Tuberous Sclerosis Alliance

EYE INVOLVEMENT IN TSC

Campbell (1905) first described the eye involvement in tuberous sclerosis complex (TSC). You will often see the terms ophthalmic or ocular involvement in the scientific and medical literature. These terms all refer to the eye. Van der Hoeve (1920) later discussed the eye involvement in individuals with TSC and gave significance to the retinal findings. The retina is the part of the eye that actually transmits what we see to the brain via the optic nerve. Retinal and optic nerve involvement in TSC are well known today, and approximately half of the individuals with TSC have some form of eye involvement.

Nonretinal and Retinal Eye Findings

Facial angiofibromas may involve the eyelids of individuals with TSC, but involvement of the outer portion of the eye is relatively uncommon. In a study at the Mayo Clinic, 13% (18/139) of the individuals with TSC had nonretinal findings. In this same group, 49% (68/139) of the individuals with TSC had hamartomas (non-cancerous tumors) of the retina or optic nerve. The most common type of retinal hamartoma is a lesion that is relatively flat, smooth-surfaced, salmon to salmon-gray in appearance, semitransparent, and circular or oval-shaped with indistinct boundaries. These were found in 57% (38/68) of the individuals with TSC with eye involvement. Either single or multiple hamartomas are usually located in the retina.

The second type of retinal or optic nerve hamartoma or tumor is the classic, relatively easily recognized, **elevated multinodular lesion** resembling grains of tapioca, salmon eggs or mulberries. The tumors are characterized by clusters of small granules, cysts or refractile glistening nodules. They are most commonly located near or at the disc margin in the retina, although they may be seen in the middle of the peripheral retina as well. This type of tumor was found in 50% (34/68) of the individuals with TSC in the Mayo Clinic study.

The third type of lesion, observed less frequently, is the **transitional or mixed tumor**. Only 12% (6/68) of the individuals with TSC in the Mayo Clinic group had tumors with characteristics similar to both of the other two types described above.

Another type of change noted was **retinal pigmentary disturbances**. In the Mayo Clinic series, 25% (18/68) of the individuals with TSC who had eye involvement had these findings. They were described as depigmented lesions of the retina that look like a “punched out” section of the retina. The significance of these lesions in not known, but they may mimic the depigented hypomelanotic macules (white or confetti spots) observed on the skin. These lesions may be suggestive of a diagnosis of TSC, but are not conclusive in and of themselves.

Vascular (blood vessel) changes in the retina and optic nerve usually accompany the hamartomas seen in these areas. Some of the hamartomas have many blood vessels (as are angiofibromas of the skin). Less than half of the individuals with TSC who have retinal involvement have bilateral (occurring in both eyes) findings.

Generally, the retinal lesions do not grow or change with age. Some feel these tumors are static, while others suggest that some of the hamartomas may in part become calcified, nodular and in part flat and transparent (mixed or transitional tumor described above). One individual had a relatively flat, semitransparent lesion that evolved into an elevated, nodular and calcified tumor over 20 years time, suggesting that some of the tumors may change with time. However, the clinical significance of this finding, or the frequency of its occurrence, is not known.

Visual Loss

Blindness in association with TSC is rare. Visual loss may be associated with retinal hamartomas, may evolve from retinal or optic nerve involvement, or from **intracranial (brain) tumors** that affect either the part of the brain that processes visual information, or that creates increased pressure in the brain and results in secondary injury to the optic nerve. One individual with TSC began having vision loss at age 7, and was practically blind at age 22, resulting from a large mulberry lesion on the retina, but this type of vision loss is uncommon with better follow-up screening. Visual decline can also accompany subependymal giant cell astrocytomas associated with the optic nerve. It is not known if there is continued visual loss in severely affected individuals with TSC since it is very difficult to determine the status of their vision. Clearly, studies that examine changes in vision over time in individuals with TSC are warranted.

Differential Diagnosis

Hamartomas of the retina in individuals with TSC are indistinguishable from those seen in individuals with neurofibromatosis. Although a retinal hamartoma may be the only recognizable manifestation of an individual suspected of having TSC, this diagnosis should be made with caution since the hamartoma may resemble other types of retinal tumors. The individual should be observed weekly if a retinoblastoma is suggested; the rapid growth of the tumor will be suggestive of a malignant tumor or retinoblastoma since hamartomas related to TSC are benign and do not grow rapidly.

Management

Since growth and change of the TSC lesions in the eye are rare, treatment is not indicated in most cases. The hamartoma should be followed in the rare event that they cause secondary effects and involvement of the retina. The recognition of a retinal hamartoma by an ophthalmologist (a medical doctor specializing in the care of the eyes) should prompt inquiries into the family history and TSC involvement. Also, ophthalmologists should remember that mental handicap is an over-emphasized symptom of TSC. More than 50% of the individuals with TSC have normal intelligence, and inasmuch as these individuals may become parents, genetic counseling should be given since TSC is a genetic disease that may be passed on to their children.

Facts About Eye Involvement in TSC

- Nearly 50% of individuals with TSC have eye involvement. This may be higher as many individuals with TSC do not receive a good eye exam that would reveal either hamartomas or depigmented areas of the retina.

- There are three types of hamartomas (tumors) observed on the retina in TSC: 1) smooth-surfaced hamartoma; 2) modular or "mulberry" hamartoma; and 3) transitional or mixed hamartoma that shows characteristics of both 1) and 2).

- Depigmented areas on the retina are seen in about 25% of the individuals with eye involvement in TSC. The significance of these findings is not known, but they may be important in the diagnosis of TSC in individuals with no other symptoms. These depigmented areas of the retina may have the same origin as those on the skin (hypopigmented macules), but this is not known at present.

- Less than 50% of the individuals with TSC with eye involvement have involvement of both eyes (bilateral). The other 50% show only eye involvement on one side.

- The retinal hamartomas are benign and usually do not change over time. Rare instances have documented tumors that change over time. It is possible that some of the hamartomas do change over time but go unrecognized since some individuals with TSC do not receive repeated eye exams where the change would be noted.

- Visual loss is not common with TSC, but some visual loss may accompany eye involvement with TSC.

- It is not known if there is increased incidence of eye involvement in individuals with TSC who are either mildly or severely affected with TSC. It is not possible to determine visual loss in a severely mentally handicapped individual where testing of vision may be difficult or impossible.

- Since growth and change of TSC lesions in the eye are rare, treatment is not warranted. What is not known is the value of eye involvement in the diagnosis of TSC where there are no other clear symptoms of the disease (e.g., in parents of children with TSC where the TSC appears to be a new mutation).

- Ophthalmologists should be able to recognize a retinal hamartoma or depigmented area and should inquire about the family's history and any possible involvement in TSC.