CASE REPORT - SUPPLEMENTARY MATERIALS

Distal corpus cavernosum fibrosis and erectile dysfunction secondary to non-ischaemic priapism

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DISCUSSION
Priapism is a urological emergency defined as a prolonged penile erection lasting for more than 4 hours in the absence of sexual stimulation (3). Of the three main priapism subtypes, non-ischaemic priapism is rare, accounting for approximately 5% of episodes and therefore limited data on the natural history of this condition is available (4).

Patients with non-ischaemic priapism usually present with a complete or partial, relatively painless erection. The characteristic lack of penile pain is due to the absence of ischaemia within the corpus cavernosum. The presentation to hospital is often delayed as non-ischaemic priapism is commonly preceded by trauma to the penis or perineum and the onset may take several days or weeks after the initial injury (5). Once the diagnosis is confirmed using cavernosal blood gas analysis and penile duplex studies, the initial management is conservative with regular follow up since the condition often resolves spontaneously (6). Although a history of trauma may precede the priapism by several weeks, rarer causes include congenital (arterial malformations) and idiopathic non ischemic priapism (5). In traumatic cases, disruption of the cavernosal artery and formation of an arterial lacunar fistula (7) leading to unregulated arterial blood inflow into the corpora cavernosa, without obstruction of venous outflow channels occurs (1).

Previous reports have indicated that non-ischaemic priapism may resolve spontaneously in 60% of cases without any long term effect on the erectile function (6). Moreover, in the early period of non-ischaemic priapism, conservative measures include direct compression of the perineum in order to encourage vasospasm and consequently thrombosis of the ruptured artery or obliteration of the fistula. Patients who fail conservative measures eventually undergo superselective embolisation which is successful in up to 89%, of patients. A further embolisation procedure may be required as the recurrence rate is 30-40% (8, 9). Currently there is no standardised time frame to perform super selective embolisation in these patients and embolisation may be delayed for several months. The absence of corpus cavernosum ischaemia should theoretically prevent the development of smooth muscle fibrosis (8). However, in this cohort of patients who presented between 3 and 15 days after the initial injury, smooth muscle dysfunction still occurred on follow up which is a phenomenon not previously reported secondary to non-ischaemic priapism. In two patients repeat angiography and embolisation was required. On both occasions a fistula was found to be in the same place and further embolisation was performed.

Serial imaging allowed identification of patients with features consistent with smooth muscle fibrosis early during follow up. Although penile MRI using T1 and T2 sequences is a useful imaging modality as it can define the extent of the smooth muscle fibrosis in ischaemic priapism (10), fibrosis was not as obvious in non-ischaemic cases although MRI was useful to demonstrate the fistula. Development of cavernosal fibrosis in non-ischaemic priapism is unexpected. However, pO2 levels within the normal penis fluctuate throughout the day between a pO2 of 20-40 mmHg in the flaccid state and approximately 100mmHg in the erect state (11, 12). We hypothesise that in this cohort of patients a persistent arterio-lacunar fistula resulted in maintenance of a high intracavernous pO2 with superoxide free radicals reacting with NO and generating peroxynitrite and hydroxyl radicals. It is possible that this free radical generation causes direct injury to the corpus cavernosum smooth muscle resulting in apoptosis and fibrosis. Provided that there is still enough healthy cavernosal smooth muscle, patients may be either be asymptomatic or respond to PDE-5 inhibitors. It is interesting distal penile flaccidity developed first, indicating distal fibrosis which is similar to ischaemic priapism. However, until myeloperoxidase activity and lipid peroxidation is measured in this tissue, it is unclear as to whether this is due to oxidative stress to the tissue.

An observation from an in vitro model of priapism (13) indicates that superfusion at supraphysiological pO2 (95% O2 and 5% CO2) levels results in a progressive reduction in the smooth muscle tone of pre contracted rabbit corpus cavernosum (unpublished findings). Initially the loss in smooth muscle tone was attributed to upregulation of iNOS but the phenomenon also persists once iNOS is inhibited using dexamethasone and indicates possible smooth muscle dysfunction due to oxidative stress.

The risk of smooth muscle fibrosis is unexpected in cases
of non-ischaemic priapism due to the absence of the parameters of ischaemia namely hypoxia, acidosis and glucopenia (13).
However, this cohort of patients has led us to postulate that sustained perfusion with supraphysiological $pO_2$ levels within the corpus cavernosum may result in the development of fibrosis due to smooth muscle injury secondary to the formation of reactive oxygen species (ROS).
Based on these findings we suggest close clinical follow up of patients presenting with non-ischaemic priapism combined with reimagining using penile Doppler and penile MRI. Features suggesting distal smooth muscle fibrosis either on imaging or the development of distal flaccidity should lead to earlier superselective embolisation to prevent long term erectile dysfunction.

References