Chapter 4.2

Acquired undescended testis: putting the pieces together

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Abstract

Acquired undescended testis is now a well-recognized disorder. It is seen in 1.5% of prepubertal boys and accounts for the 1-2% orchidopexy rate in older boys. Its pathogenesis remains largely unclear but may be caused by a fibrous remnant of the processus vaginalis. There is much controversy over its management, and the proper management awaits a randomized controlled trial. Until now, follow-up data are available only for cases of spontaneous descent or pubertal orchidopexy. It is speculated that acquired undescended testis is in fact congenital and because of a short funiculus at birth, allowing a low scrotal position early in life. However, as the boy grows, the testis might evolve into an undescended state. When testosterone surges at puberty, spontaneous descent occurs in three of every four cases.
Introduction

Undescended testis (UDT) is one of the commonest anomalies at birth in male children and is associated with impaired spermatogenesis and an increased risk of testicular cancer. UDT may be manifested at birth as congenital cryptorchidism or later in childhood as acquired UDT. Acquired UDT is defined as a testis previously residing in the scrotum, which can no longer be manipulated into a low-scrotal and stable position. It includes high-scrotal, inguinal and non-palpable forms. Acquired UDT accounts for a substantial portion of orchidopexies in boys aged 2 years or older. So far, its aetiology is unclear. In recent years, several studies have made important additions to our knowledge of acquired UDT. In this article, we will discuss the main aspects of acquired UDT and present a model for its pathogenesis.

Background

Scorer (1955) was the first to observe that testes that were thought to be completely descended at birth may ascend to a suprascrotal position with time. Since then, numerous authors have described the phenomenon of non-congenital UDT but initially only in small numbers of patients (Atwell, 1985; Gracia et al., 1997). It is only in recent years that studies with large numbers of patients have been published. Although the phenomenon of acquired UDT has only recently been accepted as a separate entity, it was as early as 1984 that Hadziselimovic et al. concluded that besides congenital UDT, there are cryptorchid boys with "secondary cryptorchidism following apparent complete descent in infancy" (Hadziselimovic et al., 1984). Furthermore, Hutson & Goh (1993) stated that "most children first presenting over the age of 5 years did not have a UDT at birth but have an acquired anomaly". Likewise, Toppari & Kaleva (1999) suggested in "to perform prospective studies on the incidence of ascending testis, because acquired cryptorchidism may partially explain relatively high prevalences reported in some school surveys".

Acquired UDT is now reported in early childhood (Wohlfahrt- Veje et al., 2009) as well as in mid and late childhood. Recently, a cumulative incidence of 7% by age 24 months was found (Acerini et al., 2009). The prevalence rate in mid and late childhood varies from 1% to 2%. However, it is likely that ascending testes are more frequent as in our experience, pre-pubertal boys with an acquired UDT are usually unaware of the condition. Therefore, we believe that it is unjust to explain late presentation by “an obvious delay in diagnosis and management of children in this age group”.
The recognition of acquired UDT

This leads to the question why acquired cryptorchidism has not been recognized previously. There are several possible explanations. First, the traditional view is that boys born with both testes fully descended are not at risk of later development of UDT. Therefore, the finding of an UDT later in childhood has been explained as observer error, misdiagnosis of retractile testes, or late referral. However, in children with UDT, there is frequently a discrepancy between the histories given by the parents and the physical signs elicited by the physician. As early as 1984, Wyllie recognized that “many parents of older boys with UDT insist that the testes were in the scrotum in infancy” (Wyllie, 1984).

Second, recognition must also be attributed to the lowering of the recommended age for orchidopexy. Since the 1940s, this age has been steadily falling from post-puberty to the age of 10–12 years in the 1950s, to 2–3 years old in the late 1970s and to 6 months to 1 year nowadays. As a result of this gradual decline, a well-defined bimodal distribution for age at surgery became apparent with the two peaks at 2–3 years old and 10–12 years old. It was this second peak that eventually led to the recognition of acquired UDT.

Third, in our country a consensus meeting in 1986 on non-scrotal testis contributed greatly to the recognition of acquired cryptorchidism. This conference was initiated to reduce the high number of late orchidopexies; it was agreed that testes, which had been descended at birth or in the early years and which were in non-scrotal position later in childhood should only be treated at puberty. This resulted in periodical registration of testis position at birth and in early years, and subsequently this led to the recognition of acquired UDT. Serial examination and registration of testis position during infancy were recommended as in 1984 by Chilvers et al. (Chilvers et al., 1984).

Acquired UDT and the late orchidopexy enigma

Orchidopexy rates have been reported to be as high as 2-3% in all males up to 14-17 years of age, despite the estimated 0.8-1.0% incidence rate of congenital UDT. At birth, UDT-rates are higher than at 3 months or 1 year of age. As a result of geographical variation the prevalence rate at 1 year of age may be higher in some countries (Boisen et al., 2004). Furthermore, a considerable number of boys undergo an operation at a median age that is well above the recommended age (Kokorowski et al., 2010). This late orchidopexy enigma has been attributed to many factors including misdiagnosis at a younger age, failure of the Child Health Surveillance to detect UDT properly, late referral, inappropriate surgery for retractile testes, family delays, insurance coverage issues and problems with the timing of subspecialty referral. As early as in 1985, Simpson et al. suggested studying the reasons for the high prevalence of orchidopexies (Simpson et al.,
Acquired undescended testis: putting the pieces together

1985). Campbell et al. (1987) and London et al. (1987) were the first to suggest that this was due to non-congenital UDT; nowadays, acquired UDT is considered to be the main cause.

Fertility outcome and risk of testicular cancer

Undescended testis is an established risk factor for developing a testicular germ cell tumour (TGCT). Orchidopexy does not protect patients from developing TGCT, but it allows for earlier detection through self-examination. The age at surgery has been shown to be a risk factor with an age cut-off point of 10-13 years (Pettersson et al., 2007; Herrington et al., 2003). However, others did not find evidence that early surgery for cryptorchidism decreases the incidence of testicular cancer (Myrup et al., 2007). The risk of testicular neoplasia in boys with UDT is higher in combination with intra-abdominal testes, abnormal genitalia, or abnormal karyotypes. In UDT patients testicular microlithiasis does not seem to be a risk factor for TGCT (Goede et al., 2010). However, testicular microlithiasis itself may be an alternative manifestation of a TGCT susceptibility allele (Coffey et al., 2007).

Recent evidence suggests that the malignancy rate in non-congenital UDT is comparable to the normal population (Ong et al., 2005). After natural descent, there is no increased risk of testicular cancer (Herrington et al., 2003). Previous treatment of UDT has no impact on the survival rate of cryptorchid patients with a TGCT. Testicular biopsies of acquired UDT show the same histopathological alterations but less pronounced than in biopsies of congenital UDT (Gracia et al., 1997). It remains unknown what the observed histological abnormalities may mean for fertility outcome and whether surgical intervention will improve or exacerbate these abnormalities.

Treatment

Surgical vs. hormonal treatment of cryptorchidism is still a controversial issue, although it has long been good clinical practice to correct an UDT surgically. Surgery is mainly based on the belief that germ-cell loss is secondary to the non-scrotal position of the testis and not due to an intrinsic developmental anomaly. Orchidopexy carries a significant risk of vascular testicular damage and can cause testicular atrophy in 1–2% of patients (Docimo, 1995).

For congenital UDT, orchidopexy is recommended at 6–12 months of age (Ritzén et al., 2007); this recommendation is based on histopathological studies documenting germ-cell loss in boys operated on after 12 months of age. Early surgery has a beneficial effect on testicular growth (Kollin et al., 2007). On the other hand, the number of germ cells
present in the testis at the moment of orchidopexy rather than the age at surgery is of more prognostic value (Hadziselimovic et al., 2007).

For acquired UDT, most authors have voiced the opinion that at diagnosis, surgical correction is also recommended. This is based on the assumption that the inguinal thermal environment may potentially result in testicular damage and subsequently in decreased spermatogenesis later in life. However, the clinical long-term outcome after pre-pubertal orchidopexy has not yet been systematically assessed, and it is still controversial whether acquired UDT can be best managed by pre-pubertal orchidopexy or by a ‘wait and see’ policy. As a result of pubertal testosterone production, the testis will drop spontaneously in three of four cases. In the past, several authors have propagated a conservative attitude. For example, in Lee (1993) concluded that “the testis which was previously normally descended but resides much of the time during mid-childhood years within the inguinal region may be a variant of normal and not require therapy”. More recently, Guven & Kogan (2008) also concluded that surgery should be deferred. In addition, a report on Nordic consensus on the treatment of UDT advocates that treatment of a high scrotal testis, which comprises 65% of all acquired UDT, is not mandatory in contrast to inguinal and abdominal forms (Ritzén et al., 2007). In addition, it has been shown that there is less spermatogenic damage after spontaneous descent than after orchidopexy. In the Netherlands, a conservative attitude is in accordance with the Dutch consensus and so far the long-term results of this policy have not given us any reason to change this conservative policy in favour of pre-pubertal orchidopexy (Hack et al., 2010).

The aetiology of acquired undescended testis

The precise aetiology of acquired UDT is not yet known but mechanical as well as endocrine factors are believed to be at play. Ascent may be due to either the partial absorption of the processus vaginalis (PV) into the parietal peritoneum (Atwell, 1985) or a fibrous remnant of the PV tethering the testis inguinally (Clarnette & Hutson, 1997). Moreover, the alteration in the length of the inguinal canal as a result of growth, the genito-femoralis nerve, and adhesions developing around a retractile testis while in the high position and prolonged cremasteric spasm, as in cerebral palsy, may also play a role. In addition, deficient or diminished androgenic activity was recently recognized as a possible aetiological factor (Tasian et al., 2010).

The basic anomaly seems to be absolute or relative failure of the spermatic cord to elongate in proportion to increasing body length. As the boy grows, the scrotum moves away from the inguinal region (descensus scroti); however, due to shortness or tethering of cord structures the testis remains stationary, becoming high-scrotal initially, but eventually, it may become inguinal. Therefore, the testis does not actually seem to ascend but rather merely remains stationary while the scrotum moves downwards (Clarnette &
Acquired undescended testis: putting the pieces together

Hutson, 1997). The term ‘ascensus testis’ may therefore be somewhat erroneous. Retractile testes are more prone to undergo ascent, which was first observed by Wyllie (Wyllie, 1984). Between 2 and 45% of retractile testes are reported to become an acquired UDT (Stec et al., 2007). However, we believe that retractility is a sign of a short or tethered funiculus rather than its cause, as shortness renders the testis more instable resulting in retractility.

Putting the pieces together

We believe that there is emerging evidence that acquired UDT is in fact a previously unrecognized congenital UDT. Rabinowitz & Hulbert (1997) were the first to suggest “that testes had originally descended to a location extremely close to their normal location”, thus appearing to be descended. Redman (2005) and Bellinger (2007) arrived at the same conclusion; however, no evidence was advanced.

A theoretical model for the aetiology of acquired UDT is shown in the Fig 1. Around birth, the testis descends to a low position at the bottom of the scrotum with an adequate length of the funiculus. However, if the cord is too short, but just long enough to allow a low-scrotal position, the testis seems descended while it is in fact undescended. As the boy grows, inadequate lengthening will result in a high scrotal position at the age of 3–6 years and in an inguinal position at the age of 7–12 years. At puberty, most testes will re-descend via a high-scrotal position to a low-scrotal position. The concept of undescended testis is therefore not static, but dynamic. It behaves like a yo-yo to reach its final position at early puberty. Retractility contributes to this effect.

The yo-yo model may explain several hitherto unexplained phenomena. It has been shown that acquired UDT shares the same histological abnormalities as congenital UDT, thus suggesting that both phenomena are the same. Moreover, in 23–76% of the cases, acquired UDT is associated with a patent PV, whereas in the normal population, the rate of an open PV is less than a few percent. Furthermore, in the majority of cases, a fibrous remnant of the PV is found. The closure, absorption and consequent disappearance of the upper part of the PV take place only if the testis has fully descended (Scorer, 1962). Therefore, the frequently observed remnant of the PV in acquired UDT is an indication that the testis has initially not reached the point of full descent. Finally, a recent study on perioperative surgical findings in congenital and acquired UDT showed congenital aspects in acquired UDT (Meij-de Vries et al., 2010).

The yo-yo model is supported by the studies by Scorer (Scorer, 1955; Scorer, 1962; Scorer, 1964), who measured the distance from the upper anterior edge of the pubic bone to the centre of the testis. At birth, the testis usually lies low in the scrotum at 5-8 cm from the pubic crest. Scorer arbitrarily defined a testis to be descended if the testis was located 4 cm or more, below the pubic crest (Scorer, 1964). In his studies, he made
Figure 1
A hypothetical model for the pathogenesis of acquired undescended testis. In the normal situation (top series), the funiculus is of adequate length to allow the testis to be in a stable scrotal position. As the boy grows and the distance between the scrotal entrance and the inguinal canal increases, lengthening of the funiculus is adequate allowing a continuous stable-scrotal position. If the funiculus is too short at birth, it still makes scrotal position possible for the testis; the testis is then declared ‘descended’ (bottom, left). However, an extra-scrotal position becomes gradually apparent over the years, resulting in high-scrotal undescended testis (bottom, middle) at 3-6 years of age. As the process evolves, the testis may become completely inguinal (bottom right). If there is some lengthening of the funiculus in the pre-pubertal period, the high-scrotal testis may remain high scrotal until puberty. If no further lengthening occurs, an inguinal position will result. At puberty, 3 out of 4 testes will drop spontaneously due to testosterone surges.
an important observation: “The testes in which descent was incomplete having merely failed to reach the normal 8 cm from the pubic crest were much more common than those in which descent had never started or had failed within or just outside the canal”. In other words, there is a relatively large group of boys with shortness of the funiculus whose testes have been declared descended and these outnumber the boys with (congenital) UDT at birth. Scorer also observed that the former mainly include late descenders (i.e. descent occurs in the first three months after birth). The John Radcliffe Hospital Cryptorchidism Study Group noted that late descendes evolve to early ascenders (John Radcliffe Hospital Cryptorchidism Study Group, 1986). Scorer’s figures suggest that boys born with a short funiculus, but with a testis location more than 4 cm below the pubic crest, are the potential source of boys with impeding acquired UDT.

Conclusion

In conclusion, we believe that our view of congenital UDT should not be limited to the first 3-6 months following birth, but should be extended well beyond it. Congenital UDT may manifest itself at birth as early-UDT but also in mid or even late childhood as late-UDT. In our opinion, for the management of UDT, two different strategies exist: for early-UDT surgical correction is needed, whereas for late-UDT, a ‘wait-and-see’ attitude might be more appropriate.
References


Chapter 4.2


