

Anaesthesia and Rubinstein-Taybi syndrome

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Synopsis of patients

Case 1: An 11 month old boy was admitted for probing and syringing of the lacrimal ducts. He had presented with history of recurrent infections of the right eye and a mucocoele of right lacrimal sac. On examination, the patient was noted to have micrognathia, heavy eyebrows, blepharophimosis, an epicanthus, broad thumbs and clinodactyly. There was no obvious micrognathia or microstomia but he was noted to have a high arched palate. His milestones were delayed - he was not yet crawling or walking. Dentition was also delayed - he had no deciduous teeth. Clinical evaluation of the cardiovascular and respiratory systems and of the abdomen was unremarkable. Anaesthesia was induced with nitrous oxide, oxygen and halothane, and was maintained with nitrous oxide, oxygen and isoflurane. At laryngoscopy, a very high arched palate was confirmed and only the epiglottis was visible. Intubation was achieved with some difficulty using posterior displacement of the larynx and a Miller size 0 laryngoscope blade. There was no evidence of laryngomalacia although this was difficult to assess. Lacrimal duct stenosis was confirmed and probe dilated. Intraoperatively the child remained haemodynamically stable and recovery from anaesthesia was uneventful.

Case 2: A 14month old boy with features of Rubinstein-Taybi syndrome (Fig 1-3) presented with recurrent chest infections. His milestones were delayed; he was somewhat hypotonic and had a strabismus involving the left eye. A series of investigations including a milk scan, and pH studies revealed significant oesophageal reflux. Following a further course of antibiotics and physiotherapy, he was presented for a Nissen fundoplication anti-reflux procedure. The open surgical procedure was performed under a combined general

anaesthetic with halothane and a thoracic epidural (T10-11), without muscle relaxants. Laryngoscopy was made difficult by the high arched palate and relative micrognathia. The larynx was normal. Recovery from anaesthesia was unremarkable. Postoperative analgesia was provided by continuous epidural infusion which was terminated after 48 hours.

Introduction

Jack Rubinstein (US paediatrician) and Hooshang Taybi (US radiologist) first described a malformation syndrome characterized by distinctive facial features, mental retardation, and a broad thumb and hallux in 1963. Since then many cases have been reported with a significant variation in the clinical presentation.^{1,2} The prevalence in the general population is unknown, but is thought to be in the order of 1:125000 births. The prevalence amongst institutionalised patients with mental retardation is about 1:600.³ It is alternatively known as the "Broad Thumb and Hallux" syndrome.

Aetiology

The gene defect of Rubinstein-Taybi syndrome has recently been clarified. It was previously thought to be X-linked with heterozygous females being more mildly affected.⁴ An autosomal dominant mutation is now believed to be the most probable cause, but it is considered a genetically heterogeneous disorder with up to 18 different chromosomal anomalies identified in patients with this syndrome.³

Most individuals with Rubinstein-Taybi syndrome (56%) have been shown to have molecular mutations or microdeletions of chromosome 16p13.3 and the EP300 gene. This region encodes the gene for the human cAMP response element binding protein (CREBBP).

CREB-binding protein is a transcriptional coactivator in cyclic adenosine monophosphate mediated intracellular protein synthesis and as such is an important regulatory of cell growth and division. CREBBP is also a critical coactivator for thyroid hormone receptors. It is essential therefore for normal foetal development, central nervous system development and

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possibly memory.

Affected individuals have an increased risk of developing malignancies, mainly central nervous (oligodendroglioma, medulloblastoma, neuroblastoma, meningioma) but also haematological (leukaemia and lymphoma).

Clinical presentation

Both our patients showed many of the typical facial features of Rubinstein-Taybi syndrome. (Figs.1-3). These included a prominent forehead and apparent hypertelorism because of the broad nasal bridge. Their eyebrows were arched and thick for their age. They had blepharophimosis and epicanthic folds with downward slanting palpebral fissures, and mild ptosis. No iris colobomata were noted in either case. Nasolacrimal duct stenosis is typical and a frequent finding.

Figure 1: Typical facial features of Rubinstein-Taybi syndrome - prominent forehead, hypertelorism, downslanting palpebral fissure, epicanthic folds, strabismus, mild ptosis, broad nasal bridge and pouting lower lip. His mother does not demonstrate any of these features.



Figure 2: Rubinstein-Taybi syndrome in profile. A beaked nose, low set ears and relative micrognathia are featured.



Both had a beaked nose to a varying degree, a pouting lower lip, a high arched palate and mild micrognathia. Their thumbs and big toes were typically broad and one deviated medially. (Fig 3) Their milestones were delayed but in view of their age it was difficult to assess their mental function. Neither mother thought that their child was retarded.

Other facial features typical of Rubinstein-Taybi syndrome include microcephaly with delayed closure of the anterior fontanelle. The hypoplastic maxilla, microstomia, micrognathia and low set or malformed external ears suggest a first and second branchial arch abnormality. Choanal atresia or a deviated nasal septum has been described. These features may compound the obstructive sleep apnoea commonly associated with a high arched palate and hypoplastic maxilla, typical of Rubinstein-Taybi syndrome.

Feeding difficulties are common in infancy and, together with the genetically based growth retardation, often result in a clinical picture of failure to thrive. Approximately one third have a congenital cardiac defect (ASD, VSD, PDA, coarctation of the aorta or bicuspid aortic valve), although neither of our patients had a cardiac defect. Respiratory infections and complications from congenital heart disease are major causes of morbidity and mortality in the first years of life. Gastro-oesophageal reflux is common and may contribute further towards the recurrent respiratory infections.⁴ Moderate to severe mental retardation is typical. Speech is delayed and hypotonia may contribute to the delay in motor milestones. Agenesis of the corpus callosum and a large foramen magnum has been described.

Generally, affected children are short in stature.

Figure 3: The typical broad thumb and clinodactyly associated with Rubinstein-Taybi syndrome.



Skeletal abnormalities include a slipped femoral epiphysis, pes planus (flat feet), patella dislocation, spina bifida occulta, pectus excavatum, scoliosis and cervical kyphosis. Typical radiographic findings include flaring of the iliac bones and retarded bone maturation.

Males may present for hypospadias repair or correction of undescended testes. Apart from cryptorchidism and hypospadias, they may have a shawl scrotum. Both our patients demonstrated these features.

Anaesthesia Considerations: Patients with Rubinstein Taybi syndrome may require surgery for a variety of reasons. These include the correction of craniofacial, orthopaedic, orthodontic, ophthalmic or cardiac lesions apart from incidental surgical conditions.

The craniofacial abnormalities may make laryngoscopy and intubation difficult particularly in the presence of micrognathia or microsomia.^{4,5} The craniofacial anomalies may also contribute to, or aggravate, obstructive sleep apnoea. Oesophageal reflux compounds these respiratory problems Laryngomalacia⁶ or laryngeal stenosis⁷, described in a recent case report, but not seen in either of our patients, may cause further difficulty.

Sedative agents should be avoided in these patients and opiate analgesia used with caution to avoid the risk of apnoea.

An anecdotal report on the occurrence of arrhythmias following the use of suxamethonium suggests that suxamethonium is best avoided.⁸ Other muscle relaxants have been used but intubation without the use of muscle relaxants is probably the safest option, particularly when hypotonia is present.

Several reports have described uncomplicated recovery after using an intravenous induction and maintenance with inhalational anaesthesia.^{4,5,9} There is no evidence to support the suggestion that recovery from

anaesthesia is delayed in these patients.¹⁰ Our patients both recovered uneventfully.

Antibiotic prophylaxis, appropriate for the planned surgery, should be given to those with an underlying cardiac lesion.

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