Clinical Vignettes

Case 1

He first presented to a paediatrician with pubertal delay age 16, but the significance of his anosmia was not appreciated and he was discharged from follow-up with "reassurance" and a diagnosis of probable constitutional delay. He was definitively diagnosed upon re-presentation to our Unit with absent puberty age 22, and was prescribed a low-dose T regime - from which he almost immediately defaulted before making any significant progress through puberty and was lost to follow-up. His sister was also found to have KS (and oxycephaly), but was likewise lost to follow-up. Decades later, their details were found on a historic departmental paper database, prompting us to contact their primary care physician to request re-referral to our Unit. At this point, aged 50.8 years, he was struggling to cope with the physical demands of agricultural labour and was facing dismissal by his employer. Improvements in physical endurance and muscle strength resulting from T therapy enabled him to keep his job, although he did rapidly develop male pattern baldness.

Case 2

He presented via primary care with sexual dysfunction aged 38. He was anosmic and gave a history of successful hCG treatment in infancy for micropenis and bilateral retractile testes. He appeared apubertal despite a history of sporadic, unmonitored T and hCG injections overseas, aged 33-35 years. There was no history of anosmia, pubertal delay, or hypogonadism among his ten siblings.

Case 3

He was referred from the neurology department at the age of 69 years, having presented with proximal myopathy of the lower limbs. An open muscle biopsy revealed disseminated atrophy of type 2B fibres. He was noted to be clinically hypogonadal with a small genitalia and an impalpable right testicle. He exhibited classical mirror movements of the upper limbs and gave a history of lifelong anosmia and poor libido. In his twenties he had received T injection over a 3-month period, but this was not continued. Upon joining the merchant navy he had been instructed to shave every day and, even in later life, had dutifully shaved off the outer layer of his epidermis on a daily basis,

even in the absence of any facial hair. A maternal nephew and great nephew were also confirmed to have KS and shared the same *ANOS1* mutation, consistent with X-linked KS.

Case 4

Having undergone bilateral orchidopexy aged 11 years, hypogonadism was strongly suspected and he was scheduled for review at age 14 to ascertain whether or not puberty had begun. However, his parents failed to bring him to that crucial clinic visit (he distinctly recalls wondering why not, but felt unable to question their judgment at the time). Aged 32 years, he was referred with myalgia to a physician, who noted his markedly eunuchoid appearance, but felt unable to broach this during the consultation and failed to initiate a specialist referral. Anosmia was attributed to chronic sinusitis. Aged 58, shortly after the death of his surviving parent, he presented to his primary care physician with fatigue, prompting test for serum testosterone and, thence, referral to our Unit. A brother and sister were reported to be phenotypically normal and had both conceived normal children.

Case 5

He was noted to be markedly eunuchoid, with bilateral gynaecomastia during an admission for minor eye surgery aged 64 years and referred for our opinion. We encountered a frail, apubertal man with short stature and extensive congenital disabilities, comprising facial asymmetry, major visual impairment, severe learning difficulty, severe bilateral hearing impairment with hypoplastic pinnae and a severely hypoplastic right kidney. He was anaemic, severely osteoporotic and exhibited proximal myopathy. He was a long-term care home resident, dependent upon others for most of his activities of daily life and, though unable to form spoken words, was able to understand simple requests and was emotionally very close to his carers. Although his carers over the years and decades were aware that he was obviously hypogonadal through the process of bathing and dressing him, this had never been communicated to his primary care physicians or learning difficulty advocates, because it was incorrectly assumed that “they must already be aware”.

Following discussion with his primary care physician and carers, a “best interests” decision was agreed to begin treating him with T in the interests of ameliorating his anaemia, myopathy,

osteoporosis and general physical frailty. This decision was supported by our Institution's Clinical Ethics Advisory Board, with the proviso that his carers should perform more frequent assessments of his overall status using a dedicated assessment tool. A year later, he had completed puberty, anaemia and myopathy had resolved and he appeared considerably less frail. No episodes of behaviour change or of increased distress were recorded.

Case 6

He was admitted aged 56 years with life-changing injuries following major self-harm episode precipitated by a misunderstanding of his financial circumstances - exacerbated by social isolation and poor self-esteem arising from lack of virilisation. He was referred to us after a nurse performing urethral catheterisation noted his poor genital development. He received the standard psychological counselling for self-harm, but particularly appreciated a bedside visit by a local "expert patient"; he consistently declined any formal psychotherapy. There was a history of childhood surgery for grade 1 hypospadias. Rehabilitation and reconstructive surgery has been ongoing over the past 5 years.

Case 7

He first presented at the aged of 7 years to paediatric services with bilaterally undescended testes. Identification of anosmia and of the existence of a similarly-affected elder brother led to a diagnosis of KS (we later ascertained the existence of numerous KS-affected nephews and great nephews). A short course of hCG injections resulted in testicular descent, without need for orchidopexy. He was later prescribed both hCG and oral TU in an attempt to induce puberty, but was largely non-adherent and was lost to follow-up. Testicular biopsy performed for infertility workup in his twenties unsurprisingly demonstrated immature pre-pubertal testicular tissue. He had suffered a history of depression throughout his life, reporting suicidal ideation during adolescence - mostly stemming from distress at the difficulties encountered at maintaining relationships with women and because he had been (wrongly) told that he could never father a biological child. Having re-presented to our unit aged 51 years with erectile dysfunction, his mood improved significantly with testosterone replacement and also indirectly through improved sexual function.