



# Tuberous sclerosis complex: multisystem hamartomas

Negar Naderi, Irina Timofte, Michael T McCurdy, Robert M Reed

Division of Pulmonary and Critical Care Medicine, University of Maryland, Baltimore, Maryland, USA

**Correspondence to**  
Dr Robert Michael Reed,  
rreed@medicine.umaryland.edu

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## DESCRIPTION

Tuberous sclerosis complex (TSC) is an autosomal dominant genetic disorder resulting in the growth of benign tumours or hamartomas affecting any organ system. Up to 90% of patients present with seizures due to growth of benign tumours in the brain.<sup>1</sup> Although significant morbidity is associated with cardiac, renal and pulmonary involvement, the neurological aspects and particularly seizures associated with tuberous sclerosis are extremely difficult to treat.<sup>1</sup> The hallmark cutaneous manifestations include ash-leaf spots (figure 1), angiofibromas, ungual fibromas, subungual red comets and splinter haemorrhages (figure 2). Up to 80% of patients also have renal tumours known as angiomyolipomas (figure 3) which can result in spontaneous aneurysmal bleeds and haemorrhagic shock due to formation of abnormal vasculature.<sup>1 2</sup>



**Figure 1** Angiomyolipoma: cortical kidney tumours composed of abnormal vascular formations, smooth muscle and fat (hypodense on CT imaging).



**Figure 2** Hypopigmented, diamond-shaped macules known as ash-leaf spots, along with angiofibromas are cutaneous manifestation of tuberous sclerosis.



**Figure 3** Splinter haemorrhages, periungual and subungual fibromas occur generally in adolescence or adulthood and are more common on the toes than the fingers.

TSC is caused by mutations in either the *TSC1* or *TSC2* genes. *TSC1* and *TSC2* form a complex responsible for the regulation of the mammalian target of rapamycin complex 1 (mTORC1).<sup>1</sup> Drugs that inhibit mTORC1, such as sirolimus and everolimus, have demonstrated efficacy for the treatment of multiple aspects of TSC, including renal angiomyolipomata, refractory epilepsy associated with brain tumours, and lymphangioleiomyomatosis.<sup>2</sup>

## Learning points

- ▶ Tuberous sclerosis complex (TSC) is an autosomal dominant disorder with an incidence of 1:6000 births.
- ▶ TSC is caused by mutations in the *TSC1* or *TSC2* genes needed for the normal expression of the mammalian target of rapamycin (mTOR) pathway.<sup>1 2</sup>
- ▶ TSC results in the growth of benign tumours (hamartomas) affecting any organ in the body; brain and cognitive abnormalities are the most common manifestations of the disease and most patients present with epileptic seizures during infancy.<sup>1</sup>
- ▶ Surgical resection is the standard treatment for those with neural lesions and refractory epilepsy; however, everolimus (an mTOR inhibitor) has shown promise in the treatment of those not amenable to surgical resection or those with renal involvement of the disease.<sup>2</sup>



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