Eponym

François de la Peyronie and the disease named after him

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Case report

A 56-year-old man presented with a 30-month history of progressive dorsal penile-curvature and loss of penile rigidity. After an initial phase of penile pain during erection, there was a palpable node at the penile dorsum. Following treatment with vitamin E and potassium-para-aminobenzoate, prescribed by the family doctor, pain ceased, although penile angulation remained unchanged. At the time of presentation at our institution, the man did not report penile pain, but penile rigidity had worsened, and sildenafil did not improve the symptoms. Besides Dupuytren's contracture on the right hand, the patients' physical status was normal. He remembered a slight penile trauma during sexual intercourse 12 months before onset of symptoms.

Clinical examination indicated a 40 mm-long and 20 mm-wide plaque in the penile dorsum. Ultrasonography showed calcification of the tunica albuginea. An intracavernosal pharmacon-injection test with 20 mg prostaglandin E1 showed incomplete erection. We used colour-encoded duplex ultrasonography during this test, which showed decreased arterial blood flow in the cavernosal arteries. Dynamic infusion pharmacocavernosometry and cavernosonography provided haemodynamic evidence of venous leakage and plaque-associated drainage as signs of cavernosal dysfunction. During this procedure, a dorsal and left-deviated curvature of 70° and hourglass-like deformity at the site of the plaque became evident (figure 1).

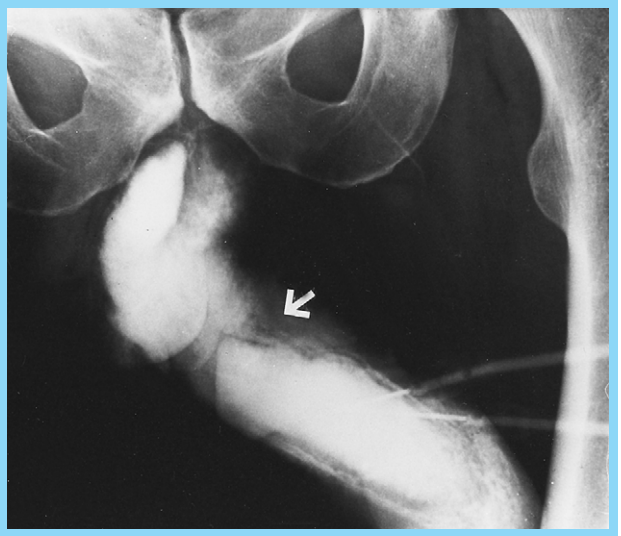

Figure 1: **Dynamic infusion pharmacocavernosography and cavernosometry**
Showing dorsal and left-deviated curvature of 70° during erection, hourglass-like deformity, contrast-medium sparing plaque, and characteristic plaque-associated venous network (arrow=plaque location).

Because of the combination of curvature, deformity, and erectile dysfunction, a hydraulic three-piece penile prosthesis was implanted after total resection of the plaque; the defect was covered with a dacron-patch. After this procedure, the penis was totally straightened, and sexual intercourse became possible to the satisfaction of the couple.

Peyronie's disease is a connective-tissue disorder with plaque formation in the tunica albuginea of the corpora cavernosa. It predominantly affects men aged 40–60 years with an incidence of about 0·3% to 3%. The plaque is usually unifocally located in the penile dorsum causing a typical dorsal deviation and hour glass like-deformity in some cases.[1] The disease may also be combined with erectile dysfunction or distal flaccidity. In the initial, acute phase, patients suffer from penile pain in flaccidity and/or during erection, which is thought to be the result of the active, inflammatory process. In most cases, pain ceases with time.[2] Spontaneous resolution of the disease is typical in the early stages in about half of patients.

Morphologically, an inflammatory reaction with thickening of the tunica with increased fibrin deposition, excessive production of collagen, and loss of elastic fibres is typical; and later on, a fibrotic, often calcified plaque develops. Although the disease was described by François de la Peyronie as early as 1743,[3] its causes remain unclear even today. Recurrent penile trauma during sexual intercourse is the most accepted theory. Hypothetically repetitive microtraumatism triggers an induction of fibrin deposition and consecutive inflammatory reaction, leading to plaque formation. Some individuals could be predisposed because of autoimmune or chromosomal factors, such as an association to the human leucocyte antigen system. Usually, the plaque is diagnosed by palpation on the stretched penis. Confirmation is simple, because most plaques are larger than 1·5 cm and therefore easily palpable.[1] Most plaques are visible using high-resolution ultrasonography, which is the method of choice to show plaque calcifications. Dynamic-infusion pharmacocavernosometry and pharmacocavernosography, which give haemodynamic insights into the function of the corpora cavernosa are restricted to those cases in which plaque surgery is planned.

Because of the absence of concrete knowledge about the definite causes, all therapeutic trials remain symptom-directed and are generally inconclusive. As a result of the high rate of spontaneous regression,[2] only results from double-blind placebo trials are really acceptable. Thus, conservative treatment is required in the earlier inflammatory, painful stages with unproven causes. With regard to intralesional treatment, none of the substances used so far in a controlled approach have shown any long-term effect. Surgical procedures should be only done after an interval of at least 12 months with no disease progression—otherwise the result might be jeopardised by

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Initial		Stable		Final stage
Pain (no calcification)	Deviation and pain	Deviation <60°	Severe deviation >60°, short penis	Erectile dysfunction (drug non-responder)
↓	↓	↓	↓	↓
Potassium-para-aminobenzoate	ESWT	Corporoplasty	Small incision grafting	Penile implant with or without grafting

ESWT=extracorporeal shock-wave therapy.

Therapeutic schedule according to the experience of the Giessen Peyronie's Disease Study Group

recurrent curvature if the disorder progresses. Surgical treatment follows an algorithm depending on the degree of penile curvature and the occurrence of concomitant erectile dysfunction.[4] In cases of normal potency and a curvature of less than 60°, plaque-contralateral corporoplasty is the treatment of choice. Unfortunately, this type of surgical straightening results in penile shortening. If angulation is severe or the penis relatively short, a combination of plaque incision or excision with grafting—eg, with vein or alloplastic material to cover the defect—should be chosen, because these techniques safeguard penile length. The advantage of incisional procedures can be seen in the lower rate of postoperative erectile dysfunction compared with complete plaque resection. If Peyronie's disease is combined with erectile dysfunction, conservative treatment with sildenafil, intracavernous injection treatment, or a vacuum erection device is judged to be in the first line of treatment. In non-responders, such as in the patient mentioned above, implantation of a penile prosthesis usually is accepted as a standard procedure. The curvature can be corrected by modelling the penis over an inflated device or alternatively by plaque incision or excision with consecutive grafting. The table shows a possible therapeutical algorithm, which has been successfully used by our Peyronie's disease study group.

Figure 2: **François Gigot de la Peyronie**
By H Rigaud.

New developments

Studies in animals

Transforming growth factor beta (TGF-β) has been implicated in many chronic fibrotic conditions. Expression of TGF-β 1, 2, and 3 proteins was detected in samples of Peyronie's plaques, but not in the tunica albuginea from a control group. In animals, intratunical injection of cytomodulin, a synthetic heptopeptide with TGF-β-like activity, can induce a Peyronie's disease-like condition in the rat penis with chronic cellular infiltration, focal and diffuse elastosis, and thickening and disorganisation of collagen bundles. Thus, studies in animals could offer the opportunity of testing the effects of drug treatment.

Diagnosis

Magnetic resonance imaging has been suggested as a new method to provide exact information about penile morphology. In Peyronie's disease, plaque formation has been associated with low-signal intensity, disruption, localised thickening, and irregularity of the tunica albuginea. Intravenous application of paramagnetic contrast medium leads to increased local signal intensity on T1-weighted images, whereby the degree of tissue perfusion indicates the inflammatory status of the plaque. Thus, magnetic resonance imaging gives some useful insight into the active or non-active status of the disease.

Management

Two new alternative conservative procedures—extracorporeal shock-wave therapy (ESWT) and iontophoresis—have been introduced for treatment of Peyronie's disease. Although ESWT is already used in the treatment of calcified and non-calcified orthopaedic diseases with obvious clinical effect, the mechanism of action is unclear. There could be a change in the milieu of free radicals with a direct effect on pain receptors in non-calcified diseases and an improvement of vascularisation with consecutive resorption of calcification in calcified plaques. The results of non-controlled studies vary widely with respect to lessening of pain, decrease of deviation, and decrease of plaque size. A case-controlled approach only showed a significant effect of ESWT on decrease of penile curvature.[5] Although these data are discrepant and technical variables have not been standardised, ESWT should be judged as an interesting, but still experimental form of treatment in Peyronie's disease.

Iontophoresis uses electrokinetic transport of charged molecules to enhance transdermal drug transport into diseased tissue, thus reaching high local drug concentrations without systemic side-effects. Different combinations of orgotein, dexamethasone, lidocain, and verapamil have been applied directly above the plaque with improvement of pain, curvature, and sexual function. Results from the only double-blind study that used an iontophoresis-type system (called electromotive drug administration) showed improvement of all symptoms in the verum group with significant differences from the controls.[6] However, although the technical basis of iontophoresis is fairly uniform, the data on drug combination and dose vary widely, and further controlled approaches are necessary.

History

The disorder is named after François Gigot de la Peyronie (figure 2), who described the condition in a treatise on ejaculatory failure in 1743.[3] He reported that rosary beads of scar tissue extended the full length of the dorsal penis, inducing a dorsally directed penile curvature during erection. It is probably because of this description that de la Peyronie has been credited with discovery of the disease,

although he was not the first to report on this condition, which had already been mentioned by Byzantine chronist Zonar and in correspondence between Fallopius and Vesalius. In 1587 Giulio Cesare Aranzi, a famous anatomist from Bologna gave a very precise description of the condition in his book on *Tumores praeter naturam: a rare affection of the genitals in people with excessive sexual intercourse: a little penile tumour palpable like a bean in the flaccid penis causing a deformity similar to a ram horn during erection.*

Although such a penile induration had already been described at an earlier date, it is de la Peyronie who is mainly remembered in connection with the disease. Perhaps the reason for this is that he was not only a brilliant teacher and academic administrator, but also a great surgeon who published numerous surgical case reports. De la Peyronie developed many principles of modern intestinal surgery such as defunctioning of bowel, resection, and back-to-back enterostomy as necessity from the battlefield.[7]

He was born in Montpellier in 1678. His father was a barber-surgeon and the young François soon became interested in his trade. He moved to Paris to receive training from a leading contemporary surgeon, Marechal, who recognised Peyronie's talent and gave him his full support. Later, de la Peyronie became professor of both anatomy and surgery at the University of Montpellier. Despite the enormous animosities which existed between the physicians and surgeons at that time, he brought the various disciplines together in the Royal Society of Sciences of Montpellier in 1706.[7] In search of a more lucrative career he went back to Paris in 1715. As his fame was growing rapidly he treated the famous kings of Europe including Peter the Great.[7] In 1731, together with his teacher Marechal, he founded a scientific society that later became known as the Royal Surgical Society of France. De la Peyronie was also in charge of the Royal Medical Military Service. When Marechal died, he succeeded him as royal surgeon to King Louis XV. Because of his influence on Louix XV, the surgeons were separated from the barbers, who were no longer allowed to practise. Consequently, the surgeons were freed from the tutelage of the medical faculty and received their own doctorship.[7] Peyronie died in Versailles in 1747, leaving behind enormous wealth that was passed on to the surgical communities of Montpellier and Paris. The money provided professorial chairs of anatomy and as well as surgery, numerous scholarships, lectures, and medals that are still sought after by French trainees today.

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Uses of error: Genetic counselling

During my second year in clinical genetics I made a mistake which imprinted my evolution as a geneticist. A young Turkish couple had been referred to me for genetic counselling. They were first degree cousins, and the wife was pregnant. She had had one spontaneous abortion and one healthy child, and another child had died shortly after birth as a result of a metabolic disorder. The couple asked for genetic counselling about prenatal diagnosis and the risk of recurrence.

As usual I ordered the dead child's hospital records. A diagnosis of G_{M1} gangliosidosis was recorded, based on phenotype, the clinical course, and some secondary laboratory results. Metabolic investigations for G_{M1} gangliosidosis were a little equivocal, supporting the diagnosis but not absolutely confirming this condition. The specific enzyme test was not successful. Necropsy revealed histological findings consistent with G_{M1} gangliosidosis. Convinced, I decided to offer prenatal diagnosis, promised a certain result to the parents, and organised the test. I was certain to have done a good job. The laboratory did the diagnostic procedures specific for G_{M1} gangliosidosis and stated that the fetus was not affected. The parents were happy, I was happy, and the pregnancy continued. However, some weeks later I got a call from the obstetrician. The wife had delivered a girl presenting with symptoms very similar to those of the previous child. Metabolic tests were underway and finally congenital sialidosis was diagnosed. It was obvious that I had investigated a disorder not present in this family, and therefore, a negative result was obtained.

What I learned from this case was the following: first, it is not enough to order old records. Second, it is not enough to believe in the most likely diagnosis, particularly when it is not proven. Third, it is necessary to check all diagnostic procedures for their reliability. Fourth, it is necessary to inform the parents, if there are any doubts.

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