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PRACTICE

A PATIENT'S JOURNEY

Klinefelter's syndrome—a diagnosis mislaid for 46 years

The patient was initially diagnosed in 1959 at the age of 14 years, but never informed of the diagnosis. He experienced physical and psychological ill effects until re-diagnosis 46 years later

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This is one of a series of occasional articles by patients about their experiences that offer lessons to doctors. The *BMJ* welcomes contributions to the series. Please contact Peter Lapsley (plapsley@bmj.com) for guidance

"Is my life a lie? Am I a man or a woman?" This was my reply in May 2006 when I was asked, "How do you feel at this moment?" I had just had my diagnosis of Klinefelter's syndrome confirmed. It had first been diagnosed 46 years previously, but I had not been told. This had led to emotional turmoil and endless questions, most of which I could not answer. I was angry, sad, bitter, guilty, and confused in no particular order.

I do remember being taken to the Birmingham Children's Hospital in my early teenage years, although the details of the visit are hazy. I do not remember a diagnosis being mentioned. My abiding memory of the period was one of lacking energy and severe muscle weakness, which led to an avoidance of sport. Unlike my peers, I did not shave and was a loner. A lack of concentration and confidence was constantly noted.

On leaving school, I trained as a chef, but an inability to cope with the pressure of the profession resulted in my quitting. I then became a clerical worker and, on being made redundant, gained employment in a local brewery. I met my future wife, a coworker in the brewery, and we married in 1968. We yearned for a child, unaware of my associated infertility. At the age of 40 years, I was diagnosed with Crohn's disease and underwent bowel surgery, leaving me with an ileostomy. This resulted in early retirement. Thus, I slipped into a quiet and mundane life that did not require energy.

This unexciting but comfortable existence was shattered in 2005 when, after a flare up of symptoms related to Crohn's disease, my GP reviewed my case notes before referral. I was shown a letter, written in 1959 by the specialist at the Birmingham Children's Hospital. This folded letter had been in my file, seemingly unread. The doctor read it out to me and said that I had been diagnosed with Klinefelter's syndrome and my father had been informed. I did not know what Klinefelter's syndrome meant and requested a copy of the letter and an appointment with an appropriate specialist. I was seen in the endocrinology clinic at Good Hope Hospital.

On my next visit, Klinefelter's syndrome was confirmed. This condition was explained to me at that point. Initially I could not take in most of what I was told. Chromosomes, sex chromosomes, X's and Y's were mentioned; my mind was confused. Was I living a lie? I did bring this up and was told that I was a man with an extra X chromosome. This was a relief as I had not being living a lie. My wife was as supportive as ever. I approached my father, and he said that he had been informed of a diagnosis but had not understood it and put it out of his mind.

The next question bothering me was how had this condition affected my life? It seemed that my low energy levels, physical weakness, and lack of facial hair were due to the reduced testosterone. What about children? It was explained that infertility was also related to the condition. We could have adopted a child if I had known. That would have given my wife and me something we longed for—a child.

I also had a bone scan, this was normal. At last, something right in my life. I was told that I needed testosterone. I perceived that the lack of this was what had ruined my life. Why did I have to wait until I was over 60 years old to have testosterone? I was asked to rub on testosterone gel, and this was followed up with blood tests. Within days I felt better, much better, and facial hair appeared. I did not shave; the facial hair now comforted me.

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Trouble once again. I was told that my red blood cell count had increased. I was sent to a haematologist, who, after more blood tests, suggested taking a pint of blood every two months depending on my blood count. I could continue to take my testosterone, and this was now increased to two sachets of gel daily. After some time, the red cell count stopped rising above the level considered dangerous.

Matters did not remain calm for long. I was told that my PSA (prostate specific antigen) level, a possible marker of prostate cancer, was raised, perhaps due to the testosterone treatment. I was sent to a urologist. More blood tests, and then the testosterone dose was dropped to one sachet daily. Biopsy was discussed, but there was a risk in view of my ileostomy. Although my PSA level came down, I did not feel well on the lower dose of testosterone—much weaker and with no life within me. I have increased the dose to a sachet and a half and will be followed-up closely.

Have I entered calmer waters? Only time will tell. After these turbulent five years, I am certain that my life is not a lie—I am a man.

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Clinicians' perspectives

Klinefelter's syndrome was first described by Harry Klinefelter in 1942 and occurs in males with an incidence of 1 in 600. An affected male has at least one additional X chromosome. Presentation symptoms vary depending on age. In children, the symptoms often involve learning difficulties such as delay and difficulties in speech, reading, and writing. Presentation in adolescence is more likely to be with abnormal breast development, while infertility is often the complaint in adulthood (Klinefelter's syndrome accounts for about 4% of all male infertility). Other features may include a characteristic appearance (tall, slender body with long legs and short torso), gynaecomastia, hypogonadotrophic hypogonadism, diminished pubic hair, osteoporosis, small firm testes, and psychosocial or behavioural issues. Diagnosis is often dependent on the clinician possessing an insight of Klinefelter's syndrome.

This patient was referred to the Birmingham Children's Hospital in 1959 with unrelated syncope attacks. The registrar in endocrinology investigated for Klinefelter's syndrome based on his clinical suspicion. A buccal mucosal smear revealed a female nuclear chromatin pattern, and a testicular biopsy showed an absence of Sertoli cells in the seminiferous tubules. Bone marrow examination revealed two cells containing 47 chromosomes. These results confirmed his initial suspicion.

On re-referral to endocrinologists 46 years later, the patient demonstrated a XXY chromosomal pattern. His testosterone level was low, 1.9 nmol/L. Testosterone gel was started and unfortunately led to polycythaemia when the dose was increased to 100 mg daily. Regular monitoring of packed cell volume and testosterone levels took place, with venesection performed when the packed cell volume exceeded 0.54. Although the packed cell volume settled, the PSA concentration increased from 4.44 ng/mL in December 2009 to 11.4 ng/mL in August 2011, and on repeat testing in September 2011 [OK?]was 12.3 ng/mL. Testosterone gel was reduced to one sachet (50 mg) daily, with the PSA level reassuringly reducing to 4.49 ng/mL, but the testosterone level not surprisingly decreased to 4.2 nmol/L. After a urology opinion, the testosterone dose was increased to 1.5 sachets.

The patient had genetic counselling upon its availability in 2010 and benefited considerably.

This is a tale of ineffective communication sadly affecting the life of a patient. A mislaid diagnosis in this case negated all the impressive work that took place in making the initial diagnosis. The end effect was the same as a diagnosis missed for 46 years. Communications between primary and secondary care when copied to the patient could prevent similar sad scenarios, and the use of electronic patient records could prevent communications from being mislaid.

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