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The CHARGE association and athyreosis

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Abstract

We report on a male infant with congenital hypothyroidism owing to athyreosis occurring with the CHARGE association (bilateral papillary coloboma, congenital heart disease, dysmorphic ears, sensorineural deafness, psychomotor retardation, cryptorchidism, facial palsy, and vesicoureteral reflux). The coexistence of these two disorders has not been described previously.

In 1981, Pagon *et al*[1] introduced the acronym CHARGE to define a constellation of malformations including Coloboma, Heart disease, Atresia choanae, Retarded growth or development or both, Genital hypoplasia, and Ear anomalies/deafness. Since then, roughly 250 cases have been published.[2 3] We present a case of a patient with the CHARGE association and congenital hypothyroidism owing to athyreosis. This combination of disorders has not been described previously.

Case report

The proband was a 30 month old male, born to a 27 year old primigravida after an uncomplicated 42 week pregnancy. The father was 29 years old and there was second degree parental consanguinity, but no family background of mental retardation, congenital malformations, or endocrine disorders. His transverse position at delivery necessitated a caesarean section, but resuscitation was not required. His weight at birth was 3950 g (90th centile) and length 50 cm (10th to 25th centile).

At 19 days old, he was admitted to our hospital with vomiting, somnolence, and refusal to eat. The physical examination showed micrognathia, low set, dysplastic ears, and a continuous systolic ejection murmur in the praecordium and back. His weight and length were normal for his age, and the results of tests did not suggest hypothyroidism. The total T4 was 55·3 nmol/l (normal 58 to 154 nmol/l) and TSH was 466 mU/l (normal 0·4 to 4·5 mU/l). Antithyroid antibodies were negative and, on scintigraphy performed with 99m-Tc and 131-I, there was no uptake of the radiolabels by thyroid tissue. The capitulum of the humerus and proximal epiphysis of the tibia were absent. At 21 days of age, replacement therapy with levothyroxine was begun. Haemodynamic studies indicated a large ductus arteriosus and atrial septal defect. Urinary cystography showed grade II left vesicoureteral reflux with a normal urethra and bladder.

At 9 months old, he underwent ductus ligation. Levels of thyroid hormones in the preceding months indicated a correct replacement dose. At this time, significant psychomotor retardation was evident, as well as craniofacial asymmetry, plagiocephaly, lower right facial palsy, and torticollis with inclination to the right side. Both ears were low set and posteriorly rotated; the left ear had a hypoplastic helix, antihelix, and lobe, and the right ear was cup shaped. Ophthalmological examination showed right microphthalmia, horizontal nystagmus, a large right papillary coloboma with macular hypoplasia, and another small papillary coloboma in the left eye. His auditory evoked potentials indicated bilateral sensorineural hearing loss. His penis was normal; the undescended left testis was palpable in the inguinal canal and the right testis was palpable in the upper region of the scrotum. The skeletal radiological study was normal. The karyotype, using Giemsa banding, was normal 46,XY. Cranial CT scan disclosed pachygyria with left cortical hemiatrophy, which was more pronounced in the frontal lobe. His EEG was normal, as was renal echography and a second urinary cystogram.

He received an implant of an auditory prosthesis and was placed in a rehabilitation and occupational therapy programme. In subsequent checks, significant psychomotor retardation was confirmed: at 17 months, his age was 7 months on the Bayley Scales

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of Infant Development. Throughout the entire follow up period, his weight and height growth curve remained within the 10th to 25th centile (Tanner) with a normal growth rate.

At 28 months of age, endocrinological testing confirmed hypothyroidism owing to athyreosis with normal hypophyseal function and somatomedin C level, and normal testosterone response to human chorionic gonadotrophin.

Discussion

Our patient exhibits five of the anomalies that define the CHARGE association. Only choanal atresia is missing, a fact which does not rule out the diagnosis given that its incidence ranges around 56%.[1-4] In our opinion, the psychomotor retardation is not secondary to hypothyroidism since the latter was detected and treated early. On the other hand, he has facial dysmorphism, vesicoureteral reflux, and facial palsy, which frequently appear in this disorder.[4] The absence of swallowing defects, malnutrition, and severe hypoxaemia probably accounted for his normal weight and height, in contrast with that usual in patients with choanal atresia, tracheo-oesophageal fistula, or cyanotic heart disease.

Oley *et al*[4] reported a patient with CHARGE association and a normally functioning ectopic thyroid gland, but to our knowledge no other cases with anomalies of thyroid development have been described. However, alterations in the development of other structures derived from the floor of the primitive pharyngeal intestine have been related to this association. Thus, four cases of full blown DiGeorge's syndrome[1 5] and two cases of 'partial' DiGeorge's syndrome, with a very atrophic thymus and a diminished number of parathyroid glands,[6 7] have been reported. Alterations in the development of the middle ear, which is derived from the first pharyngeal pouch, are very frequent in the CHARGE association.[3]

In conclusion, we consider that the study of the morphological and functional condition of the thyroid gland should be included in the assessment of patients with the CHARGE association, as it may lead to the early detection of eventual alterations which further hinder the mental development of these subjects.

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