

## Varicocele

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### Case

A 15-year-old adolescent male was referred urgently by his family doctor with painless left-sided scrotal swelling detected on a routine physical examination. The family doctor had concerns that this finding could represent a testicular tumour. On history, the patient had not noticed the swelling and he is completely asymptomatic. On examination, the swelling is consistent with a high-grade, left-sided varicocele with bilaterally normal sized symmetrical testes. Ultrasound assessment confirms the left varicocele and documents normal symmetrical testes bilaterally. His parents are concerned and asked many questions, such as, "Is this dangerous? Does it cause testicular damage? What should we do with it?"

### Background

Varicoceles are common, affecting up to 15% of males, and become more prominent during puberty due to the increased venous drainage of the developing testis.<sup>1</sup> Virtually all varicoceles are left-sided, likely due to anatomical differences between the venous drainage of the right and left testicles and the nutcracker effect of the superior mesenteric artery. This inadequate venous drainage leads to enlargement of the pampiniform venous plexus of the spermatic cord, causing blood to pool around the scrotal structures, which results in increased heat and stress to the testicle.<sup>2,3</sup> Although the exact pathophysiology of varicoceles is unknown, they are associated with hypoplasia of the developing testicle in adolescence and have been shown to negatively impact semen parameters, the molecular and ultrastructural features of sperm, testicular endocrine function, and fertility in men.<sup>2,3</sup>

Despite these associations, only 20% of men with a varicocele will have future issues with fertility,<sup>3</sup> making treatment decisions in the adolescent population very challenging.

### Challenges

Most studies evaluating different aspects of varicocele management in adolescents use surrogate endpoints, such as testicular size or semen analysis parameters, to guide decisions. Diamond et al reported that the presence of testicular hypotrophy and a discrepancy in testicular size, especially 20% or more difference, was associated with a low total motile sperm count (less than 20 million total motile sperm).<sup>4</sup> Taking into account both testicles, a total testicular volume of less than 30 cc was also associated with a low total motile sperm count in Tanner V boys.<sup>5</sup> Additionally, a peak retrograde venous flow velocity of 38 cm/sec or higher on Doppler ultrasound of the varicocele has been associated with a higher risk of persistent testicular asymmetry over time.<sup>6</sup>

The decision to treat the adolescent varicocele should be based on the ability to improve the most clinically relevant outcomes, such as paternity rates; however, the challenge facing the pediatric urologist is predicting which subgroup of patients will benefit from active early treatment. A recent survey of pediatric urologists studying indications for varicocele treatment in adolescents reported that 96% recommend treatment for smaller ipsilateral testicular size, 79% for testicular pain, and 39% for altered semen parameters.<sup>7</sup> This survey demonstrates the significant heterogeneity in the management of adolescent varicoceles in the pediatric urology community.

The evidence supporting the early treatment of the adolescent varicocele is mixed. A recent meta-analysis of randomized controlled trials demonstrated intermediate and low level of evidence to support radiological or surgical intervention for varicoceles in children and adolescents in order to improve testicular volume and sperm concentration, respectively.<sup>8</sup> Surgical outcomes and adverse events associated with varicocele treatments are not reported consistently in the literature, but all of these procedures do have some level of inherent risk that has to be taken into account. Two reports address the question of paternity rates in men who

underwent varicocele treatment in adolescence. In the first study, the paternity of 286 men who underwent microsurgical varicocelectomy between the ages of 12 and 19 were compared with 122 matched controls.<sup>9</sup> The overall paternity rate was significantly better in the treatment group (77% vs. 48%), supporting the notion that adolescent varicocele repair is beneficial for future paternity. Conversely, a Belgian study assessing paternity rates had contradictory results; after a median of 14 years followup, 78% of adolescents with a varicocele treated with sclerotherapy had documented paternity compared with an 85% paternity rate in those conservatively managed.<sup>10</sup>

In addition to the controversies of whether to treat or not treat an adolescent with a varicocele, there are other considerations and unknowns that add to the complexity of the decision to transition these patients to an adult urologist. The first caveat is relying on discrepancy in testicular size alone as an indicator to treat a varicocele. Studies have shown catch-up growth of testicles in patients with a varicocele that have not been treated but just observed.<sup>11</sup> Secondly, there are significant barriers to adolescents obtaining a semen analysis. Although the American Society of Reproductive Medicine recommends that adolescents presenting with a varicocele in the absence of testicular atrophy should obtain a semen analysis,<sup>12</sup> many do not. In a survey of pediatric urologists treating adolescents with varicoceles, 48% of respondents were uncomfortable asking an adolescent to obtain a semen analysis and 90% of those practitioners who were uncomfortable did not order them for their patients.<sup>13</sup> The survey also determined that the majority of patients and families were not comfortable pursuing the test, primarily due to a lack of knowledge about it. Third, even if a semen analysis is obtained, normal values have not been defined for the adolescent population to predict future fertility potential. The normal reference ranges for the 2010 WHO Standards for Semen Analysis are based on fertile adult men. Even in those adolescent patients with an initial abnormal semen analysis, 47% will normalize over time without intervention.<sup>14</sup> Lastly, the link between developing hypogonadism and the presence of a varicocele and the potential positive endocrine effects of treating a varicocele have not been adequately studied in the adolescent population. Fideleff et al performed a prospective study of 93 adolescents (mean age 12.8 years) with a left varicocele and found no correlation between the presence of a varicocele and hormonal findings when controlling for Tanner stage.<sup>15</sup> In those patients that underwent varicocelectomy, there were no statistically significant differences in pre vs. postoperative hormonal parameters.<sup>15</sup> Given these results, more research is needed before recommendations regarding hormonal testing or discussion of the benefits of adolescent varicocele treatment in preventing hypogonadism can be provided.

## The transition process

Transitioning adolescent patients with a varicocele to adult urology colleagues has historically been inconsistently performed. One survey of pediatric urologists showed that 89% of respondents did not know if their varicocele patients later went on to develop infertility and 42% reported no followup data on their patients after varicocele treatment.<sup>7</sup> Unfortunately, there are no established guidelines for adult urologists to follow when transitioning young patients with varicoceles.

In those patients that are transitioned to an adult urologist, I suggest performing a baseline history that includes questions about symptoms associated with the varicocele and future fertility plans, if known. A scrotal examination is also performed, documenting testicular size (and discrepancy in size), testicular consistency, and grade of the varicocele. After the history and physical examination, I discuss the importance of obtaining a semen analysis and I ask the patient to obtain at least one, but ideally two semen analyses, especially if a semen analysis has not already been performed. I do not routinely order a scrotal ultrasound, but I will obtain one if the physical examination is challenging or to further document any palpable abnormalities of the testicles or scrotal structures. I also do not routinely order a hormonal profile, but would consider ordering one if the patient had any hypogonadal symptoms, which is rare in this age group. After the tests have returned, I bring the patient back to discuss the results and discuss the pros and cons of proceeding with a varicocele procedure, if indicated.

In asymptomatic patients with a normal semen analysis, I do not recommend active treatment. If the semen analysis demonstrates oligospermia and/or asthenospermia with a palpable varicocele, the patient is offered a varicocele procedure immediately or can defer a varicocele procedure until they are looking to start a family or have documented infertility. In those that have a varicocele procedure, I will bring them back for followup at three months for a scrotal examination and repeat semen analysis. In those patients that choose to defer, I counsel them about their risk of infertility in the future and suggest that they come back for re-assessment when they are looking to start a family, have scrotal discomfort on the side of the varicocele, or develop symptoms of hypogonadism. Patient education is key because many years may go by before fertility is an issue and having a known infertility risk factor should streamline future fertility evaluations and treatments, if required.

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## Case summary

The patient and his family are reassured by the discussion with the pediatric urologist regarding his varicocele. The decision is made to observe the patient and a review appointment is arranged for one year. At his review, he remains asymptomatic and his scrotal examination and ultrasound continues to demonstrate normal bilateral symmetrical testes and a left Grade 3 varicocele. The patient is offered an opportunity to perform a semen analysis, but declines at this time. In discussion with the patient and his family, a decision is made to transition the patient to an adult urologist when he turns 18 years old.

The patient is seen by the adult urologist approximately two years later. The patient is now in his first year of university and remains asymptomatic. He is not sexually active and does not have a partner currently, but thinks he would like to have children in the future. His scrotal examination demonstrates normal bilateral symmetrical testes and a left Grade 3 varicocele with no other abnormalities. He agrees to have two semen analyses, which both demonstrate normal sperm concentrations of over 30 million sperm/cc, but progressive sperm motility is somewhat low at around 30% in both samples. After reviewing the results and options of proceeding with a varicocele procedure or waiting for future fertility concerns, the patient decided not to proceed with treatment at this time. He was counselled to return if he became symptomatic with pain or when he wants to start a family.

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