Ophthalmologic Findings of Susac’s Syndrome

Autoimmune Endotheliopathy in the Retinal Vasculature

Patients with SS typically notice “dark spots” in one or both of their visual fields. This “dark spot” obstructs their vision in that particular portion of their visual field, so that they “can’t see anything” in that particular spot. Some patients describe this as a “black spot,” a “pink spot,” a “shadow,” or a sensation that a “curtain has been drawn” over a portion of their vision.

When a patient with SS is evaluated by an ophthalmologist, routine examinations may be normal—i.e., visual acuity is usually normal and routine retinal exam (with an ophthalmoscope) and retinal photos may look normal. This may be true, despite presence of retinal vasculopathy.

Routine retinal exam (and retinal photos) may, however, reveal “cotton wool spots,” which represent parts of the retina that have been ischemically injured, due to branch retinal artery occlusions (BRAO) that have blocked flow of blood (with its oxygen and nutrients) to that portion of the retina. (See Figure 2.)

Formal Visual field testing might reveal a visual field deficit, and fluorescein angiography (FA) might reveal Branch Retinal Artery Occlusion (BRAO) or fluorescein “staining” or “leakage,” even in patients who have no eye symptoms:

Before going further, let’s review how fluorescein angiography (FA) is performed. The procedure begins with a rapid intravenous injection of fluorescein “dye” into a peripheral vein. Immediately after injection, this “dye” flows throughout the body’s circulation, including the blood vessels in the retina. As soon as possible after injection of the “dye,” multiple sequential photographs are taken of the retina. In a normal FA study, the central retinal artery and all of its branches “light up” normally (look white) with this fluorescent “dye.” Specifically, the “dye” flows normally through the channel of each retinal blood vessel, and we are able to visualize each dye-filled channel.

In Figure 18, note how the dye (white in color) flows nicely through most of the vessels. However, the bottom yellow arrow points to a place along that particular arterial branch where the white dye suddenly stops...
flowing (due to obstruction). No dye is visible beyond that point, causing the rest of the vessel to look black beyond the point of obstruction. This is what is meant by branch retinal artery occlusion (BRAO).

*Figure 17* schematically depicts FA in a normal situation (top drawing) and in a patient with SS (bottom drawing). At the top of *Figure 17* is a normal tiny blood vessel (like a branch retinal artery, or even a capillary). The outside wall of the blood vessel is represented by the “basement membrane” of the vessel, shown in pink. The inner lining of the wall is represented by the endothelial lining cells (EC), shown in pale blue. Note that normally the EC are snug to one another, with “tight junctions.” The yellow fluorescein dye is shown freely and normally flowing through the open channel of the vessel (from right to left).

At the bottom of *Figure 17* is a branch retinal artery, the left half of which has become completely occluded (completely obstructed) due to extreme swelling of endothelial cells (EC). Along the right half of the vessel the endothelial cells have become moderately swollen and are only partially occluding the channel. (Note that the “tight junctions” between these moderately swollen EC have been pulled apart.) Along the left half of the vessel, the EC are so swollen that they have completely occluded the channel. It is this complete or partial occlusion of the vessel that results in the BRAO seen on FA (See *Figure 18*).

Go back to *Figure 18*, which depicts two obvious BRAOs. In both of those blood vessels the fluorescein dye travels only to a certain point, and then abruptly is not seen, for the reason depicted in the bottom of *Figure 17*.

When a patient with SS develops a BRAO, *Figure 2* reveals what ophthalmologists may see when they look at the retina with an ophthalmoscope, or otherwise take retinal photos. *Figure 2* reveals an area of the retina (the white-gray patch at the bottom) that has suffered from ischemic injury, due to lack of blood flow (and, therefore, lack of oxygen and nutrients) to that part of the retina. This finding (often called a “cotton wool” spot) is directly due to the BRAO in that location and represents ischemic injury to the retina. Some “cotton wool” spots can later resolve and no longer be visible.

*Figure 5* reveals a less appreciated, but very important finding in SS. In this actual patient with SS, there is very obvious “leakage” of fluorescein dye through the walls of three of the branch retinal arteries.

*Figure 10* shows another example of “leakage.”
Figures 19 and 20 explain what is happening in Figures 5 and 10.

In Figure 19 the top blood vessel is normal, with its normal sized endothelial cells that are snug together at their tight-junctions. In the bottom blood vessel, the endothelial cells (EC) are moderately swollen, their tight-junctions are spread apart, and the channel of the vessel in narrowed, but not occluded. The loss of tight-junctions allows dye to move between the EC and accumulate between the basement membrane and the EC. Accumulation of dye in this space is abnormal and is due to the loss of tight-junctions.

In Figure 20 we see the next step in severity of disease---“leakage,” shown in the bottom drawing. In this case, the dye has not only passed between the EC and into the space between the EC and the basement membrane, the dye has also “leaked” through the basement membrane (or wall of the blood vessel) into the surrounding space. This “leakage” is due to the combination of loss of tight-junctions and loss of integrity of the blood vessel wall.

Figure 21 shows an even more florid version of this “leakage.”

Whenever this “leakage” is seen, it is usually an indication of active disease. This “leakage” (particularly if mild) can be seen on FA even when the patient is asymptomatic and even when the patient has a normal appearance of the retina when viewed with an ophthalmoscope or other routine retinal photos. Therefore, “leakage” upon FA is one of the most sensitive ways to detect evidence of active disease---even in asymptomatic patients. Accordingly, frequent FA is a wise way to keep track of a patient’s status. It represents a “bio-marker” of disease activity.

Other retinal findings in SS “Silver streaks”

Figures 22 and 23 demonstrate typical “silver streaks,” or “sheathing.” These vessels look this way because their walls have become thickened and opacified, and this results in
greater reflection of light when viewed with an ophthalmoscope.

The thickening and opacification have occurred because of chronic “leakage,” with chronic long-standing accumulation of serous material between the endothelial cells and the basement membrane.

• Sometimes these deposits appear less plaque-like and more “pearl-like,” or like a “string of pearls.”
• Gass plaques are not, and should not be mistaken for emboli or for cholesterol deposits.
  - The retinal disease of SS does not involve emboli.
  - Furthermore, emboli are located at bifurcations of vessels, whereas Gass plaques are found away from sites of bifurcation.

"Silver streaks," “sheathing," “Gass plaques," and “pearls” all represent chronic changes—changes that gradually develop over a long time, due to past active disease. These changes, by themselves, do not indicate currently active disease.

All of the abnormalities shown in this section represent visual images of the “autoimmune endotheliopathy” occurring in the microvasculature of the retina. These depictions have focused on involvement of the branch retinal arteries, but the “autoimmune endotheliopathy” also occurs in the smaller branches of these branches—particularly in the capillaries out in the periphery of the retina. In fact, the main action of SS is out in the peripheral capillaries. This is important to realize, because routine ophthalmoscopic views of the retina, and even routine FA views do not extend very far into the periphery. Furthermore, being so small, the peripheral capillaries are more difficult to see and to interpret. Moreover, autoimmune endotheliopathy out in the periphery is much less likely to cause any symptoms, compared to disease in the more central and easily seen part of the retina. Peripheral capillary disease primarily causes gradual loss of peripheral vision, not loss of visual acuity.

These images help us to better understand and appreciate the fundamental role of “autoimmune endotheliopathy” in causing the symptoms and signs of SS.
The same “autoimmune endotheliopathy” that is going on in the retina can occur in the brain and in the inner ear.