Gyrate Atrophy: A Study in a Degenerative Eye Disease

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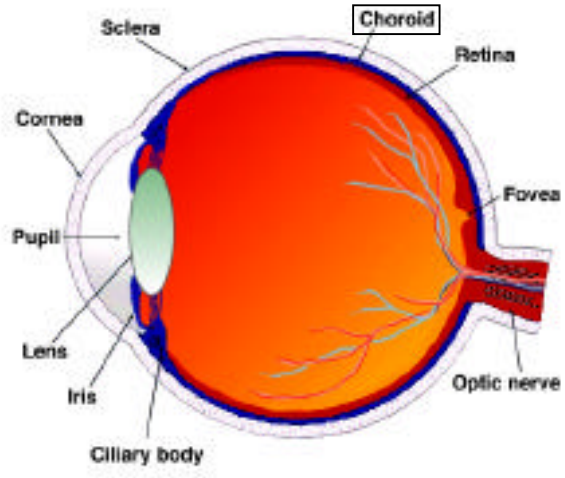
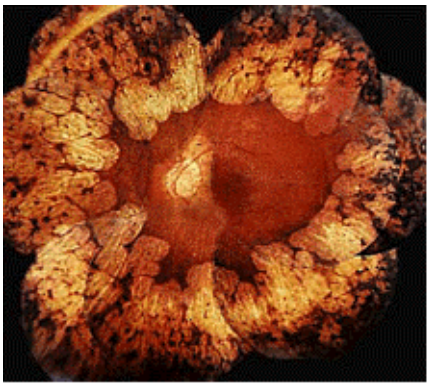
Maxwell, a highly active five years old, visited his pediatric doctor complaining of myopia (nearsightedness), loss of peripheral visual field and night vision. Upon investigation of his eyes, the doctor noted damage of the retina. Visual tests proved a visual acuity of 20/200 (nearsighted). Blood chemical analysis showed highly elevated levels of Orinthine, a rare amino acid in humans, but abundant in plants. His plasma orinthine levels were recorded at 773 uMol/l where normal orinthine levels are 24-132 uMol/l (Jaissle, G. et al). The pediatric doctor recommended further retinal investigation by an ophthalmologist.

The ophthalmologist investigated the conditions of all the parts of the eyes. His analysis showed atrophy of the circular gyrate choroid. The gyrate choroid is the capillary bed layer of tissue in the eye between the retina and the sclera (white of the eye). The main function of the choroid is to feed the retina with a constant flow of blood. Without a functioning choroid, the retina would not receive a constant flow of nutrients and oxygen. The result would be a gross atrophy of the layer to tissue responsible for the neural response to visual information. Examination of Maxwell's retina showed degeneration mainly in



the peripheral retina (area's furthest from the optic nerve) resulting in the patient's complaint of a narrower visual field.



The retina of a patient with gyrate atrophy of the choroidand retina of the eye caused by ornithine aminotransferase (OAT) deficiency. [Image credit: Muriel Kaiser-Kupfer, NEI, NIH, Bethesda, MD, USA and David Valle, Johns Hopkins University, Baltimore, MD, USA.]

After confirming the diagnosis of Gyrate Atrophy with Maxwell's pediatric specialist, Maxwell is placed on a restricted diet devoid of high amounts of protein and he is placed on dietary supplements containing essential amino acids. After three months of treatment, Maxwell's plasma orinthine levels fell to 120 uMol/l and his vision improved to 20/50, or only slightly nearsighted. The patient will be examined on a yearly basis for visual acuity, plasma orinthine levels and retinal examination by an ophthalmologist.

Gyrate Atrophy is the result of a deficiency of Orinthine Ketoacid Aminotransferase, an important enzyme in the urea cycle. The primary purpose of the urea cycle is to convert the amino groups from amino acids and proteins into urea, a soluble compound, composed of two amino groups that can be passed successfully in the urine. This enzyme is responsible for carrying the amino group from orinthine to an _-keto acid. In the case above, the amino group is transferred to _-ketogluterate for ultimate insertion in the urea cycle. The increase of orinthine in the choroid show causes destruction of the vital blood vessels that feed the retina.

Questions:

1.) Why would a diet low in the amino acid arginine alleviate the Gyrate Atrophy?

2.) Several years after the beginning of his treatment, Maxwell experienced a recurrence of symptoms. By this time, he his diet consisted solely on plant matter, of this, his favorite foods were raw legumes such as soybeans and peanuts. Consider two reasons why he is having a recurrence of the Gyrate Atrophy.

3.) After treatment, Maxwell complains of a general loss of energy. Discuss the role of the urea cycle in the catabolism of glucose into ATP, specifically cite why Maxwell is experiencing a loss of energy.

Clinical Discussion of Gyrate Atrophy

4.) Why would a diet low in the amino acid arginine alleviate the Gyrate Atrophy?

In the urea cycle, arginine is broken down into urea and orinthine by arginase. With lowered levels of arginine, the urea cycle would slow down, especially at this step. Since this would lower the levels of orinthine. This would give orinthine an alternative route of degradation. Instead of transamination, the cells would be able to slough the excess orinthine into the slowed urea cycle, thus lowering the cellular concentration of orinthine

5.) Several years after the beginning of his treatment, Maxwell experienced a recurance of symptoms. By this time, he his diet consisted solely on plant matter, of this, his favorite foods were raw legumes such as soy beans and peanuts. Consider two reasons why he is having a recurance of the Gyrate Atrophy.

Although orinthine isn't used as an amino acid in humans, plants use it a great deal. Because of their function as germinating bodies, legumes have a large pool of energy storing molecules. Specifically, legumes store their energy as proteins. The proteins in the storage structures of the plant material are high in orinthine and arginine. This boost in arginine and orinthine would cause a rapid regression of the degenerative eye disorder. After examining Maxwell's eating habbits, his doctors suggested a diet without many legumes. After three weeks on his new treatment, Maxwell quickly regained his sight.

6.) After treatment, Maxwell complains of a general loss of energy. Discuss the role of the urea cycle in the catabolism of glucose into ATP, specifically cite why Maxwell is experiencing a loss of energy.

Now that orinthine is primarily degraded using the urea cycle, Orinthine Ketoacid Transaminase now lies dormant. If you will remember, the main role of this enzyme is to

transfer the amino group off of orinthine, ultimately to end up as a-ketogluterate, a key intermediate in the TCA cycle. With the bodies lowered a-ketogluterate, the body is unable to maintain the TCA cycle at the rates that it was able to previous. This would ultimately slow the formation of ATP. In Maxwell's case, he was supplemented with Creatine Monophosphate to boost his metabolism enough to fill in the energy void from the nonfunctioning transaminase.

References

Gyrate Atrophy of Choroid & Retina. Oxford University, Oxford England. http://oxmedinfo.jr2.ox.ac.uk/Pathway/Disease/5181.htm

Genes and Disease. NCBI. http://www.ncbi.nlm.nih.gov/disease/GyrateA.html

Jassie, G. et al. Long-Term Benefit of Dietary Treatment in Gyrate Atrophy. 97th DOG Annual Metting, 1999. http://www.dog.org/1999/e-abstrac99/431.html