

What You Should Know About Incontinentia Pigmenti

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Incontinentia pigmenti (IP) is a genetic disease affecting the skin, brain, eyes, teeth, and sometimes the bones and other organ systems. The condition stems from a mutation on the X chromosome, which is one of two chromosomes determining a person's sex. Females have two X chromosomes and males have one X chromosome and one Y chromosome. The genetic defect leads to a defective protein called nuclear factor Kappa B essential modulator, which is required to activate a series of enzymes called I Kappa B kinases. Without proper activation of these enzymes, multiple organs experience deranged development. If a male inherits the mutated gene on his single X chromosome, it is almost always fatal and the pregnancy ends in miscarriage. In females, inheriting the mutated gene on one of the X chromosomes leads to the disease, but not necessarily to death. The second X chromosome, which has the normal copy of the gene, allows the cell to produce enough normal protein to prevent death, but not disease. Because of these genetic considerations, 97% of living patients with Incontinentia Pigmenti are females, and the rare males who survive often have an additional genetic abnormality such as three sex chromosomes (eg. XXY). This is a useful fact for the physician; if a patient presents with eye findings of incontinentia pigmenti (IP), but the patient is male, then other diseases come to mind, and IP is usually rejected as a possible diagnosis.

A family history of IP is obtained in 15-40% of cases. The remainder of cases are sporadic, that is, there is no family history of disease. In these cases, the genetic defect is a new one.

What Are The Eye Abnormalities In Incontinentia Pigmenti?

Ocular abnormalities occur in approximately 35% of cases with IP. The most common ocular problem in IP is failure of the blood supply to the peripheral retina to develop. The retina is the neural lining of the back of the eye, where light is focused and converted to a signal that travels to the brain. The normal retina is densely packed with capillaries, but in IP the peripheral retina fails to develop vessels. As a result, the tissue is oxygen starved, leading to reactive growth of abnormal blood vessels. These can bleed, leak fluid into the retina, and produce scar tissue, which can contract and detach the retina. Other less common ocular problems in IP include cataract, a swollen cornea (the clear watchglass over the pupil), crossed eyes, and a smaller than normal sized eye. Frequently, the eye abnormalities are asymmetric in IP for unknown reasons. Blindness of an affected eye occurs in approximately 35% of cases. An example of leakage of lipid into the retina from the abnormal blood vessels is shown in figure 2. For comparison, a normal retina is shown in figure 1.

FIGURE 1. NORMAL RETINA

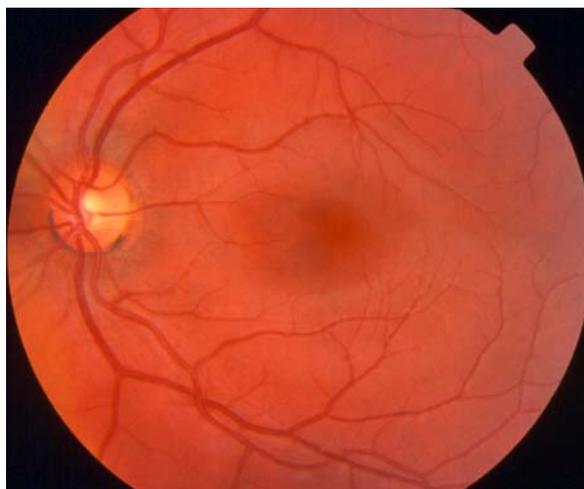
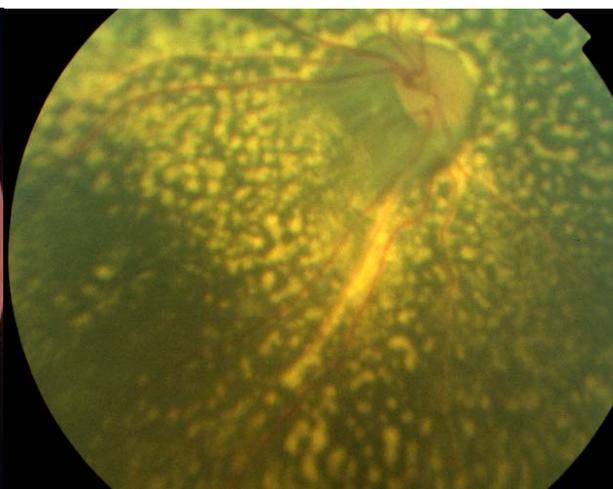


FIGURE 2. LIPID LEAKAGE IN IP



What Are The Systemic Abnormalities Of Incontinentia Pigmenti?

Most patients with IP have some of the following problems, but it is rare for a single patient to show all of these: mental retardation, seizures, abnormalities of the teeth, a variety of skin problems from pigmentary changes to blisters and roughened areas, abnormal skull shape, loss of hair, and heart defects. Figure 3 shows the small skull (microcephaly) and the scaly skin of the forehead, both of which can arise from this disease.

FIGURE 3.



Is There Any Treatment For The Eye Condition?

The most common treatment for the abnormal blood vessel growth in the retina is laser or cryo (freezing) treatment to destroy the area of the retina that has poor circulation. This usually causes the abnormal blood vessels to regress, although some cases progress to scar tissue growth and contraction with retinal detachment. In such advanced cases, vitreoretinal surgery to remove scar tissue and reattach the retina may be modestly helpful.

Genetic Testing

The position of the responsible abnormal gene for IP has been identified on the X chromosome. A goal of current research is to find a way to repair the

defective protein that is generated by the genetic mutation. This is likely to be difficult, and achieving this goal may take decades.

Final Comments

Because IP involves so many organ systems, families of affected patients need to consult with multiple physicians from different specialties. Good communication between all of the physicians involved and the patient and family is critical. Genetic counseling of affected females is also important so that the probabilities are understood that offspring may be affected.

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