CHERYL KING, MS, CCRN • Section Editor

CE 2.3 HOURS Continuing Education

Treacher Collins Syndrome

A Case Review

Ginger Jensen-Steed, MSN, NNP, NCC-BC

ABSTRACT

Treacher Collins syndrome is named after the English surgeon Edward Treacher Collins, who initially described the syndrome's traits in 1900. This rare autosomal dominant disorder affects approximately 1:50 000 live births. It primarily affects the development of facial structures through a mutation in the TCOF1 gene found at the 5q32-33.1 loci. While common facies and phenotype can be described with this syndrome, the gene has a wide variation of expressivity, thus making the diagnosis of mild cases challenging. This study involves a term female diagnosed with Treacher Collins syndrome, who was also diagnosed with Tracheal Esophageal Fistula. She is expected to be of normal intelligence but, as is typical for Treacher Collins syndrome, has conductive hearing loss and therefore is at risk for developmental delay. This article describes her hospital course and outcomes thus far and is intended to guide the bedside practitioner in recognition and guidance of families in the future.

KEY WORDS: mandibulofacial dysostosis, TCOF1 protein, Treacher Collins syndrome

GENETIC BACKGROUND

Treacher Collins syndrome is a rare autosomal dominant genetic disorder that affects 1:50 000 live births.[1-3] In approximately 40% of cases, it results from the transmission of the affected gene from a parent to their offspring.[2-4] Treacher Collins syndrome is also known as mandibulofacial dysostosis or Franceschetti-Klein syndrome and is caused by a mutation in the TCOF1 gene found at the 5q32-33.1 loci. It directly affects the development of the facial structures arising from the first and second brachial arches. Defects of the first arch arise around the 4th week of development and are thought to occur from an insufficient migration of neural crest cells into the first arch, such is thought to be the case with Treacher Collins and Pierre Robin syndromes.[5] This occurs through an alteration of the encoding of the Treacle gene leading to variable hypoplasias and malformations of the facial bones. At this time, TCOF1 is the only gene known to be associated with Treacher Collins syndrome.[3] In fully expressed cases of Treacher Collins syndrome, diagnosis based on clinical characteristics can typically be made early; however, because of the vast degree of variability in expression of the mutation, and the fact that approximately 60% of cases are caused by a new mutation of the gene, diagnosis is often difficult.[1-7]

With advances in genetic testing, it can be determined whether the mutation was new or the result of being passed from parent to offspring. If genetic testing reveals that the gene was passed from parent to offspring the recurrence risk is 50% for future pregnancies, and this risk affects male and female offspring equally. If the mutation was new, the risk of recurrence is relatively low.[3,4,6,8-11] Chorionic villous sampling or amniocentesis can be done early in subsequent pregnancies to determine the presence of the gene mutation. High-resolution ultrasonography may also be helpful in determining the presence of facial feature abnormalities, depending on the degree of affect. Because of the variability in expression, however, neither of these techniques can absolutely determine the severity of the condition for a particular fetus.[3,6,8]

CLINICAL MANIFESTATION

The most common manifestation is that of facial anomalies. According to a review of literature, facial anomalies can include the items listed in Figure 1. Malformation of the facial structures can also lead to

Author Affiliations: *Regis University, Denver, Colorado.*

The author declares no conflict of interest.

Correspondence: *Ginger Jensen-Steed, MSN, NNP, NCC-BC, PO Box 3254, Coeur d'Alene, ID 83816 (gingersteed@gmail.com).*

DOI: 10.1097/ANC.0b013e3182338070

FIGURE 1.

Hypoplasia or absence of the cheek bones
Hypoplasia of the side wall or floor of the eye socket
Hypoplasia of the mandible
Beak-like nose- pointed nasal prominence
Choanal atresia/stenosis
Increased anterior facial height
Small oral cavity with high arched palate
Small chin with an open anterior bite
Steep angle of the lower jaw
Cleft lip and or palate
Shortened soft palate
Malocclusion of teeth
Coloboma- notched lower eyelids
Down slanting palpebral fissures
Total or partial absence of lower eyelashes
Hypoplasia, malformed, or prominent external ears
Conductive hearing loss

Common Clinical Characteristics of Treacher Collins Syndrome.

difficulties in hearing, breathing and eating. Most individuals with Treacher Collins syndrome have normal intelligence and development; however, associated hearing loss and oral malformation can lead to delays in speech and language. Less commonly, Treacher Collins syndrome has been associated with heart defects, visual disturbances, malformed or absent thumbs, and cryptorchidism.[1,2,4,6,7,10,11]

The association of conductive hearing loss is high, affecting approximately 40% to 50% of individuals with Treacher Collins syndrome. This is because of abnormal formation of external ear and middle ear cavities. Early determination of the degree of hearing loss with follow-up by an audiologist, and ear, nose, and throat (ENT) specialist for early intervention is essential for promotion of speech and language development.[2,3,7]

Case Study Infant: Maternal Prenatal Course

This baby girl was a 2593-g infant born at 38⅐ weeks' gestation to a 23-year-old mother. Mother's prenatal labs were noncontributory and she had comprehensive prenatal care during the pregnancy. Her pregnancy was complicated with hyperemesis and polyhydramnios. She was in good general health, and the only medication taken during the pregnancy were prenatal vitamins. Despite comprehensive prenatal care and being informed of the presence of polyhydramnios, the parents state they were not informed of any potential complications associated with polyhydramnios.

Case Study Infant: Labor and Delivery and Admission Findings

The mother went into spontaneous labor with rupture of membranes 12 hours prior to delivery. She delivered vaginally without complication. The NICU staff was called to evaluate the baby after delivery for respiratory distress and inspiratory stridor. The infant was admitted to the NICU and noted to have copious amounts of oral secretions, coughing, inspiratory stridor, and mild hypoxia. The infant breathed easier and was able to maintain her color and saturations if she was placed on her side or prone, but she had significant respiratory distress and desaturation when placed supine.

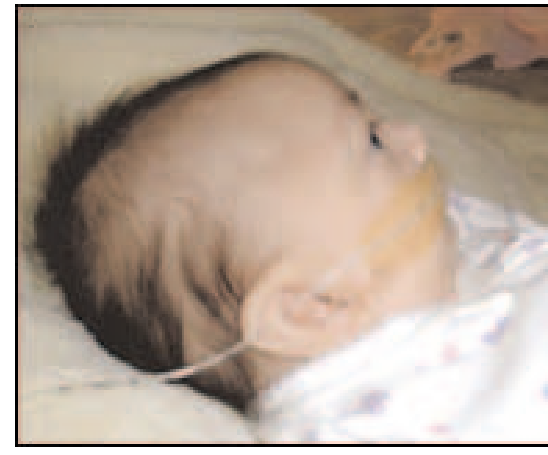
Physical examination of the infant was normal except for a posterior soft palate cleft, low set, posteriorly rotated ears with 3 skin tags in front of the right ear, and a small back hairy nevus. The left ear revealed one skin tag and a pointed helix. She was also noted to have micrognathia with a small recessed jaw (Figures 2 and 3).

Respiratory distress and copious amounts of oral secretions prompted staff to place an orogastric tube, which would not pass beyond 10 cm. Chest x-ray revealed the orogastric tube to terminate in the upper one-third of the esophagus. Air was noted in the bowel prompting surgical consult for suspected esophageal atresia (EA) with a distal tracheoesophageal fistula (TEF) (Figure 4).

Case Study Infant: Differential Diagnosis

At this time, it was suspected that the infant was at risk for VATER/VACTERL association. VATER/VACTERL associations are acronyms for commonly associated defects. VATER stands for Vertebral

FIGURE 2.



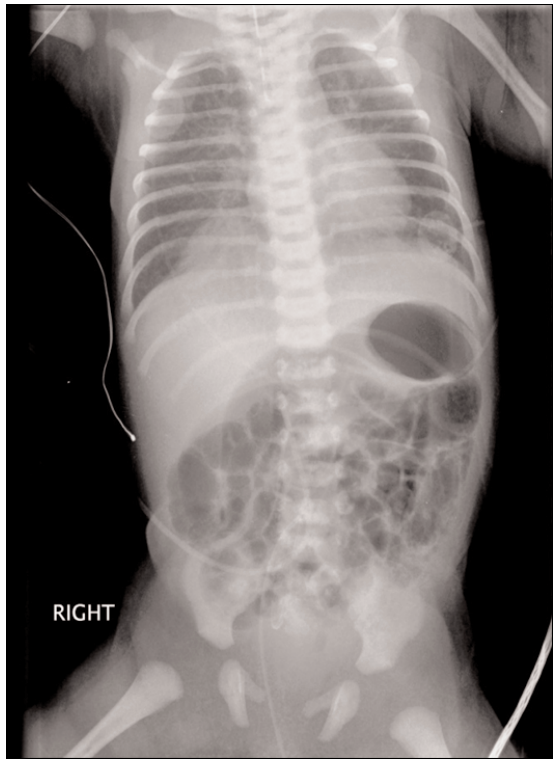
Profile picture showing skin tags, low posteriorly rotated ears, and foreshortened recessed chin.

FIGURE 3.

Picture showing foreshortened recessed chin, low posteriorly rotated ear, with skin tag and pointed helix.

anomalies, Anal atresia, TEF, and Radial or Renal dysplasias. The incidence of this association is 1.6:10 000, and diagnosis requires presence of 3 or more of the listed defects. VACTERL adds in Cardiac anomalies, and Limb defects.[8,11]

FIGURE 4.



X-ray image showing Replogle that ends in upper esophagus, and air in the stomach indicating esophageal atresia with distal tracheoesophageal fistula.

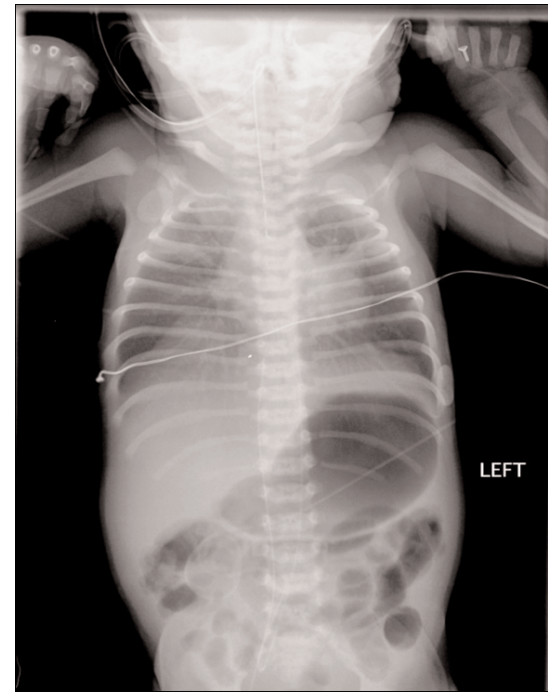
As indicated, an echocardiogram, x-rays, renal ultrasound, head ultrasound, chromosomes, and a genetic consult were all ordered. The echocardiogram showed no cardiac malformations, and renal and cranial ultrasounds were also normal. Chest x-ray a day later, due to the large air-filled stomach bubble, did reveal 13 ribs on the left side (Figure 5). However, the chest x-ray remained unremarkable for malformations other than the diagnosis of EA with distal TEF.

Surgery to repair the EA/TEF was performed on day of life 3. The length of the EA was sufficient to allow an end-to-end anastomosis of the esophagus, and the tracheal esophageal fistula was repaired without incident. As is commonly associated with TEF, the infant did go on to experience reflux and had mild laryngomalacia. Despite these issues and having the small cleft palate, the baby was able to nipple most of her feedings. Unfortunately she was not able to take in enough orally to support adequate growth; therefore, the decision was made to do a Fundoplication and place a gastrostomy tube (GT) prior to discharge. She did well with these procedures, recovered quickly, and went home soon after.

Case Study Infant: Genetics

Chromosome testing showed a 46, XX, or normal female karyotype. Genetics evaluation was done on day of life 8 and in addition to the soft palate cleft,

FIGURE 5.



X-ray image of infant showing presence of 13th rib on the left side.

preauricular tags, micrognathia, and low-set dysplastic ears, the geneticist also noted a somewhat hypoplastic mid-face, low posteriorly rotated ears with poorly formed helices, lack of lower eye lid lashes, a wide mouth with thin upper lip, and a short neck. She felt the infant's features were consistent with a mild form of Treacher Collins syndrome, however, needed to research TEF in association with Treacher Collins syndrome. Her research lead her to another diagnosis of Treacher Collins syndrome with TEF; however, this is not a common association. In-depth molecular analysis is available to determine the presence of the TCOF1 gene mutation. This testing was offered to the parents, but due to the cost and the lack of insurance coverage for such testing, it was not done at this time. The geneticist discussed with the family Treacher Collins syndrome. They were informed of the associated normal learning abilities, but significant risk for hearing loss and need for hearing evaluation and follow up. Genetics plan to follow up with the family on an outpatient basis.

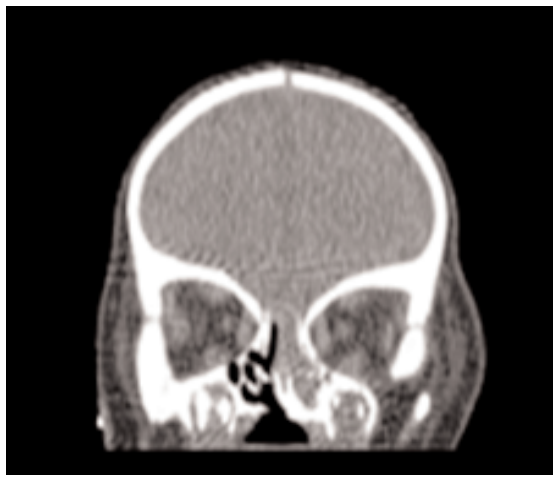
Case Study Infant: Consultations and Findings

The infant failed the initial auditory brainstem response hearing screening. She was referred to audiology for consultation. This testing suggested severe hearing loss in both ears with results suggesting abnormal middle ear function. The baby will be followed by audiology for hearing aids and further testing.

It was determined by ENT that the baby had left-sided unilateral choanal atresia (Figure 6), a slightly posteriorly displaced tongue with moderate micrognathia, and mild laryngomalacia. The physician was unable to visualize the right ear canal because of stenosis. Furthermore, he found the left auditory canal to be partially patent with an opaque tympanic membrane suggestive of a mucoid middle ear effusion.

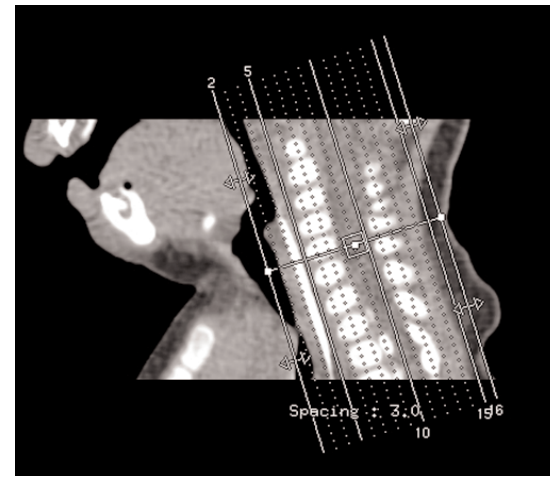
Computed tomography and magnetic resonance imaging were ordered on this infant to determine the extent of central facial bony formation and defects. These tests revealed normal structures other than a slightly foreshortened mandible, and thickening of mucosa in the superior left nasal cavity. Cervical spine analysis also showed normal formation (Figure 7).

FIGURE 6.



Computed tomographic image showing left unilateral choanal atresia.

FIGURE 7.



Computed tomographic image showing normal spine formation, as well as foreshortened mandible with open anterior bite apparent.

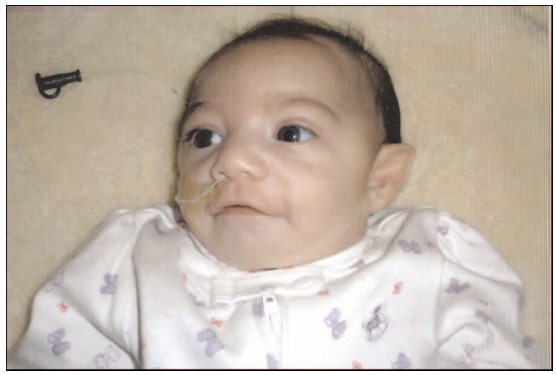
Case Study Infant: Discharge and Follow-Up

This infant was discharged from the hospital on her 67th day of life and was progressing well after her Fundoplication and gastrostomy tube (GT) placement (Figures 8 and 9). They will continue ongoing support with a primary pediatrician, pediatric surgeon, audiologist, ENT specialist, plastic surgeon, geneticist, ophthalmologist, and the early intervention developmental services.

Case Study Infant: Where are They Now?

This baby is now 4 months old (Figure 10). She has been receiving home health and dietary services since discharge. She has been receiving physical therapy services on a monthly basis and is meeting age-related developmental milestones. Despite her hearing loss, she is quite verbally expressive. She continues to take most of her feedings from a bottle, and the family is beginning some introduction to

FIGURE 8.



Picture A of infant near discharge.

spoon feedings, which she is doing very well with. She is currently beginning occupational therapy follow-up on a weekly basis and is also enrolled in an early developmental intervention program.

She had recent placement of tympanic tubes and is scheduled for follow-up hearing evaluations with audiology in 1 month's time. It will then be determined whether she will need subsequent placement

FIGURE 9.

Picture B of infant near discharge.

FIGURE 10.

- FACES: The National Craniofacial Association: www.faces-cranio.org
- Treacher Collins Family support Group: www.treachercollins.net
- Reflections on Treacher Collins syndrome: www.treachercollins.org
- The craniofacial Center, Dallas, TX: www.thecraniofacialcenter.org/
- Seattle Children's Craniofacial Center: www.seattlechildrens.org/clinics-programs/craniofacial/
- National Institute for Health; Pub Med. Treacher Collins Syndrome: www.ncbi.nlm.nih.gov/pubmedhealth/PMH0002624
- National Center for Biotechnology Information: National Institute of Health: Gene Reviews: www.ncbi.nlm.nih.gov/books/NBK1532/

Resources for families.

of hearing aids. Often these patients can have atresia of the auricular ducts; however, this infant's computed tomography and magnetic resonance imaging appeared to show complete communication.

A cleft palate repair is planned at 12 to 14 months of age. While recovering, she will be unable to take anything orally for approximately 2 months, during which time the GT will prove useful for feedings. Removal of the GT is then planned when the infant can intake adequate feeding volumes by mouth. With her current enthusiasm for oral feedings, it is hoped that this will be a rapid transition.

Plastic surgery for removal of the ear skin tags, reformation of the helixes, and choanal atresia repair are all being considered for repair at the same time as the cleft palate surgery. The patient will not undergo repair of the mandible until later in life.

Conclusion

Treacher Collins syndrome is a complex diagnosis, which requires extensive evaluation and care in the hospital as well as after discharge to ensure these infants reach their full potential. There are many helpful resources available for families affected by Treacher Collins syndrome, see (Figure 11). These sites offer families medical, social/emotional, and financial support.

Follow-up by a primary pediatrician is essential to ensure ongoing coordination of services with specialist including audiology, ENT, maxillofacial surgeons, geneticists, orthodontists, ophthalmologists, and occupational/physical and speech therapy services as well as social services as needed. Given proper care, follow-up, and love these children can live happy productive lives (Figure 12).

FIGURE 11.

Follow-up picture of baby after discharge.

FIGURE 12.

Baby and her family after discharge.

References

1. Malone KJ, Cook SS. Introduction to genetics for otorhinolaryngology nurses. *ORL-Head Neck Nurs.* 2006;24(2):8-18.
2. Magalhaes MH, Barbosa da Silveira C, Moreira CR, Cavalcanti MG. Clinical and imaging correlations of Treacher Collins syndrome: report of two cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2007;103:836-842.
3. Katsahis SH, Cutting GR. *Treacher Collins Syndrome.* GeneReviews [electronic resource]. MLN ID: 101256853. http://www.ncbi.nlm.nih.gov/books/NBK1532/. Published 2006. Accessed February 18, 2011.
4. Dalben GD, Costa B, Gomide MR. Prevalence of dental anomalies, ectopic eruption and associated oral malformations in subjects with Treacher Collins syndrome. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2006;101:588-592.
5. Moore KL, Persaud TN. *The Developing Human: Clinically Oriented Embryolog.* 8th ed. Philadelphia, PA: Saunders Elsevier; 2008.
6. Jackson L. What is it? Treacher Collins Syndrome. *Central Lines.* 2004;20(4):10. Copy received from NANN Archives, January 2011.
7. Jones KL. *Facial Defects as Major Feature. Smith's Recognizable Patterns of Human Malformation.* 6th ed. Philadelphia, PA: Elsevier Saunders; 2006:280-282.
8. Verklan MT, Walden M, Schiefelbein J. Genetics: from bench to bedside. In: Hayden MD, Gower LK, eds. *Core Curriculum for Neonatal Intensive Care Nursing.* St Louis, MO: Saunders Elsevier; 2010:399-414.
9. Nussbaum RL, McInnes RR, Willard HF. Patterns of Single-Gene Inheritance. In: Nussbaum RL, McInnes RR, Willard HF, eds. *Thompson and Thompson: Genetics in medicine.* 7th ed. Philadelphia, PA: Saunders Elsevier; 2007:115-149.
10. FACES: The national craniofacial association. http://www.faces-cranio.org/disord/Treacher.htm. Accessed October 22, 2010.
11. Merenstein GB, Gardner SL. Genetic disorders, malformations, and inborn errors of metabolism. In: *Handbook of Neonatal Intensive Care.* 6th ed. St Louis, MO: Mosby Elsevier; 2006:812-837.