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CASE REPORT

Treacher Collins syndrome: a case report

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Abstract

Treacher Collins syndrome is an inherited and rare, autosomal dominant condition that presents several craniofacial deformities at different levels. The disorder is characterised by abnormalities of the auricular pinna, hypoplasia of facial bones, antimongoloid slanting palpebral fissures with coloboma of the lower eyelids and cleft palate. This condition affects an estimated 1 in 50,000 people. Upper airway obstruction and difficult tracheal intubation are often encountered in patients with this syndrome. Neonates and small infants with craniofacial abnormalities may represent great challenges regarding the management of the airway. We present a 40-day-old baby girl with Treacher Collins syndrome. The infant was seen in our hospital for sudden-onset respiratory distress that progressed rapidly to respiratory failure. Chest X-ray was consistent with pneumonia. The patient developed worsening respiratory distress and was transferred to the intensive care unit and mechanically ventilated. She proved difficult to intubate and difficult to wean. Tracheostomy and gastrostomy were necessary in the management of this patient. We discuss the importance of a multidisciplinary planned approach in the management of this rare syndrome.

Introduction

Treacher Collins syndrome, otherwise known as mandibulofacial dysostosis, is a congenital disorder of craniofacial development,[1] mainly characterised by maxillary, zygomatic and mandibular hypoplasia, a high arched palate and temporomandibular joint abnormalities. Patients with this syndrome are particularly difficult or even impossible to mask, ventilate or intubate.[2]

Treacher Collins syndrome can present one of the most difficult airway management problems encountered by an anaesthesiologist, because children with this condition can have many craniofacial abnormalities and they often require a variety of corrective surgical procedures, thus confronting the anaesthesiologist with a possibly difficult intubation.[3]

Treacher Collins syndrome is well known to present difficulties in intubation, and many techniques aiming at successful airway management have been reported, such as intubation under fibre-optic bronchoscopy, the use of a laryngeal mask airway, fibre-optic intubation through a laryngeal mask airway, and even tracheostomy as a last resort.[4]

The care of individuals affected by Treacher Collins syndrome requires a multidisciplinary approach and may involve intervention from a number of healthcare professionals both preoperatively and postoperatively.[5,6]

We describe the case of a 40-day-old baby girl with Treacher Collins syndrome. By presenting this case, we intend to show that in small infants with this syndrome, in whom difficulties in ventilation and intubation are expected, thoughtful airway management planning is very important. A multidisciplinary team should be formed to coordinate the available expertise to manage these complex situations. An appropriate algorithm of airway management should be clearly envisaged.

Case report

A 40-day-old baby girl, weight 2 kg, was seen in our emergency room with a three-day history of sudden-onset shortness of breath, poor feeding and lethargy. In the previous 12 hours, she had developed respiratory distress and cyanosis. Her mother denied having a history of fever or chills. The infant was started on antibiotic therapy without any improvement.

History

The baby was born vaginally at full term; weight at birth was 2 kg and there was no delay in crying. This patient was the youngest of the three children born to parents with no family history of any syndrome. She had two normal siblings. Her parent's marriage was not consanguineous; there was no history of exposure to known teratogenic agents or of maternal diseases. The mother also had no history of alcohol, smoking and drug abuse. The baby was having difficulty in feeding and not gaining weight. She developed pneumonia at the age of 6 days and aspirated several times.

Physical examination

On her arrival to the emergency room, the infant looked ill, with a temperature of 38.5°C, a respiratory rate of 55 breaths/min, and a pulse rate of 150 beats/min. The blood pressure was 85/60 mmHg and the oxygen saturation was 78% by pulse oximetry while breathing room air. Examination of her chest revealed crackles at both lungs, cardiac examination was normal.

The infant had a characteristic appearance with antimongoloid slanting of the palpebral fissures, bilateral coloboma of the lower eyelids with absence of cilia of the lower eyelids, hypertelorism of the eyes, proptosis, normal-sized pupils with a normal reaction to light, malar hypoplasia of the zygomatic arch with a 'sunk-in' appearance, sad facial expression, a 'bird-like' face with trigonocephaly, mandibular hypoplasia, micrognathia, retrognathia, low-set ears, malformations of the auricular pinna, atresia of the auditory meatus, microcephaly, 'beak-like' nose, macrostomia 'fishlike mouth' and thin hair *(figures 1 and 2)*.

Intraoral examination revealed a high arched cleft palate without cleft lip *(figure 3)*.

A detailed examination of this patient revealed clinical features of mandibulofacial dysostosis, bilaterally symmetrical but abnormal face characteristics. Computed tomography showed bilateral choanal obstruction and bilateral atresia of the external auditory canals. Echocardiograph and abdominal ultrasound revealed normal findings.

Based on the phenotypic and radiographic findings, the diagnosis of Treacher Collins syndrome was made.

Hospital course

During the first day, the patient's condition deteriorated, her

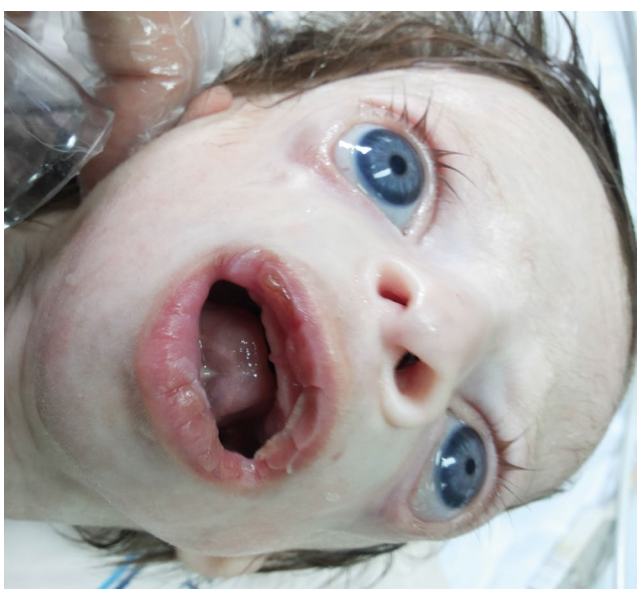
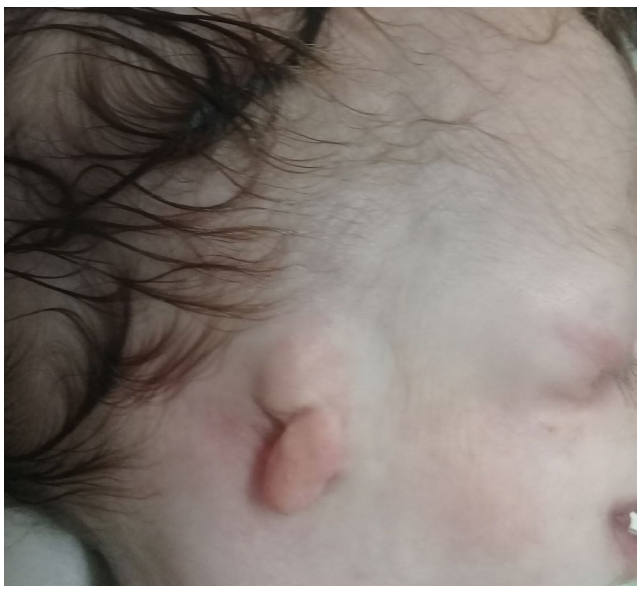


Figure 1. The clinical view of the 40-day-old baby girl with Treacher Collins syndrome. Consent of the patients family was obtained for the publication of these images.



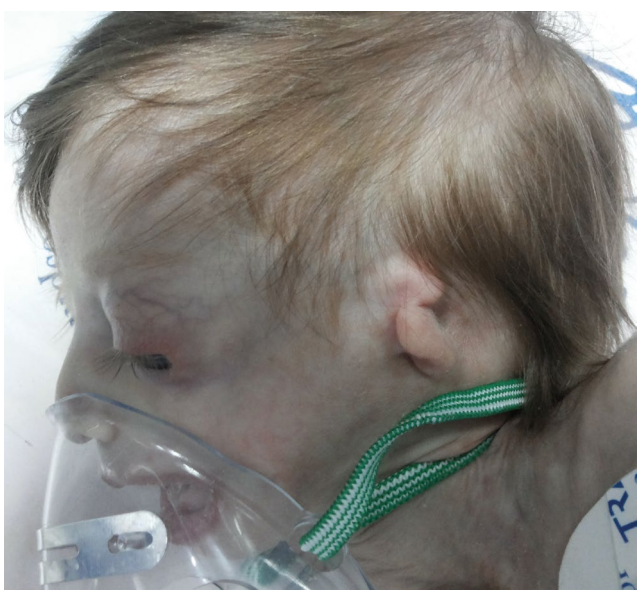


Figure 2. The clinical manifestations of Treacher Collins syndrome

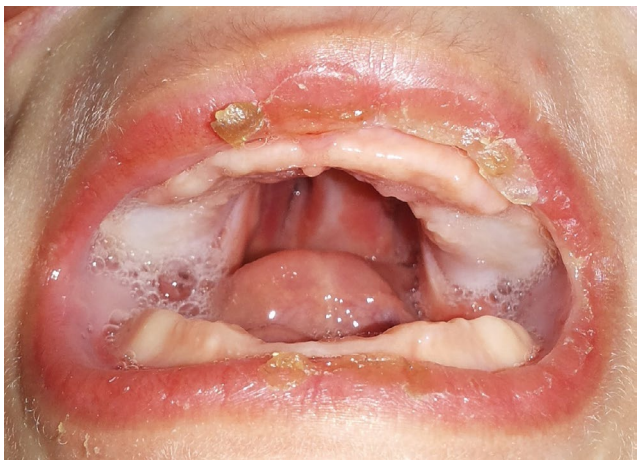


Figure 3. A high arched cleft palate

dyspnoea worsened, and she experienced respiratory distress. Two hours after admission to the hospital, she was transferred to the paediatric intensive care unit (PICU). Examination of the chest X-ray indicated bilateral infiltrates consistent with pneumonia. The patient was treated with a combination of antibiotics. Bronchoalveolar samples showed *Streptococcus pneumoniae*. However, the blood culture which was collected for the bacteriological diagnosis was negative.

During the next day, she underwent intubation for worsening hypoxia and respiratory distress, and a three-way central venous catheter (CVC) was inserted into the right internal jugular vein. As great difficulty was anticipated in securing the airway, the otorhinolaryngologist and anaesthesiologist teams were urgently requested to be present at the procedure. These teams were waiting in the adjacent room with all the necessary equipment laid out and ready, including a paediatric intubation set and a tracheostomy set.

The intubation of the infant was very difficult with two unsuccessful attempts at orotracheal intubation. One intubation attempt was with a video laryngoscopy and one was through the laryngeal mask airway. Finally, we decided to perform tracheal intubation via a fibreoptic bronchoscope. The fibreoptic bronchoscope was checked and loaded with a 3.5 mm endotracheal tube. We were ready to perform an emergency tracheostomy if required with the otorhinolaryngologist and anaesthesiologist on hand. The fibrescope was inserted into the mouth. The trachea was entered and the tube was passed into the trachea.

After seven days, the patient's condition had improved. The chest X-ray showed no infiltrates. Computed tomography of the rhinopharynx showed bilateral choanal obstruction. The diagnosis of choanal atresia was confirmed by nasofibroscopy. The patient underwent successful correction of bilateral choanal atresia.

Three days after the operation, the pulmonary situation had stabilised enough for the ventilator device to be removed. The patient was extubated; however, this led to shortness of breath, a rapid heart rate and elevated blood pressure with no improvement after high flow oxygen inhalation and noninvasive ventilator-assisted respiration. Therefore, she was intubated again.

During the period she was connected to the ventilator, she proved difficult to wean. Weaning was attempted 24 hours after using a T-piece and 4 l/min of oxygen was administered. She had a good cough reflex. Three attempts were made to remove the endotracheal tube but all of them failed due to immediate respiratory distress with documented low saturation requiring reintubation. Therefore, after consulting the paediatric otolaryngologist, the decision was made to perform a tracheostomy.

Because of feeding problems, the patient was commenced on central total parenteral nutrition. After a discussion with the paediatric gastroenterologist, the decision was made to perform a gastrostomy to aid in growth and development, and for prevention of aspiration.

The treatment of this baby girl required the coordinated efforts of a team of specialists, including a paediatrician, paediatric otolaryngologist, paediatric nurse, plastic surgeon, audiologist, ophthalmologist, geneticist and other specialists to systematically and comprehensively plan the child's treatment. Multiple surgeries would have been needed to treat the various craniofacial abnormalities associated with Treacher Collins syndrome.

Unfortunately, her clinical condition deteriorated; 36 days after admission, she developed septic shock. Cultures of blood from the CVC and peripheral vein, and culture of urine were obtained. Because ventilator-associated pneumonia was suspected, diagnostic bronchoalveolar lavage culture was performed to evaluate for pneumonia as a sepsis source. The antibiotic treatment was empirically changed to wide-spectrum antibiotic therapy (linezolid and colistin). She required high inotropic support and high ventilator settings. Inotropes and vasopressors were used to maintain her mean arterial pressure within the normal range. Chest X-ray revealed bilateral infiltrates. A nosocomial, ventilator-associated pneumonia was diagnosed. The results of blood cultures from the CVC and peripheral vein, and bronchoalveolar samples yielded *Pseudomonas aeruginosa*. Urine culture was negative.

The CVC was removed and a new catheter was inserted into the left internal jugular vein. She was switched to high-frequency oscillatory ventilation but the patient never responded adequately to any therapy.

Despite appropriate treatment, she remained critically ill with unstable systemic blood pressure.

Forty days after admission, she went into cardiac arrest. Although cardiopulmonary resuscitation was performed for 30 minutes, the patient succumbed to her illness.

Discussion

Treacher Collins syndrome is a rare congenital disorder of craniofacial dysmorphism characterised by numerous developmental anomalies restricted to the head and neck.[7]

Early descriptions were attributed to Berry (1889), Treacher Collins (1900) and Franceschetti and Klein (1949) and hence the names Berry's syndrome and Franceschetti-Zwahlen-Klein syndrome.[1,9,11]

The frequency of Treacher Collins syndrome is 1 in 50,000 live births.[5,7,8] The most frequent clinical manifestations are antimongoloid palpebral fissures, malar and mandibular hypoplasia, malformation of auricular pinna, coloboma of the lower eyelids, conductive deafness, cleft palate and dental anomalies.[9]

Additional abnormal structures that are occasionally found in Treacher Collins syndrome include absent parotid glands, cervical spine malformation, cryptorchidism, extremity malformation, renal anomalies, and congenital heart disease.[8,10]

Treacher Collins syndrome is caused by mutations in the *TCOF1*, *POLR1C* or *POLR1D* genes that affect facial development before birth.[9,11,12] Mutations in the *TCOF1* gene ac¬count for 81% to 93% of all cases. *POLR1C* and *POLR1D* gene mutations are responsible for 2% of Treacher Collins syndrome cases.[9] The three genes have been involved with a dominant (*TCOF1, POLR1D*) or a recessive (*POLR1D, POLR1C*) autosomal mode of inheritance.[13]

Forty percent of the cases are associated with previous family history and those affected have a 50% chance of passing it on to their next generation. The remaining 60% of the cases are thought to arise because of new mutation.[6,9,13] Our case did not report a familial history of the syndrome and the cause was likely a new mutation.

The diagnostic features of Treacher Collins syndrome include abnormalities in eyes, ears, nose, mouth and facial bone. The vast majority of these features were present in our case. Based on these clinical features five clinical forms of Treacher Collins syndrome were identified by Franceshetti and Klein: the complete form presenting with all known features, an incomplete form presenting with less severe ear, eye, zygoma, and mandibular abnormalities, the abortive form with only lower lid pseudo coloboma and zygoma hypoplasia, the unilateral form with anomalies limited to only one side of the face and the atypical form presenting with other abnormalities not usually part of this syndrome.[1,7,9] In our case, the patient presented with the complete form of this syndrome.

Treacher Collins syndrome has been recognised to be associated with upper airway obstruction and difficult tracheal intubation.[14] In neonates and other paediatric patients with predicted difficult ventilation and intubation, thoughtful airway management planning is mandatory. Usually, difficult intubation in these patients is anticipated, which gives us some time to prepare.[2]

Management of difficult airway in children remains one of the most relevant and challenging tasks for anaesthetists. Many airway management techniques had been described in paediatric patients with craniofacial malformations.[2] In our case we used different devices: intubation with video laryngoscopy was attempted once but failed, then we used the laryngeal mask airway once which also failed and, finally, intubation was achieved by a fibreoptic bronchoscope. Each device was only used once in order to prevent the risk of airway trauma which is associated with multiple attempts.

We formed a multidisciplinary team consisting of paediatric critical care doctor, anaesthesiologist and otorhinolaryngologist to manage intubation difficulties.

Nagamine et al. reported a 13-year-old girl with Treacher Collins syndrome who had a history of difficult intubation and was scheduled for plastic surgery. They took three-dimensional computed tomography images to better evaluate the anatomical features of the upper airway. The patient's anaesthetic airway management was influenced successfully by the findings of the images.[15] In our case, airway management was urgent and there was not enough time for additional investigations.

Grohskopf et al. carried out a study to determine the prevalence of ICU-acquired infections, which is a major cause of morbidity in PICU patients. They concluded that age-adjusted risk factors for infection included central intravenous catheters, arterial catheters, total parenteral nutrition, or mechanical ventilation.[16] In our case, the patient had multiple risk factors for infection such as central intravenous catheters, parenteral nutrition, and mechanical ventilation

Çelik et al. performed a study to determine the prevalence of infections and the predominant organisms. They concluded that the rate of nosocomial infection is high in ICU patients, especially for respiratory infections. The most frequently reported infection was ventilator-associated pneumonia. The predominant bacteria were *P. aeruginosa* and *S. aureus*.[17] In our case, a nosocomial, ventilator-associated pneumonia was diagnosed. The results of blood cultures and bronchoalveolar samples yielded *P. aeruginosa*.

Vincent et al. provided an up-to-date, international picture of the extent and patterns of infection in ICUs. They concluded that infections are common in patients in contemporary ICUs, and the risk of infection increases with the duration of ICU stay.[18] In our case, the baby girl stayed in the PICU for 40 days.

Treacher Collins syndrome can be detected using prenatal screening ultrasound. Three-dimensional sonographic imaging has been shown to detect these subtle features including downslanting palpebral fissures, micrognathia, and lowset ears/microtia. Polyhydramnios is seen as well.[10] In our case, the syndrome was not detected before birth. For a good outcome it is mandatory to anticipate problems in securing the airway and have a plan ready on how to proceed. Ideally appropriate prenatal planning is needed and prompt intervention after birth by a team of experienced medical and surgical personnel.

There is no cure for Treacher Collins syndrome. Treatment is aimed at the specific needs of each individual. Many children require a multidisciplinary approach involving a craniofacial team, including a paediatric otolaryngologist, audiologist, plastic surgeon, geneticist, psychologist, dental surgeons and other healthcare professionals.[1]

Of primary concern are breathing and feeding problems that present at birth as a consequence of micrognathia and tongue obstruction of the hypopharynx.[5,9]

A tracheostomy may even be necessary in some cases to maintain an adequate airway. Furthermore, a gastrostomy could be necessary to ensure an adequate caloric intake while protecting the airway. Surgery to restore a normal structure of the face is generally performed at defined ages, depending on the developmental stage.[9] Tracheostomy was required at some stage in childhood in 41% of children with TCS, and the ratio increased to 84% in TCS patients who also had choanal atresia or stenosis.[4]

In our case, tracheostomy, gastrostomy and surgical repair of bilateral choanal atresia were essential in the management of the baby girl. We made a plan with our team of specialists to systematically and comprehensively treat the patient.

Conclusion

Each case of Treacher Collins syndrome is unique and needs to be managed individually. Many manifestations of the disease can be improved by surgery and other supportive treatments. Early detection and well-planned treatment, tailored to the individual patient, can reduce disease symptoms and produce excellent results for complete restoration of the form and function of the patient. Airway management should also be specific for each individual patient. A multidisciplinary approach and careful planning is mandatory for the appropriate management of these patients. The members of the team are determined by the complexity of the case. Preparing for potential difficulties and communicating effectively can lead to successful results and avoid catastrophic outcomes.

Disclosures

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Informed consent was obtained from the patient's family for the publication of this case report (and the accompanying images).

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