrome and its management

MALARMATHI. M

TUTOR

COLLEGE OF NURSING

JAWAHARLAL INSTITUTE OF POSTGRADUATE MEDICAL EDUCATION & RESEARCH (JIPMER)

Abstract

A group of symptoms known as Eisenmenger syndrome (ES) are brought on by a congenital abnormality in the heart that results in strong anatomical connections between various heart components. The flow of blood first produces a transfer from the left side to the right side due to anatomical variations that exist from birth. This ultimately results in an increase in blood vessel resistance and the onset of pulmonary arterial hypertension (PAH), a dangerous condition. In conclusion, as the pulmonary vascular resistance rises, the left-to-right shunt will ultimately change to a right-to-left shunt. Cyanosis will develop as a result of the drastic drop in oxygen levels.

Key words: Eisenmenger syndrome, Pulmonary arterial hypertension, Congenital heart defect

Introduction

Victor Eisenmenger was the first to describe Eisenmenger syndrome (ES) [1]. The case of a patient in 1897 who had bluish discolouration and dyspnea from a young age. The person eventually passed away from severe bloody coughing, which became known as Eisenmenger syndrome, after developing heart failure over time [2]. It was defined by Paul Wood in pathophysiologic terms as "pulmonary hypertension (PH) at systemic level, caused by a high pulmonary vascular resistance (PVR), with reversed or bidirectional shunt at aorto-pulmonary, ventricular, or atrial level [3]. It is the most severe hemodynamic phenotype of pulmonary arterial hypertension (PAH) associated with congenital heart disease (CHD) and arises when there are complex forms of CHD, such as univentricular hearts with unrestricted pulmonary blood flow, large, unrepaired atrial or ventricular septal defects, or arterial shunts [4].

In addition, ES patients had the highest prevalence of impaired kidney function and worst exercise tolerance among CHD patients [5]. Their quality of life is considerably lower than that of people with PAH of various etiologies and other patients with CHD due to their poor physical abilities and multiorgan involvement [6].

Etiology

A cardiac defect can lead to aberrant blood circulation, which can result in Eisenmenger syndrome. People who have this ailment are typically born with a ventricular septal defect, which is a hole between the left and right ventricles, the heart's two pumping chambers. Blood that has already taken up oxygen from the lungs can return to the lungs through the hole rather than leaving for the rest of the body [7].

Clinical manifestations

Secondary erythrocytosis, iron deficiency, and hyperviscosity syndrome

Chronic hypoxemia causes the kidneys to release more erythropoietin, which in turn causes the bone marrow to produce more red blood cells, increasing the mass of red blood cells in circulation and hemoglobin [8]. In patients who are iron-repleted, this physiological reaction is proportionate to the level of hypoxia [9]. In such that in an attempt to maintain proper oxygen transport to peripheral tissues, more severe hypoxemia causes larger levels of hemoglobin to be in circulation. Although the hemoglobin level may still be within the "normal" range for an acyanotic patient, this response decreases in iron-deficient patients because of decreased hemoglobin production, which results in an improperly low hemoglobin level. Because iron shortage is a risk factor for a poor prognosis, monitoring and proper replacement of iron stores are crucial components of care for ES patients [10].

In the past, noticeably elevated red blood cell mass caused worries about hyper-viscosity syndrome, a condition that can cause cardiac ischemia, mucosal bleeding, and neurological symptoms [11].Although this does happen when cyanosis and secondary erythrocytosis are present, there is only a weak relationship between hematocrit and viscosity, iron deficiency, or the intensity or frequency of a patient's symptoms [12].

This is especially significant because phlebotomy or apheresis, the primary therapies for hyper-viscosity syndrome, may be detrimental. Compared to the general population, ES patients are more likely to experience iron insufficiency, dehydration, thyroid dysfunction, pheochromocytoma or paraganglioma, and cerebral abscesses, all of which can resemble hyper-viscosity symptoms [8].

Only patients with hemoglobin >22 g/dL (or hematocrit >65%), definitive hyper-viscosity symptoms, properly volume resuscitated, and no other reversible causes should undergo therapeutic phlebotomy (drawn in small volumes with equal volume fluid replacement to avoid hemodynamic embarrassment) or red cell apheresis [12].

Renal disease

In ES, chronic renal disease is common. Lower glomerular filtration rate (GFR) and proteinuria are risks for those with secondary erythrocytosis and chronic hypoxemia [13]. According to one study, up to 30% of cyanotic individuals had proteinuria, and their serum creatinine levels are higher than those of their acyanotic counterparts [14].

Patients with cyanotic congenital heart disease had a significantly lower GFR than those without the condition, which was linked to a worse prognosis, according to a larger cohort research [15].

Notably, compared to creatinine-based GFR estimates, estimated GFR derived from cystatin C more accurately predicts non-elective cardiovascular hospitalization and all-cause death in people with congenital heart disease [16].

Coagulopathy

Derangements in platelet function and coagulation pathways brought on by cyanotic heart disease make people more susceptible to thrombosis and hemorrhage [17]. Up to 20% of patients may have pulmonary artery thrombus, which is linked to both left or right ventricular dysfunction and deeper pulmonary arteries with decreased blood flow velocity [18].

Another problem is cerebral thrombosis; one study found that although only 21% of individuals with cyanotic congenital cardiac disease (of whom 70% had ES) had a history of a clinically diagnosed stroke, 47% of them had MRI-detected evidence of previous cerebral infarctions. Although 75% of the participants in this same study had no known medical history of pulmonary thrombus, 38% of them had imaging evidence of the condition.

It might be challenging to recognize the clinical alterations caused by thrombotic illness. It's interesting to note that in the two studies mentioned above, the incidence of pulmonary or cerebral thrombosis was not linked to variations in coagulation factors, platelet function, or degree of erythrocytosis, despite the platelet and coagulation pathway abnormalities linked to cyanotic disease previously described [19].

Given the conflicting threats of thrombosis and hemorrhage, routine anticoagulant use is not advised, i.e., when there is no known thrombus or significant risk factor for thromboembolism, such as atrial arrhythmias. Uncertainty about the function of routine subclinical thrombosis screening and treatment in ES [20].

Hypoxemia

One of the main signs of ES is chronic hypoxemia, which can be caused by a right-to-left or bilateral shunt as well as inadequate pulmonary diffusion in the setting of pulmonary vascular remodeling. Comorbidities and physiological aftereffects of ES associated with the effects of hypoxemia [21].

Eisenmenger syndrome patients frequently have a history of temporary pulmonary congestion during infancy due to a significant pulmonary blood flow brought on by a massive intracardiac shunt that runs from left to right. As pulmonary vascular resistance rises later in infancy or early childhood, pulmonary blood flow falls and pulmonary congestion symptoms subside. Cyanosis and erythrocytosis appear when the shunt reverses, or when shunting moves from right to left. Less frequently, patients seek medical attention for developing fatigue, dyspnea, or cyanosis and acquire Eisenmenger syndrome in adulthood without any apparent symptoms in childhood.

The majority of Eisenmenger syndrome patients eventually suffer from one or more of the following ailments: 1) signs of poor systemic output (e.g., fatigue, syncope, or dyspnea upon exertion); 2) mild neurologic abnormalities (e.g., headache, lightheadedness, or vision disturbances) brought on by erythrocytosis and hyperviscosity; or 3) signs of congestive heart failure. Hemoptysis and arrhythmias are also frequent, and the former might result in unexpected death. Pulmonary infarction, rupture of a pulmonary artery dilated by an aneurysm or a thin-walled pulmonary arteriole, or bleeding diathesis which frequently begins as mucosal (i.e., gingival or epistaxis) bleeding are the causes of hemoptysis. A cerebral abscess, paradoxical embolism, or hyperviscosity are common causes of cerebrovascular accidents [22].

Pathophysiology

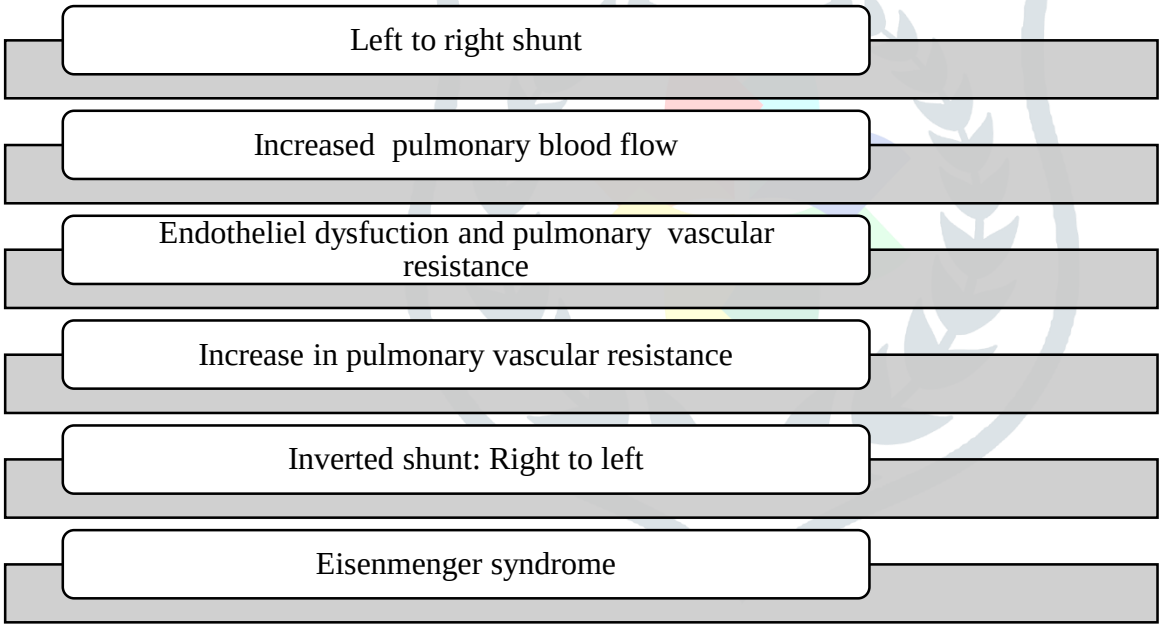

Fig. 1. Pathophysiology of Eisenmenger syndrome.

It is unclear whose pathophysiologic processes cause the pulmonary microvascular alterations that occur in Eisenmenger syndrome patients. The production of elastase enzymes and growth factors, such as insulin-like growth factor I and transforming growth factor, is stimulated by pulmonary microvascular injury in experimental animals. This can lead to medial hypertrophy, cellular intimal proliferation, progressive occlusion, and ultimately the destruction of small arterioles [23, 24]. Eisenmenger syndrome patients exhibit increased pulmonary endothelin production, impaired endothelium-dependent pulmonary arteriolar relaxation, and elevated plasma thromboxane B2 concentrations, indicating that endothelial dysfunction or platelet activation may be a contributing factor [25].

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moves from right to left. Less frequently, patients seek medical attention for developing fatigue, dyspnea, or cyanosis and acquire Eisenmenger syndrome in adulthood without any apparent symptoms in childhood [25, 26].

Physical Examination

A physical examination of the Eisenmenger syndrome patient shows clubbing of the nail bed and central cyanosis. The degree of right-to-left shunting and cyanosis rises if systemic vascular resistance decreases, which might happen due to hot weather, exercise, fever, or a systemic infection. Differential cyanosis, or clubbing of the nail beds on the left hand and both feet, and normal, pink nail beds on the right hand are possible in patients with a patent ductus arteriosus. This happens as a result of venous blood entering the aorta distal to the right subclavian artery after shunting through the ductus**.** If tricuspid regurgitation is present, the jugular venous pressure may be normal or high, with a noticeable "V" wave. Usually, the arterial pulse is either normal or reduced [27].

Visualizing intracardiac defects and detecting related cardiac or valvular abnormalities are made easier with the use of two-dimensional echocardiography. The flow of color Intracardiac shunting is typically detectable by Doppler imaging. However, the pressure gradient and flow across the intracardiac defect may be minor and thus challenging to see by color flow in individuals with Eisenmenger syndrome since their pulmonary and systemic arterial pressures are similar. Doppler imaging [28].

Contrast echocardiography should be done on these individuals. When a right-to-left intracardiac shunt is present, an intravenous contrast agent (such as hydrogen peroxide, agitated normal saline, or indocyanine green) rapidly appears in the left heart chambers; the extent of intracardiac right-to-left shunting can be qualitatively classified as small, moderate, or large, but it cannot be precisely measured [29, 30].

Management

Digoxin, chronic angiotensin converting enzyme inhibitors (ACEi), and angiotensin receptor blockers (ARB) did not reduce mortality, according to this analysis. It's interesting to note that the advantages of beta-blocker use in this cohort were almost significant [31].

Heart-related vasodilators ES is characterized by elevated pulmonary vascular resistance. Recent years have seen a lot of study on the use of pulmonary vasodilators for PAH in general, and encouraging findings in that field have led to an increase in use in ES patients in particular [31].

PDE-5 inhibitors

PDE-5 inhibitors Improvements in exercise capacity, functional class, and hemodynamics have been linked to the PDE5 inhibitors sildenafil and tadalafil in ES patients [32,33].

Riociguat

Riociguat is a soluble guanylate cyclase (sGC) stimulant that has antiproliferative and vasodilatory properties. Both pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension (CTEPH) can be treated with it. Although there is currently insufficient data on Riociguat use in ES, subgroup analysis of the trials that demonstrated benefit in PAH revealed that Riociguat use was linked to long-lasting improvement in hemodynamic and functional parameters (6MWD, PVR, NTproBNP, and WHO functional class) at two years in patients with persistent or recurrent PAH after CHD correction (PAH-CHD) [34,35].

Prostanoids

Inhaled iloprost improves subjective quality of life metrics, RV function, and 6MWD [36]. although when combined with maximal oral medication, this effect might be reduced [37].

Following four weeks of nifedipine medication, a small randomized investigation of persons with Eisenmenger syndrome revealed a slight improvement in exercise capacity. However, we do not advise using calcium-channel blockers because they can result in syncope and unexpected death if administered carelessly [38].

A small nonrandomized trial found that children with congenital heart disease and concurrent pulmonary vascular disease had better survival rates when they received long-term home oxygen therapy [39].

Phlebotomy

Secondary erythrocytosis and systemic hypoxemia are caused by blood being diverted from the venous to the systemic circulation. Blood viscosity rises in proportion to the amount of erythrocytes (hematocrit), which ultimately results in a decrease in blood flow and oxygen transport 40. Due to decreased tissue oxygenation, patients with hyperviscosity may experience headache, exhaustion, lightheadedness, anorexia, or lethargy. Without sufficient volume replacement, phlebotomy can exacerbate symptoms and further impair brain perfusion, oxygen delivery, and cardiac output. On the other hand, isovolumetric hematocrit lowering relieves symptoms both at rest and during exercise, lowers systemic vascular resistance, and enhances cardiac output and systemic oxygen transport [41]. Within 24 hours, hemodynamic and clinical improvements are typically noticeable [42].

Thrombocytopenia, platelet dysfunction, and other coagulation abnormalities frequently seen in polycythemic individuals with cyanotic congenital heart disease are also corrected by isovolumetric reduction in erythrocyte mass [43,44].

Although the exact mechanism behind these advantages is unknown, it might have something to do with the liver and bone marrow receiving more oxygen. Phlebotomy can be successfully carried out as an outpatient procedure in people with Eisenmenger syndrome who have concomitant hyperviscosity. This involves drawing 500 mL of blood in 30 to 45 minutes and infusing it with an equivalent volume of isotonic saline [45].

As an alternative, fresh frozen plasma, dextran, or salt-free albumin may be used for volume replacement with comparable effectiveness, but at a higher expense and with a higher risk of allergy and exposure to blood-borne infections. Throughout phlebotomy, blood pressure should be regularly checked to prevent hypotension. When an erythrocytotic patient exhibits symptoms of hyperviscosity, phlebotomy should be carried out; it is not recommended for patients with an increased hematocrit who do not exhibit hyperviscosity symptoms [46, 47].

It is rarely necessary to remove more than two units of blood over two days, though phlebotomy might be repeated if symptoms do not get better. Instead of aiming for a predetermined hematocrit, phlebotomy aims to alleviate hyperviscosity symptoms. Despite several phlebotomies, iron deficiency should be recognized if hyperviscosity symptoms continue. Blood viscosity rises and the erythrocyte becomes less deformable when the mean corpuscular volume decreases 48. Patients with microcytosis or biochemical signs of iron shortage (lower serum levels of iron and ferritin and decreased transferrin saturation) should get iron replacement treatment. Iron replacement therapy patients need to be properly watched since their hematocrit can rise quickly, which can induce hyperviscosity [49].

Transplantation

Compared to combined heart-lung transplantation, lung transplantation offers a number of benefits, such as improved availability of donor organs, reduced transplant waiting times, and the prevention of cardiac allograft rejection and transplant coronary vasculopathy [50]. In summary, patients with Eisenmenger syndrome who have normal left ventricular systolic function, no coronary artery disease or severe left-sided valvular disease, a simple congenital cardiac defect (such as an atrial septal defect, a ventricular septal defect, or patent ductus arteriosus), and a right ventricular ejection fraction greater than 0.10 are best treated with lung transplantation combined with repair of congenital cardiac defects [51].

Nursing perspectives

Monitoring: To keep fluid equilibrium, weigh yourself every day. Monitoring to make sure oxygen saturation is higher than 90%. Medications: Giving out drugs including iron supplements, diuretics, antibiotics, anticoagulants, and extra oxygen .Position: Promoting an upright posture to facilitate breathing and lessen cardiac strain. Limiting intense or isometric activity and ceasing if symptoms arise are examples of exercise limits.. Maintaining proper dental hygiene lowers the chance of infection. Promoting a nutritious diet and adequate water Using efficient contraceptive techniques, such as a hormone implant, vasectomy, or an intrauterine device (IUD),

Eisenmenger syndrome concerns also include:

Pregnancy should be avoided since it might be fatal for both the mother and the unborn child. Steer clear of high elevations. Preventing the depletion of the volume. Preventing anemia due to iron shortage. Using peripheral

vasodilating drugs with caution . One disorder that can result in a shorter life expectancy is Eisenmenger syndrome. Cyanosis, clubbing, dyspnea, edema, and an irregular heartbeat are among the symptoms [52].

Complications

Pregnancy

Women with Eisenmenger syndrome should not become pregnant because of the 30–50% risk of maternal death and the generally poor chances of a successful pregnancy, particularly if the mother's arterial oxygen saturation is less than 85% [53].

Neurological complications

Eisenmenger patients frequently experience neurologic problems, which need to be treated very away. These comprise both infection-related consequences (cerebral abscess) and ischemia events (paradoxical embolism or air embolism). Air-eliminating filters must be used anytime intravenous lines are inserted for Eisenmenger patients due to the danger of paradoxical/air embolism.

Problems with thrombosis and embolism

Numerous Eisenmenger patients have been found to have pulmonary thrombosis, which can be both an in-situ thrombosis and a result of thromboembolism. Regular anticoagulation for Eisenmenger patients has therefore been recommended; however, this must be weighed against the typically elevated risk of bleeding resulting from co-occurring hematological disorders with an inherent, elevated risk of bleeding. No research has demonstrated that Eisenmenger patients using oral anticoagulants survive [54].

Prevention of infectious complications

Patients should be carefully encouraged to get vaccinated against pneumococcal illness every five years and against influenza every year. In order to prevent pulmonary or cardiac consequences, respiratory infections should also be identified early and treated appropriately. Current recommendations state that before receiving dental work, Eisenmenger patients should be given the proper antibiotic endocarditis prophylaxis [55].

Conclusions

The majority of Eisenmenger syndrome patients who are children go on to become adults. Understanding the pathogenesis, clinical appearance, natural history, consequences, and therapy (medical and surgical) of the condition is necessary for the proper evaluation and treatment of these patients. These patients frequently have erythrocytosis, but careless phlebotomy can exacerbate hyperviscosity and raise the risk of a cerebrovascular accident. In people with Eisenmenger syndrome, procedures and events that are often well tolerated by healthy adults like pregnancy or noncardiac surgery are linked to higher rates of morbidity and mortality. Such patients should be monitored in tertiary care facilities that specialize in complex congenital cardiac disease and can offer a multidisciplinary approach when difficulties emerge, in addition to the care given by the primary caregivers.

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