



Subependymal Giant Cell Tumours in Tuberous Sclerosis Complex

There are essentially three abnormalities that occur in the brain in people with Tuberous Sclerosis Complex (TSC).

1. Tubers
2. Subependymal nodules (SENs)
3. Subependymal giant cell tumours* (SGCTs)

* SGCTs are sometimes called subependymal giant cell astrocytomas (SEGAs).

All three brain abnormalities are thought to have a common origin. We believe that they are abnormalities in the development of the brain during the embryonic period. Normally, cells that form the outer part of the brain (the cortex) start deep within the brain (in the periventricular area) as primitive parent cells and migrate outwards. The abnormalities found in TSC relate to this migration.

Tubers occur in the brain substance itself along the embryonic migration path of the primitive cells.

Subependymal giant cell tumours (SGCTs) and Subependymal nodules (SENs) are found around the lining of the ventricles (cavities in the brain containing cerebrospinal fluid (CSF)). They are thought to arise from abnormal growth of the primitive cells of the brain before they even migrate outwards. SENs and SGCTs are the same when examined under the microscope but are very different in the way they behave. In order to understand SGCTs it is important to understand SENs also.

SENs

- These are small lesions found in the lining of the ventricles
- They can occur anywhere in the ventricles and do not cause hydrocephalus (an accumulation of CSF leading to raised intracranial pressure).
- They are seen at any age.

- They occur in 92-100% of people with TSC.
- They are calcified and are therefore seen easily on CT scans.
- They do not enhance with contrast either with CT or MRI.
- They do not grow and are not therefore considered to be tumours.

NB A lesion that grows or causes hydrocephalus is an SGCT

- SGCTs
- These are usually slow growing tumours that are found in the ventricles.
- They are also called subependymal giant cell astrocytomas (SEGAs). This is controversial as they don't exclusively contain astrocytic cells - they are mixed.
- They are mainly found at the foramen of Munro (an opening between the ventricles through which CSF flows) and can cause hydrocephalus.
- They are found mainly in children.
- They occur in around 10% of children with TSC and comprise 1.4% of all brain tumours in children. There have been rare reports of SGCTs occurring in people without TSC.
- It is unclear whether they arise from SENs though most experts feel that they probably do.
- They are benign tumours in almost all cases. There have been single reports of a malignant SGCT and an SGCT that has spread to the spine.
- SGCTs are not calcified and enhance with contrast. They are best seen with MRI.

	SENs	SGCTs
Size	<10 mm	>10 mm
Growth	None	All grow
Site	Anywhere in ventricles	Near foramen of Munro
Obstruction	No obstruction Do not cause hydrocephalus	Often obstruct the foramen of Munro and cause hydrocephalus
CT	Best seen on CT because of calcification	Enhances with contrast
MRI	1/3 missed on MRI	Best seen on MRI and enhance
Surgery	Never need surgery	If causing hydrocephalus or growing

Table: The main differences between SGCTs and SENs

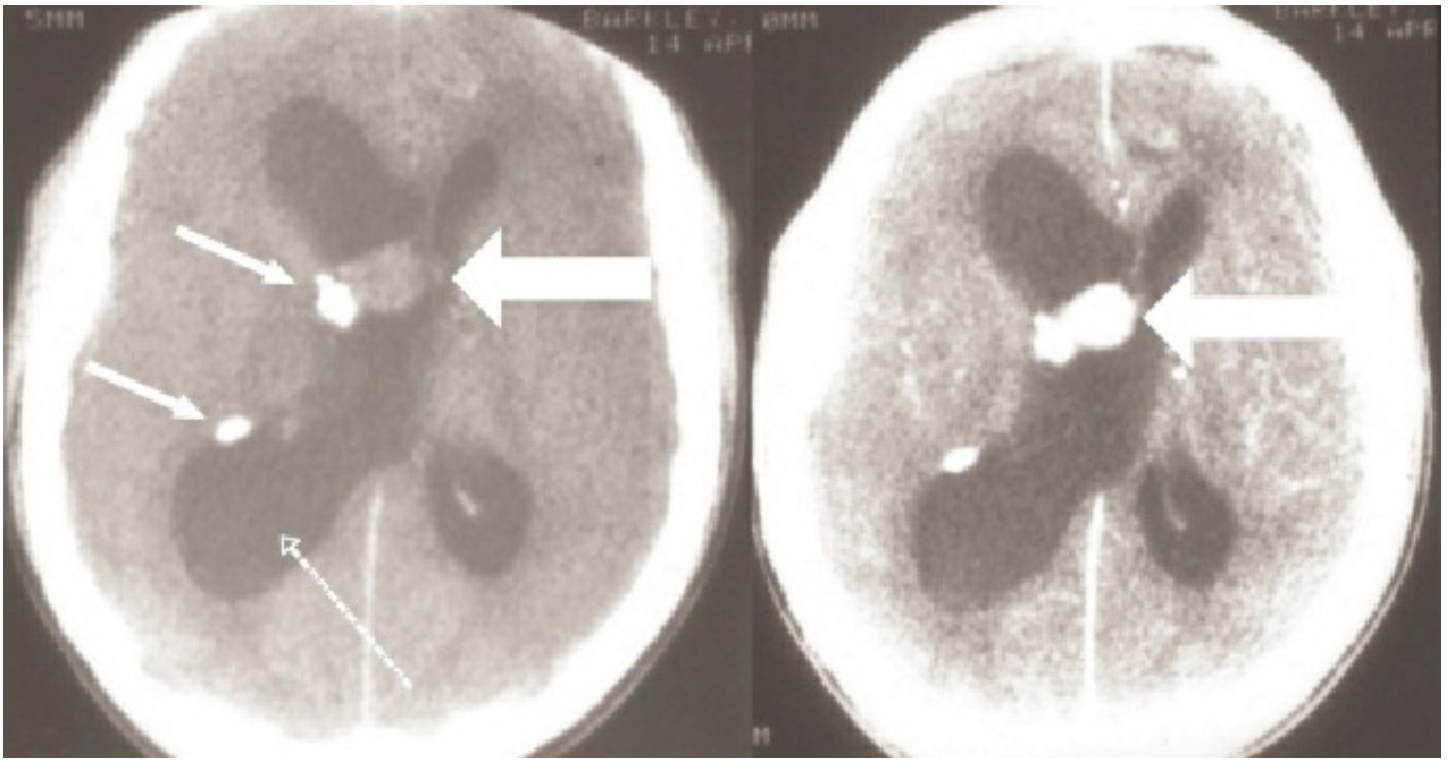


Figure 1: Pre- and post-contrast axial CT scan showing SGCT enhancing (large arrow in both pictures). This is causing hydrocephalus on one side (dashed arrow). SENs are also seen in the right ventricle (thin arrows). These are calcified.. The options here would be to excise the SGCT or to insert a ventriculoperitoneal shunt on the right side.

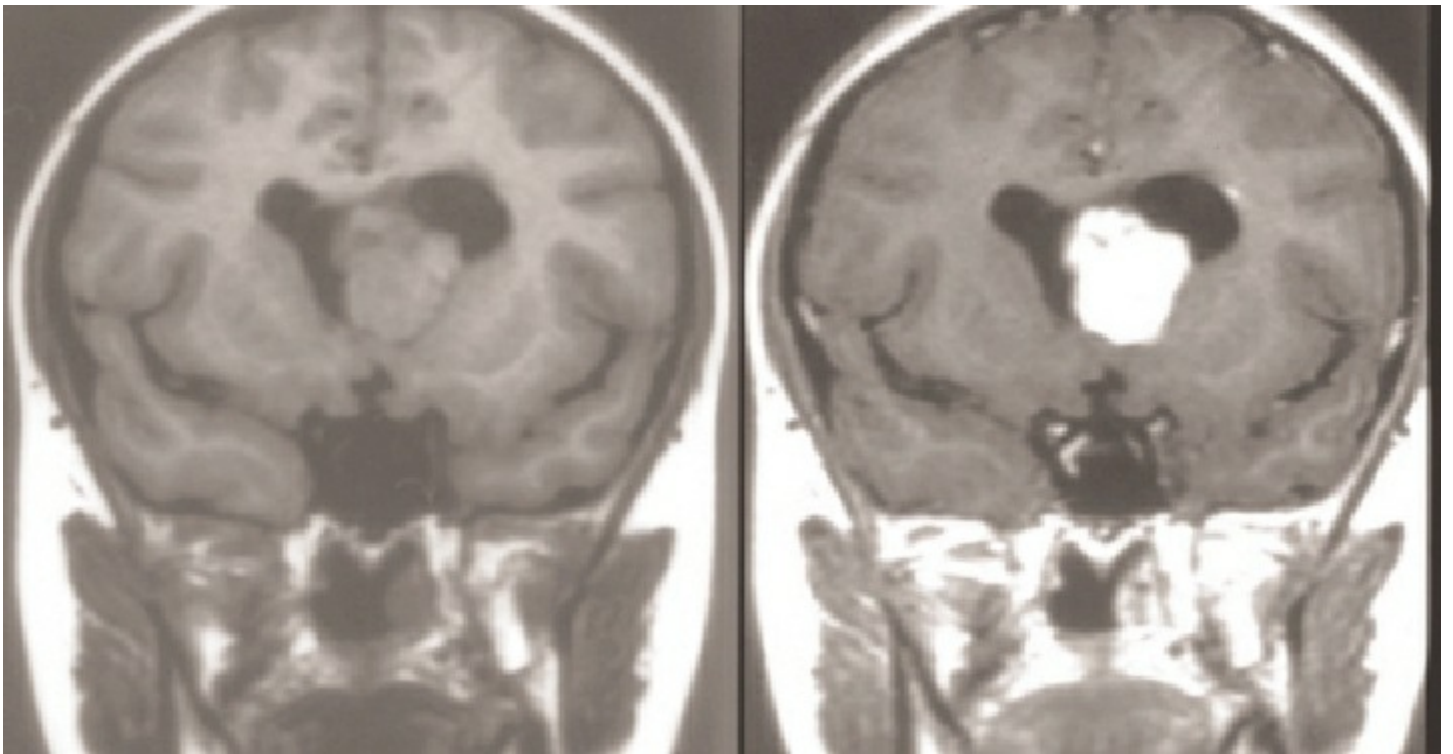


Figure 2: Pre and post-contrast coronal MRI showing an SGCT enhancing brightly. This is the same patient as above.

Clinical features of SGCTs

SGCTs can remain asymptomatic but those that grow can cause obstruction of the foramina of Munro and cause hydrocephalus. This will cause headaches, vomiting, drowsiness and papilloedema (swelling at the back of the eye indicative of raised intracranial pressure). Hydrocephalus can sometimes be less obvious and cause generalised delay in development or increased frequency of seizures. Occasionally an SGCT can cause specific deficits such as weakness or visual disturbance because of pressure on adjacent structures in the brain.

Surgery for SGCTs

SGCTs can be removed surgically. Not all need to be removed however, and the indications for surgery are

1. Evidence of raised intracranial pressure (symptoms, papilloedema or hydrocephalus on imaging)

2. New focal deficit attributable to the tumour

3. Increase in tumour size on serial imaging of the brain

In those who have hydrocephalus, it is best treated by complete removal of the tumour. Completely removed tumours will not recur. Partially removed tumours tend to recur and the hydrocephalus will persist and may need other treatments.

The main risk of surgery is paralysis (weakness of one side of the body usually opposite to the SGCT). This unfortunately occurs in about 1 in 5 cases. The majority of children who undergo surgery, suffer no permanent deficits and can be discharged from hospital within a week of the operation. They will usually have an MRI scan afterwards to ensure complete removal of the SGCT has been achieved.



Figure 3: Ventriculoperitoneal shunt taking CSF from the ventricles of the brain to the abdomen and ventriculoatrial shunt taking CSF from the ventricles to the heart (less commonly used nowadays)

About 1 in 12 children who have hydrocephalus secondary to an SGCT will need a ventriculoperitoneal shunt even if the tumour is completely removed. More than that will need a shunt if removal is incomplete or where surgery is not possible. This is an artificial tube that drains fluid (CSF) from the ventricles down to the abdomen. Though shunts treat hydrocephalus well and relieve the raised pressure associated with it, they are prone to failure. About 30% of shunts need to be revised within a year of their insertion due to blockage, infection, underdrainage or overdrainage. The symptoms of shunt malfunction are essentially the same as the symptoms of the initial hydrocephalus.

Screening for SGCTs

In the USA National Institute of Health guidelines (Hyman 2000) suggest that patients should be screened every 1 to 3 years up to the age of 21. In the UK Clinical Guidelines for the care of patients with TSC recommend screening when symptoms of hydrocephalus show. Screening is by cranial CT or MRI. Once a tumour is seen to be growing, management must be more aggressive (either more frequent screening or surgery). Children who have SGCTs removed before symptoms develop (ie because of growth on screening) do better than those who already have symptoms.

Other treatments

Radiotherapy is of no benefit in treatment of SGCTs. They do not respond to it. In fact, theoretically there is an increased risk of secondary malignancy if radiotherapy is given. There are no chemotherapy regimes known to affect SGCTs. Recently, however, evidence has come to light that Sirolimus (Rapamycin) (an immunosuppressive drug that is already commercially available for transplant patients) can cause regression of growing SGCTs. None disappeared completely and they regrow when treatment is stopped. For this reason and the fact that it has potentially serious sideeffects and may interact with anti-epileptic drugs, it is not recommended for treatment of SGCTs at present. More studies are underway in the USA.

Prognosis of SGCTs as tumours

The prognosis of SGCTs is excellent. There is low mortality associated with them even with radical surgery and eighty percent of children do well in the long term. The main concern is to monitor them clinically and radiologically when they are discovered and to remove them if they are growing or causing symptoms.

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Further information on TSC and the work of the Tuberous Sclerosis Association can be obtained from our website at: www.tuberous-sclerosis.org

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