Rob W. Meijer · Willem W. M. Hack
Krijn Haasnoot

Successful treatment of acquired undescended testes with human chorionic gonadotropin

Received: 21 March 2000 / Accepted: 8 August 2000

Human chorionic gonadotrophin therapy may have its place in the management of acquired undescended testes and surgery should be reserved for those who fail to respond to therapy. Further studies are necessary to evaluate these preliminary results.

At present, congenital and acquired forms of undescended testes are recognised [2]. Congenital forms are usually treated by orchiopexy (ORP) at an early age. Although ORP is also frequently performed in acquired forms, this therapy is under debate and it is estimated that a significant percentage of all ORPs are accounted for by acquired forms [6]. We report human chorionic gonadotrophin (HCG) treatment in 13 prepuberal boys with acquired undescended testes (AUT) and found that HCG-stimulation may have its place in the treatment of AUT.

A group of 13 prepuberal boys (aged 7.7–12.2 years, mean 9.1 years) with AUT were seen at the out-patient clinic during a period of 5 years between 1991 and 1995. Eleven boys had unilateral AUT (6 right-sided and 5 left-sided) and two boys had bilateral AUT. All patients were treated with intramuscular injections of HCG (PregnylR, Organon) as recommended by the World Health Organisation (two doses of 1.000 IU weekly for 5 consecutive weeks in boys older than 5 years). Testicular position was re-evaluated at the end of the treatment and again 6 and 12 months later. All successful cases were requested by letter to attend for long-term assessment. As shown in the Table, 11 cases consented and one (case 3) did not respond to our request. Mean duration of long-term follow-up assessment after HCG-therapy was 5.7 years (range 3.9–7.5 years). In 14 out of 15 gonads, complete testicular descent was observed during HCG therapy. In one gonad (case 10) HCG therapy was not successful and ORP was performed. At long-term assessment, in 11 out of 11 boys, testes remained fully descended. In 10 out of 11 patients, testes were symmetrical and of normal size.

In the management of undescended testis, HCG therapy is used with rates of success ranging from 20–55% [5] and various protocols of HCG injections are being used. For several reasons, HCG can be expected to be effective in obtaining testicular descent in AUT. It has been shown that hormonal therapy is highly effective in obtaining testicular descent in gliding forms [1]. Therefore, acquired forms, which, according to our observations are preceded by gliding forms, can also be expected to be treated successfully with HCG therapy. Furthermore, several studies have shown better results in older children and with testes located low in the inguinal region. In AUT both these criteria are met. In addition, Hutson and Beasley [4] predicted acquired forms to respond well to HCG because these gonads had been previously fully descended. Therefore, anatomical abnormalities accounting for failure to respond to HCG therapy are presumed to be absent. It can only be speculated whether acquired forms may offer an explanation for the observed influence of age on the results of HCG treatment as reported in various studies.

The results of our study show that HCG therapy may have its place in the management of AUT, which suggests that surgery should be reserved for those who fail to respond to hormonal therapy. However, since in this study numbers are small, further longitudinal studies including larger numbers will be necessary to give more accurate evaluation of the results. Also, although in this group long-term assessment showed in most cases symmetrical normal-sized testes on orchiometry, these data do not allow for conclusions about fertility. Finally, since acquired forms seem to respond well to HCG stimulation, we do not recommend the use of HCG as a diagnostic tool to distinguish retractile from undescended testes as suggested by others [3].

References

1. Bierich JR (1982) Undescended testes: treatment with gonadotrophin. Eur J Pediatr 139: 275–279
2. Hack WWM, Hirasing RA (1996) De verworven niet-scrotale testis bij jongens: een onderschat fenomeen. Ned Tijdschr Geneeskd 140: 1809–1812
3. Hazebroek FWJ, de Muinck Keizer-Schrama SMPF, Molenaar JC (1993) Role of hormone treatment in the management of the undescended testis. Eur Urol Update Series 2: 170–175
4. Hutson JM, Beasley SW (1992) Descent of the testis. Chapter 4: Classification and causes of undescended testes in humans. Edward Arnold (Ed.). London Melbourne Auckland, pp 57–59
5. Pyörälä S, Huttunen NP, Uhari M (1995) A review and meta-analysis of hormonal treatment of cryptorchidism. J Clin Endocrinol Metab 80: 2795–2799

Table Clinical data of patients (n = 13) with AUT treated with HCG

Patient	Age at presentation (years)	Localisation of AUT	Year of HCG treatment	Testis volume			
				Age (years)	Right (ml)	Left (ml)	Puberty stage
1	8.8	Left	1991	14.8	10	10	P_2G_3
2	9.0	Right and left	1992	16.5	20	20	P_4G_4
3	9.3	Left	1992	One year after HCG-treatment both testes fully descended (volume 2 ml). No long-term follow-up			
4	8.0	Left	1992	15.0	10	12	P_3G_4
5	8.3	Right and left	1993	14.3	22	12	P_4G_4
6	7.8	Right	1993	14.3	8	10	P_4G_3
7	9.3	Right	1993	15.7	15	20	P_4G_4
8	12.2	Left	1993	18.4	25	22	P_4G_4
9	7.7	Left	1993	13.8	6	6	P_1G_2
10	10.7	Right	1993	HCG therapy unsuccessful. ORP performed. No long-term follow-up.			
11	10.0	Right	1994	14.8	15	20	P_4G_4
12	8.0	Right	1995	11.9	4	4	P_1G_2 Still in follow-up
13	9.6	Right	1995	14.7	20	20	P_4G_4

6. Rabinowitz R, Hulbert WC (1997) Late presentation of cryptorchidism: the etiology of testicular re-ascent. J Urol 157: 1892–1894

R. W. Meijer
Department of Surgery, Medical Centre Alkmaar, Alkmaar, The Netherlands

W. W. M. Hack (✉) · K. Haasnoot
Department of Paediatrics, Medical Centre Alkmaar, Wilhelminalaan 12, 1815 JD Alkmaar, The Netherlands
Tel.: +31-72-5484444

Muge Yemisci · Serap Saygi

Partial agenesis of the corpus callosum with partial seizures and bilateral congenital lacrimal duct atresia

Received: 14 March 2000 / Accepted: 5 July 2000

Patients with partial agenesis of the corpus callosum can be readily detected by magnetic resonance imaging.

Although there are many asymptomatic cases of agenesis of the corpus callosum (ACC), the condition often is associated with mental retardation (73%), seizures (42%), ocular anomalies (42%), gyral abnormalities (32%), hydrocephalus (23%), other central nervous system lesions (29%) and costovertebral defects (24%) [4, 6]. Here we report a case presenting with juvenile onset partial epilepsy and previously undescribed association of partial ACC and congenital lacrimal duct atresia with other subtle eye findings such as minimally restricted conjugated eye movements and mild bilateral ptosis.

An 18-year-old right-handed female having complex partial seizures occuring at least once a month since the age of 16 was admitted to our hospital. She was the first child of first degree consanguineous parents. She had been diagnosed as having bilateral lacrimal duct atresia and underwent reconstructional surgery for this at the age of 6 years. Except for bilateral mildly ptotic eyelids and a minimal limitation of bilateral horizontal conjugate gaze, her mental development and her physical and neurological examinations were perfectly normal. The patient has a brother with short fingers. The family history was negative for any other mental or physical handicaps. Her EEG showed non-specific slow wave paroxismal activity in the centro-temporal regions. Her cranial CT was reportedly normal, but cranial MRI revealed posterior agenesis of the corpus callosum (Fig. 1). She became seizure-free after daily administration of 900 mg valproic acid. Her sib refused having further investigation as he did not have any neurological deficit.

The actual frequency of ACC in the general population is unknown because of many asymptomatic cases, but in an unselected hospital population, the prevalence was estimated at approximately 1–3 per 1,000 [4]. Although the pathogenesis is still unknown there is evidence of genetic heterogeneity in ACC. According to the findings in the different reported families, autosomal dominant, autosomal recessive, X-linked recessive and polygenic inheritance have been proposed causing a disturbed developmental process during embryogenesis. There have been previous reports on familial versus sporadic occurrence of ACC. A destructive necrotising process, toxic metabolites, nutritional deficiency or an inborn error of metabolism may also be the cause of ACC [7].

Unilateral or bilateral congenital lacrimal duct obstruction is also a common malformation in the newborn period, occurring in 2–6% among a series of unselected infants but in most of them, obstruction opened spontaneously or after few probing procedures during infancy and only a few of them required surgery depending on the severity of atresia [2]. Lacrimal duct atresia is also seen in some genetically determined (mostly autosomal dominant) ectodermal dysplasia associated syndromes such as occurring in 59% of cases in ectodermal dysplasia-ectrodactyly-clefting syndrome [5]. The lacrimal duct and the corpus callosum start proliferating at about the 9th week of gestation from ectoderm. The oculomotor muscles are derived from mesoderm [1]. The subtle ocular abnormalities in this patient (mild ptosis and gaze paresis) may have been caused by the defective interaction of mesoderm and ectoderm as they both interact to produce the specialised structures and a fault in the ability of mesodermal tissue to organise ectoderm might produce the picture of ectodermal dysplasia [3]. The facial features approach normal appearance at about the 16th week and it correponds to late corpus callosum morphogenesis [3, 4]. The prevalence of both ACC and lacrimal duct atresia is high so there can be an incidental association; however, in large series of cases with ACC, the ocular anomalies were reported to occur in 42% without an associated lacrimal duct atresia being reported before [3].

In this case, the history of consanguineous marriage, the presence of a family history for ectodermal defect (short fingers in her brother) and the knowledge about development of both the lacrimal duct and the corpus callosum from the ectodermal germ

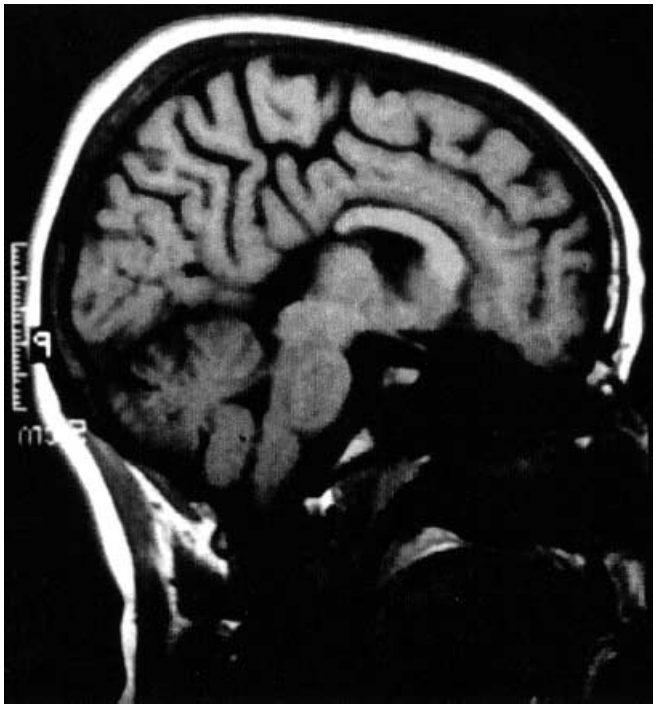

Fig. 1 The patient's T1-weighted sagittal cranial MR image showing posterior corpus callosum agenesis