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Short Running Title: A queer presentation of Carmi syndrome

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SUMMARY

Carmi syndrome is a rare disease affecting multiple organ systems. Not much has been documented in literature about this disease. Respiratory papillomatosis, on the other hand, is a common benign disorder affecting the respiratory tract of children. Here, we report an interesting case of Respiratory papillomatosis along with posterior urethral valve in a 9-year-old male child with features of Carmi syndrome.
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ABSTRACT

Introduction
Congenital pyloric atresia with junctional epidermolysis bullosa and congenital cutis aplasia is known as Carmi syndrome.

Case Report
We report a case of squamous papilloma of the respiratory tract with posterior urethral valve in a case of Carmi syndrome.

Conclusion
Such presentation is extremely unusual and has not been documented yet.

Keywords: Carmi syndrome, pyloric atresia, epidermolysis bullosa, respiratory papilloma, posterior urethral valve
TITLE: Respiratory papillomatosis in a case of Carmi Syndrome: An unusual presentation

INTRODUCTION
Carmi syndrome is an extremely rare disease manifesting with congenital pyloric atresia and junctional epidermolysis bullosa, with the inheritance pattern being autosomal recessive. [1, 2]

CASE REPORT
A preterm male infant was delivered by lower uterine Caesarean section, with a history of polyhydramnios in the mother. The newborn infant developed repeated episodes of vomiting with regurgitation of feeds since birth. A diagnosis of congenital pyloric atresia was made for which he underwent gastroduodenostomy(Figure 1) on the fifth day of life. He also developed bullous lesions over the trunk and extremities, with new lesions developing with trivial trauma (Figure 4). At six months of age, the child developed poor stream of urine with discharge of whitish flecks with fever. Urine culture was positive for Pseudomonas aeruginosa, sensitive to Gentamicin. Ultrasound showed hydronephrotic changes in both kidneys with dilatation of bilateral ureters. He was diagnosed to have posterior urethral valve(Figure 6) for which vesicostomy(Figure 2) had to be done after attempts of cystoscopy guided valve fulguration were deemed ineffective in a setting of recurrent urinary tract infection and hydronephrosis. The child presented with respiratory distress and hoarseness at four and a half years of age. Thereafter, direct laryngoscopy was done which revealed multiple masses occupying bilateral false cords, left aryepiglottic fold and anterior commissure (Figure 5). The masses were firm, fleshy, pedunculated and did not bleed on touch. Biopsy was taken and surgical excision of the masses was done. The histopathology report revealed squamous papilloma(Figure 7). The child again presented with acute severe respiratory distress with cyanosis two months following discharge, for which emergency tracheostomy had to be done. Attempts of weaning were tried but the child was unable to tolerate it. At present, the child is nine and a half years old, tracheostomized, school-going with age-appropriate neurodevelopment. His six-and-a-half-year-old sister underwent
gastroduodenostomy for congenital pyloric atresia on 21st day of life and vesiectomy for posterior urethral valve at two years of age. She was also diagnosed with junctional epidermolysis bullosa at four years of age. Interestingly, the mother suffered from polyhydramnios during the birth of her second child also. There is a history of sibling death within first week of life in his father’s generation following a blistering disorder.

**DISCUSSION**

Respiratory papillomatosis is a benign tumor of the respiratory tract, usually caused by Human Papilloma Virus 6 or 11 infection, often presenting with hoarseness of voice, stridor and acute airway obstruction requiring emergency tracheostomy. The reported incidence of recurrent respiratory papillomatosis in a population based Danish study is 3.62 per 100,000[3]. Such population based data in the Indian subcontinent is limited. Hence, to strengthen the database, a national registry [4] has been introduced. Surgical excision of the papillomas remain the mainstay of treatment, though medical therapy including intralesional antivirals [5] and HPV vaccines [6] have also been tried. Here we report an unusual case of respiratory papillomatosis and posterior urethral valve in addition to junctional epidermolysis bullosa with congenital pyloric atresia, which constitute Carmi syndrome. JEB with congenital pyloric atresia has been associated with mutation in the α6β4 integrin genes (ITGA6, ITGB4)[2], leading to the formation of blisters which rupture on mechanical insults. Congenital heart disease [7] has also been reported in Carmi syndrome. Peptic perforation [8] and enterocolitis [9] are known complications of Carmi syndrome. Prenatal diagnosis of Carmi syndrome is made by ultrasonographic findings like polyhydramnios, gastric dilatation, “snowflake sign” in amniotic fluid and complete separation of chorioamniotic membrane [10]. Preimplantation genetic detection [11] and immunofluorescence assisted villous trophoblast analysis [12] have also been as diagnostic tools. Although management of this rare disorder is early diagnosis and timely symptomatic intervention, gene therapy may yield promising results and creates ample scopes of research.
CONCLUSION

Respiratory papillomatosis is a common disease in the paediatric population that may have syndromic association as highlighted in the case report above. Hence formulation of a multidisciplinary approach to the diagnosis of respiratory papillomatosis with thorough systemic examination, keeping such multi-system affection in mind is imperative to rule out any syndromic association, that may be often missed. Moreover, further studies may help to expand the spectrum of symptoms that define this rare disease-Carmi syndrome.

CONFLICT OF INTEREST

None

AUTHOR'S CONTRIBUTIONS

Dr. Sandipta Mitra
Group 1 - Conception and design, Acquisition of data, Analysis and interpretation of data
Group 2 - Drafting the article, Critical revision of the article
Group 3 - Final approval of the version to be published

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Group 3 - Final approval of the version to be published

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FIGURE LEGENDS

Figure 1: Child with tracheostomy tube in-situ with scar of gastroduodenostomy incision

Figure 2: Bullosa involving right limbal conjunctiva

Figure 3: Scar of vesicostomy

Figure 4: Healed scars of ruptured bullosa over extremities

Figure 5: Fleshy masses in bilateral false cords, left aryepiglottic fold and anterior commissure

Figure 6: Voiding cystourethrogram showing dilatation and elongation of posterior urethra and bladder trabeculation

Figure 7: Photomicrograph showing multiple squamous papillae (H and E, x40)
Figure 1: Child with tracheostomy tube in-situ with scar of gastroduodenostomy incision
Figure 2: Bullosa involving right limbal conjunctiva

Figure 3: Scar of vesicostomy
Figure 4: Healed scars of ruptured bullosa over extremities
Figure 5: Fleshy masses in bilateral false cords, left aryepiglottic fold and anterior commissure
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Figure 7: Photomicrograph showing multiple squamous papillae (H and E, x40)