Anemia in CKD Patients

Genetics 208-01 Bunker Hill Community College

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Slide 2- STATEMENT ABOUT WHAT YOU'RE DOING A PROJECT ABOUT

My project is about anemia in CKD patients. Anemia in CKD patients is important to me because my 17-year-old cat has stage 2 chronic kidney disease with anemia.

Slide 3- OBJECTIVES

Today we will be answering the following questions [LIST QUESTIONS] additionally, we will look at a real world example

1. Types of anemia
2. What happens when you have anemia?
3. How does anemia affect CKD patients vs an otherwise healthy person?
4. Why are chronic kidney disease patients prone to anemia?
5. How do you treat anemia?
6. A Real World Example
7. Conclusion

Slide 4- TERMS TO KNOW

Before we jump in, we should understand a few terms [LIST TERMS AND EXPLAIN]

1. Anemia → a blood disorder that occurs when the body doesn't have enough healthy red blood cells or hemoglobin that carries oxygen to the body's tissues.
2. Autosomal recessive disorder → a pattern of inheritance characteristic of some genetic disorders. Autosomal refers to a gene in question that is located on 1 of the numbered or non-sex chromosomes. Recessive means that 2 copies of a mutated gene (1 from each parent) are required to express the disorder.

3. CKD → chronic kidney disease (aka chronic kidney faliure); involves a gradual loss of kidney function. Occurs in 5 stages: in stages 1-3, the kidneys are still able to filter waste out of the blood but at a reduced effectiveness . Stage 4, kidneys work as hard as they can to filter the blood. Stage 5, kidneys fail and cannot filter the blood.
4. EPO → Erythropoietin; a hormone necessary for red blood cell production.
5. Germline mutation → a gene change in a body's reproductive cell (either egg or sperm) that becomes incorporated into the DNA of every cell within the body of the offspring.
6. HBB → gene; gives instructions for making the beta-globin protein (which is a component of hemoglobin, which is a larger protein and is located within red blood cells).
7. Pica → a syndrom that drives individuals to chew on or eat inedible and/or hard objects (like pottery shards, ice, etc)
8. Splice (site) mutation → a genetic alteration in the DNAs sequence that occurs at the boundary of an exon and an intron (splice site). This change may disrupt the RNA splicing, resulting in the loss of exons or the inclusion of introns and an altered protein-coding sequence.
9. Substitution point mutation → when one base is incorrectly added during the replication process and replaces the pair in the corresponding position on the complementary strand (ex: sickle cell anemia).
10. TMPRSS6 → gene containing 18 exons; provides instructions for making a protein called matriptase-2, which controls levels of the protein hepcidin (which is an iron regulatory hormone). Mutations in this gene cause iron-refractory iron deficiency anemia (IRIDA).

Slide 5- TYPES OF ANEMIA (EXPLAIN ABOUT THE GENES and LIST DIFFERENT KINDS OF ANEMIA)

There are a few different types of anemia, which include [LIST ANEMIAS]

1. Aplastic anemia
2. Iron deficiency anemia
3. Sickle cell anemia
4. Thalassemia
5. Vitamin deficiency anemia

Slide 6- Today, we will be focusing on Iron deficiency anemia, sickle cell anemia, and Thalassemia, as they result from gene mutations. And all of which are autosomal recessive disorders. The example in this slide is SCA.

Slide 7- IRIDA

1. Iron-refractory iron deficiency anenemia (IRIDA) is caused by germline mutations to the TMPRSS6 gene.
2. The TMPRSS6 gene is located on chromosome 22, between the q12 and q13 regions.

Slide 8- SCA

1. Sickle cell anemia is the result of a change in a single nucleotide, a point mutation. Changes in DNA sequence may also occur in the chromosome, where large segments of the chromosome become altered.
2. The HBB gene is found on chromosome 11p15.5.
3. HBB mutations result in the production of abnormally shaped hemoglobin (or Hb. called HbS).
4. 4 chains make up hemoglobin, 2 are alpha chains and 2 are beta chains. In sickle cell anemia, a single point mutation causes a change in amino acids from glutamic acid (Glu) to be replaced by valine (Val) within the beta chains of HbA. That results in abnormal HbS. Red blood cells that have HbS and low oxygen levels will distort their shape into sickle shapes.

Slide 9- Thalassemia

1. Caused by splice (site) mutations within the DNA of cells that create hemoglobin.
2. Hemoglobin molecules are made of alpha and beta chains, these chains are affected by the mutation, resulting in a reduced production of either alpha or beta chain
3. The mutations are located in the alpha-globin (HBA1 and HBA2) and the beta-globin (HBB) genes on chromosomes 16 and 11.
4. 4 genes are involved in making the alpha hemoglobin chain, which you gain 2 from each parent. If 1 gene is mutated, you may not experience any symptoms but are still a carrier of the disesase. If 2 genes are mutated, you may experience mild symptoms of the disease. However, if 3 genes are mutated, your symptoms may be moderate to severe. And while rare, if 4 genes are mutated, the offspring would either be stillborn or die soon after thier birth.
5. 2 genes are involved in making the beta hemoglobin chain, which you gain 1 from each parent. If 1 gene is mutated, you may experience mild symptoms. If 2 genes are mutated, you may experience moderate to severe symptoms of the disease.

Slide 10- WHAT HAPPENS WHEN YOU HAVE ANEMIA?

Anemia symptoms vary from patient to patient because anemia can range from asymptomatic, mild, moderate, and severe. Possible symptoms of anemia include [LIST SYMPTOMS]

1. Fatigue
2. Weakness
3. Shortness of breath
4. Pale or yellowish skin
5. Irregular heartbeat
6. Dizziness/lightheadedness
7. Chest pain
8. Cold, numb, or tingling hands and feet
9. Headaches
10. Difficulty concentrating
11. Irritability
12. Loss of appetite
13. Blue color to the whites of eyes
14. Brittle nails
15. Pica symptoms
16. Lightheadness upon standing
17. Sore/inflamed tongue
18. Mouth ulcers
19. Abnormal menstruation in women
20. Loss of labido in men

Slide 11- HOW DOES ANEMIA AFFECT CKD PATIENTS VS AN OTHERWISE HEALTHY PERSON?

CKD

1. In CKD patients, anemia is caused by the kidney's lack of ability to produce enough EPO
2. CKD patients experience anemia more frequently and more severely than an otherwise healthy person
3. CKD patients often require EPO stimulating agents

HEALTHY PERSON

1. In otherwise healthy patients, anemia can be caused by nutrient deficiencies, infections, inflammation, chronic diseases, and inherited blood cell disorders.
2. These patients tend to experience anemia less frequently than CKD patients unless the anemia is

a result of genetic mutations, in which the patient would experience anemia chronically
3. Otherwise healthy patients can typically treat anemia quicker than a CKD patient and are ususally treated with iron-rich diets and supplements

Slide 12- WHY ARE CKD PATIENTS PRONE TO ANEMIA?

CKD patients are prone to anemia for various reasons [LIST REASONS]

1. The kidneys are damaged so blood filtration is reduced and the production of EPO reduces
2. Lack of filtration means that waste and fluids build up
3. Less EPO means the body makes fewer red blood cells and as a result, less oxygen is delivered to organs and tissues
4. In addition to the body producing fewer red blood cells, red blood cells tend to live shorter periods in CKD patients with anemia and those cells end up dying quicker than they can be replaced.
5. Many CKD patients have low levels of nutrients necessary to make healthy red blood cells, including iron, folate, and vitamin B12

Anemia is a common complication of CKD and becomes more common as stages progress

Slide 13- HOW DO YOU TREAT ANEMIA?

To treat anemia, a healthcare provider will take into account any physical symptoms you might have and run a few tests to assess what steps should be taken. These tests include [LIST TEST SECTION]

Tests to run:

1. CBC → a complete blood count, capable of examining blood shape, size, and count.
2. Hemoglobin test → detects hemoglobin; hemoglobin is the main component of red blood cells
3. Hematocrit test → measures the percentage of red blood cells in the blood
4. Peripheral blood smear → examination of red blood cell size and shape under a microscope
5. Reticulocyte count → reticulocytes are immature red blood cells; the test checks if the bone marrow is producing enough healthy red blood cells

Once a test has concluded anemia, a provider may offer several options of treatments based on the severity of the anemia [LIST TREATMENTS]

Treatments available:

1. Iron supplements
2. Folate (B9); folic acid supplements
3. B12 supplements
4. Erythropoietin → a medication that helps your bone marrow to produce more blood stem cells
5. Corticosteriods → a medication that suppresses the immune system for patients whose immune system is attacking blood cells that belong in the body
6. Blood transfusion
7. Bone marrow transplant

Slide 14 and 15- A REAL WORLD EXAMPLE

Slide 14- This is Alison, an anemia patient with CKD.

Slide 15- This a graph of Hematocrite (or HCT) levels, red blood cell counts (or RBC) and white blood cell counts (or WBC).

Varenzin, an erythropoietin treatment, began November 17th, 2024 and continued until November 25th, 2024. During that time, hematocrite levels climbed from 23.8% to 27% in just 8 days of treatment, a 3.2% increase. This increase can be noted on the far right of the graph. Usually, this treatment is used for around 30 days but the patient suffered side effects, prompting the recheck of HCT levels just 8 days later.

Slide 16- CONCLUSION

Anemia as a result of a genetic mutation can be either a germline mutation, a splice (site) mutation, or a Substitution point mutation.

Genetic mutation anemias are autosomal recessive disorders.

TMPRSS6 gene mutations cause germline mutations on chromosome 22.

HBB gene mutations cause substitution point mutations on chromosome 11.

(Alpha-globin and beta-globin) HBA1 and HBA2 gene mutations cause splice (site) mutations on chromosome 16.

CKD patients experience anemia often due to a lack of EPO hormone, which is responsible for RBC production.

Slides 17, 18, and 19- I have included my sources. I hope you learned something today!