Tuberous sclerosis
Anaesthetic considerations

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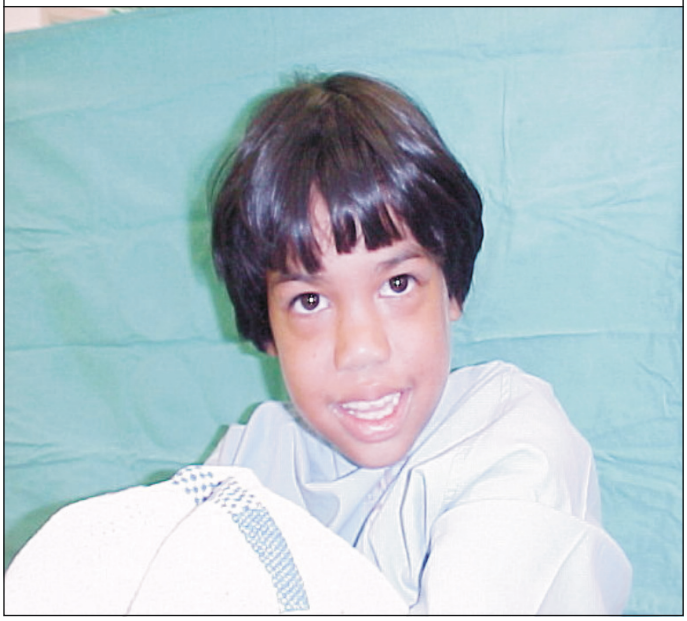
Synopsis of patient

An eight year old female, weighing 28kg (Fig 1), presents for removal of a large 10 by 10cm mass on her left flank, extending towards her left scapula. She is mentally handicapped with a mild left hemiplegia. She has small adenoma sebaceum in the malar region, a number of hypo-pigmented skin lesions over her arms and body, and an area of roughened skin on her lower back. Previous investigations demonstrated calcified subependymal nodules at the Foramen of Munro; a right parietal cortical tuber; fibrodysplasia of the 6th rib on the left; rhabdomyomas in the right atrium, and left and right ventricle, in addition to multiple bilateral renal angiomyolipomas. An electrocardiogram shows regular ventricular extrasystoles for which she is on no treatment. There are no signs of raised intracranial pressure and no focal pulmonary lesions. She is on anticonvulsive therapy but her seizure activity is not well controlled. Family history is negative. She has been diagnosed as having tuberous sclerosis.

Figure 1: The patient - an eight year old female with tuberous sclerosis



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Tuberous sclerosis

Tuberous sclerosis(TS) was first described by Bourneville in 1880.[1] TS is said to be one of the commonest autosomal dominant diseases. Epidemiological studies report an incidence ranging between1:10000 to 1:170000.[2,3] Two gene loci have been identified on chromosone 9q34 (TSC1) and 16p13.3 (TSC2) and they occur in all racial groups. New mutations are common but since gene expression is variable the clinical manifestations may vary widely from the obvious to the subtle.[2,4-5] No single feature is invariably present but the disease progresses with age making the clinical manifestations more obvious in adults. The classic triad of mental retardation, seizures and adenoma sebaceum or fibroangiomas[5] is present in only 30% of cases and about 6% have none of the triad.[2]

These children, or adults for that matter, may present for a variety of surgical procedures as a result of the uncontrolled widespread proliferation of hamartomas throughout the body.[2,3] From the anaesthesiologists point of view there are a number of potential pitfalls into which the unwary may fall. Some of these could be life threatening.

Communication with the patient may be difficult since mental retardation is common (about 60% of cases).[2] Hyperactivity or autistic behaviour may compound this problem. Most patients (80-90%) have seizures but seizure activity is often difficult to control.[2] "Salaam seizures", a particular type of infantile spasm, are also common. Visual impairment may further challenge the anaesthesiologist with respect to communication with the patient. This visual impairment may be caused by retinal astrocytomas or choroid hamartomas which may be present or may have been surgically removed.

Tuberous sclerosis is one of the congenital neurocutaneous disorders or phakomatoses. Others include Sturge-Weber syndrome, von Reckling-hausen's disease and von Hippel-Landau's disease. The phakomas are associated with a wide variety of endocrinopathies including phaeochromocytoma. The cutaneous manifestations of TS are typical and are seen in more than 50% of affected individuals. These include hypopigmented elliptical or lenticular-shaped (ash leaf) macules anywhere on the body but usually on the torso (Fig 2). Areas of roughened skin - "shagreen patches"- are typically seen over the lower trunk (Fig 3). The fibroangiomas in the malar region secondarily involve the sebaceous glands - the "adenoma sebaceum," (Fig 4) often referred to, is not a true adenoma.[3,8] A variety of other skin tumours may be seen but periungual fibromas around the fingertips are

Figure 2: A typical elliptical and lenticular hypopigmented macule resembling an "ash leaf" on her forearm (tertiary feature).

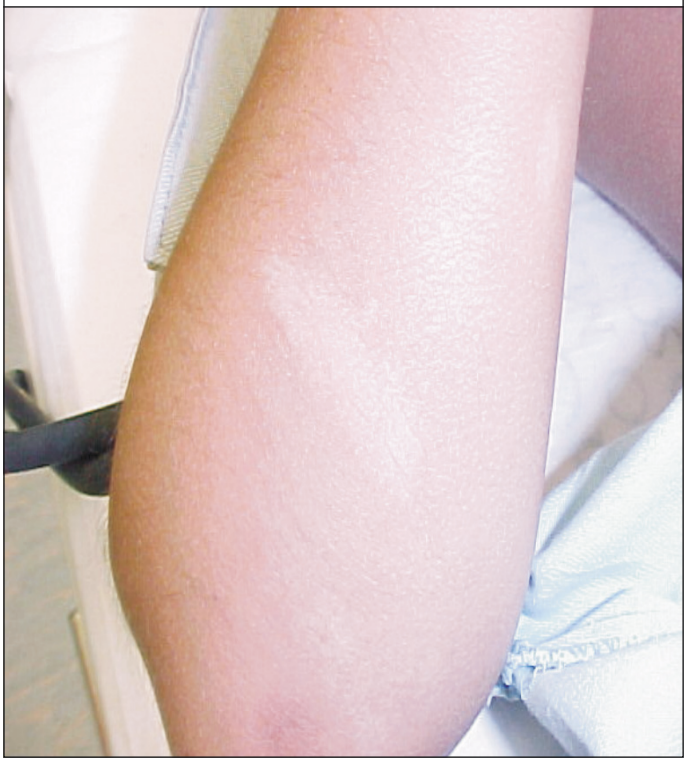


Figure 3: A "shagreen patch" of roughened skin on her lower back (secondary feature)

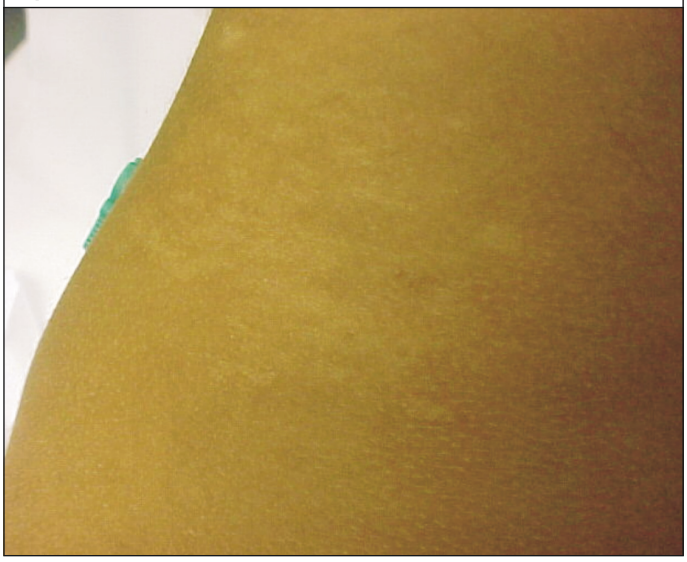
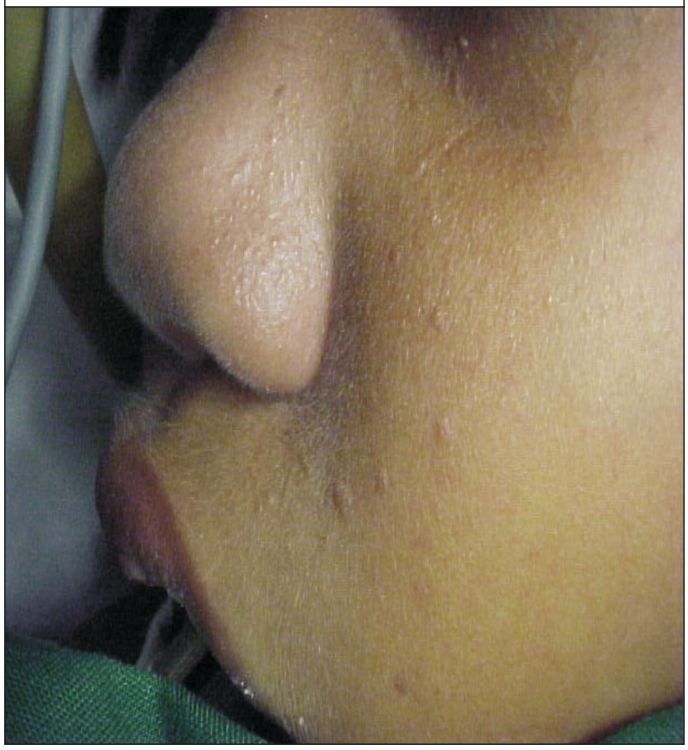


Figure 4: A close up of "adenoma sebaceum" in the malar region close to the alar nasi (primary feature).



pathognemonic of this disease.[5]

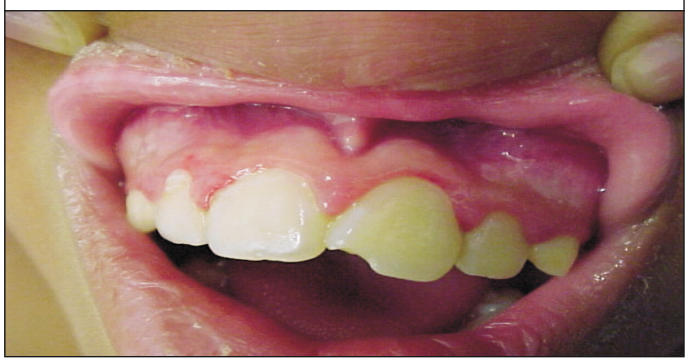
Cardiovascular manifestations, seen in more than 50% of affected individuals, can have major anaesthetic implications. Cardiac rhabdomyomas are almost pathognemonic of the disease[4,6,7] are usually asymptomatic but should be suspected in patients with arrhythmias or a localised loss of electrical activity.[2,3] The rhabdomyomas may be single or multiple and may occur in any chamber. These tumours may cause sudden obstruction to blood flow or behave like a valvular stenosis[6], in addition arrhythmias[6,7] and or heart block.[7] Abdominal aortic aneurysms have been reported[7] as well as narrowing of major arteries.[2,3,8] Hypertension may occur secondary to renal tumor or renal arterial stenosis.[4,8] A baseline cardiac evaluation is therefore essential part of the preoperative workup even in asymptomatic patients.

Pulmonary involvement is rare (<1%)[2] and tends to occur in females in the third or fourth decade. However hamartomatous growths may involve the lungs or pleura and there have been a number of reports of spontaneous pneumothorax in patients with undiagnosed pulmonary manifestations of the disease. A preoperative chest Xray is therefore indicated to exclude silent pulmonary or mediastinal masses and ventilatory pressures should be kept low.[3]

Endotracheal intubation may be a further challenge. Oropharyngeal or laryngeal tumours, fibromata and papillomata, (11% patients)[2] may obscure the view of the larynx. The presence of pitting of the teeth enamel should be noted preoperatively. (Fig 5) otherwise they could be mistakenly considered to be due to intubation trauma.

Neurological lesions are common (>50%) and are also considered pathognemonic.[2,5] These include single or multiple cerebral tubers (from whence the term tuberous is derived); astrocytomas and multiple subependymal periventricular nodules. These nodules may calcify or cause hydrocephalus by obstructing the circulation of cerebrospinal fluid. Astrocytomas may cause focal

Figure 5: Enamel pit on the left incisor (tertiary feature).



neurological deficits, raised intracranial pressure, behavioural changes or loss of seizure control. Sacro-coccygeal chordomas should be sought prior to placing a caudal or sacro-intervertebral block.

These patients may undergo surgery for a variety of gastrointestinal or renal tumours.[2,3] These hamartomatous tumours may occur at any level of the gastrointestinal tract including the mouth, oesophagus, stomach, pancreas, liver or intestines.[4] They have an insidious onset and may be asymptomatic for many years. They may cause delayed gastric emptying or intestinal obstruction.[2-4]

Renal angiomyolipomas and cysts[2,9] are characteristic of the disease and are present in 50-80% of affected individuals.[2] They may be asymptomatic initially but may even progress to renal failure. The angiolipomatous process may also involve the adrenals. These tumours are highly vascular and spontaneous haemorrhage into these lesions may occur.[2,3]

Tuberous sclerosis, is a disease which affects many organ systems. These patients may present for surgery at any age on the operating lists involving almost every surgical discipline. A cursory preoperative examination may only reveal the tip of the iceberg. What lies beneath may catch the unsuspecting anaesthesiologist by surprise.[2,9] A potentially fatal outcome may be the result.

Table 1: Diagnostic criteria for tuberous sclerosis (TS). Definite TS = either one primary, two secondary or one secondary plus two tertiary; probable TS = either one secondary plus one tertiary; or three tertiary; suspect TS = either one secondary or two tertiary features.[5]

Primary features	Secondary features	Tertiary features
Facial angiofibromas	Affected first degree relative	Hypomelanotic macules
Multiple ungual fibromas	Cardiac rhabdomyoma	"Confetti" skin lesions
Cortical tubers *	Other retinal hamartoma	Renal cysts #
Subependymal nodule*#	Cerebral tuber #	Pits in teeth enamel
Giant cell astrocytoma *	Non-calc subependymal	Rectal polyp-hamartoma
Retinal astrocytomas	Shagreen patch	Bone cysts
	Forehead plaque	Gingival fibromas
	Pulm lymphangiomyoma *	Pulm lymphangiomyoma #
	Renal angiomyolipoma	Hamartoma of other organs
	Renal cysts *	Cerebral heterotopias
		Infantile spasms

* = histological diagnosis # = radiological diagnosis

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