S6：シンポジウム6 「過活動膀胱（Overactive bladder）の基礎と臨床」

司会のことば

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本シンポジウムで取り上げた過活動膀胱（Overactive bladder, OAB）は、Abrams&Weinにより提唱された疾患名であり、尿意切迫感（突然、強い尿意が出現し、尿が漏れそうになる）、と頻尿の二つの症状が必要な条件である。2002年ICS用語規約では以下のようにまとめられている。1. Urgency, with or without urge incontinence, usually with frequency and nocturia, can be described as the overactive bladder syndrome, urge syndrome or urgency-frequency syndrome. 2. These symptom combinations are suggestive of urodynamically demonstrable detrusor overactivity, but can be due to other forms of urethro-vesical dysfunction. 3. These terms can be used to if there is no proven infection or other obvious pathology. Sentence 3. の意味するところがあいまいであり、膀胱炎、膀胱結石症などは除外されることには異論がないものの、前立腺肥大症も除外されるのではとの解釈も可能である。このような点においても、統一された見解は得られていないものの、蓄尿時の症状が患者のQOLを強く損ねることから、治療を重視する観点からOABを疾患名として捉えようとの提案は広く認知されるべきものと思われる。本シンポジウムを通して本邦におけるOABの基礎と臨床のいくつかの課題が解決され、OABの診療が充実することを期待したい。

S6-基調講演

Are we treating symptoms or urodynamics-the way forward

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Symptomatic bladder outlet obstruction due to prostatic enlargement is a common problem in urological practice. Hyperactive detrusor function, "detrusor instability", occurs in up to 80% of patients presenting with prostatic obstruction and in most cases it resolves post-operatively when the obstruction has been relieved. This dysfunction is generally regarded as a modern concept but, in 1786, John Hunter recognized the complex nature of prostatic obstruction and reported: "The disease of the bladder arising from obstruction alone, is increased irritability, and its consequences, by which the bladder... becomes quick in its action and thick and strong in its coats."

Animal models have confirmed the relationship between obstruction and instability. Several hypotheses have been proposed to explain this link and include: (1) post-junctional hypersensitivity-possibly related to denervation, (2) altered adrenoceptor function, (3) afferent nerve dysfunction, (4) an imbalance of peptide neuro-transmitters, and (5) a primary or acquired myogenic deficit.

The principal motor control of the intraprostatic musculature is mediated by the sympathetic nervous system; however, the mechanism of action and specific localisation of prostatic adrenoceptors and the importance of non-adren-ergic neuro-transmission in man is poorly understood.

A study of patients with symptomatic prostatic obstruction was undertaken to investigate the influence of neural pathways in determining the pathogenesis and clinical presentation of prostatic and detrusor dysfunction. Sixty-two patients were investigated using modern uro-dynamic techniques and sub-divided into three groups; control, stable obstructed and unstable obstructed. Biopsies of prostate, bladder neck and bladder muscle were taken at the time of surgery, and pharma-

cological, autoradiographic and histochemical studies performed. The prostate, bladder and bladder neck were found to be innervated by a complex network of noradrenaline-, acetylcholine-, neuropeptide-, and amine-containing nerves. Separate quantitative analyses of these neurons were carried out and corrections applied to compensate for muscle hypertrophy and hyperplasia. The histological findings were complemented wherever possible by biochemical assay of neurotransmitters.

There was a significant reduction in the acetylcholinesterase positive innervation of the obstructed bladder compared with control, which was most marked in tissue from patients with detrusor instability. A similar reduction in the non-adrenergic, non-cholinergic sensorimotor neurotransmitters was evident. Biochemical changes within the detrusor included an increase in noradrenaline content and a decrease in the putative sensory neurotransmitter substance P.

Detrusor muscle strips from obstructed patients showed increased contraction in response to acetylcholine, suggesting that denervation hypersensitivity might contribute to the pathogenesis of post-obstructive detrusor instability. Normal detrusor muscle relaxed in response to noradrenaline. In contrast, detrusor muscle from unstable obstructed patients contracted; a response most marked in detrusor muscle from patients who had presented in acute retention.

In vitro prostatic muscle-strip experiments confirmed that contraction of prostatic muscle is produced by α_1 adrenoceptor stimulation. Radioligand binding assays endorsed the results of these experiments by demonstrating a clear excess of α_1 receptors over α_2 receptors in histologically normal and adenomatous prostate. Autoradiography showed the precise localization of the two types of adrenoceptor and confirmed the predominance of α_1 receptors within prostatic musculature.

The complexity and potential importance of the autonomic nervous system in the pathogenesis and symptomatic expression of prostate-mediated bladder outflow obstruction is demonstrated by this work. Marked changes in the innervation of both the prostate and bladder accompany obstructive benign enlargement of the prostate. The characterisation and localisation of the prostatic adrenoceptor is of considerable relevance since it validates the therapeutic use of selective prostatic α_1 blockade in the clinical management of obstructed patients. Preliminary immunohistochemical studies of bladder, bladder neck and prostate are presented, which provide an histological basis for further functional investigative studies.

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OVERVIEW

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過活動膀胱（症）は切迫性尿失禁の有無に関わらず、尿意切迫感と頻尿とを有する疾患名とされ、積極的に治療されるべきと提唱されている。欧州6カ国の40歳以上、約16000人の調査結果によれば、尿意切迫感、頻尿、切迫性尿失禁の頻度はそれぞれ、14%、9%、6%であり、本邦においても同様の頻度であることが予想される。過活動膀胱（症）の患者の診察に際しては、まず、病歴の聴取、症状の評価、理学的所見、検尿、尿流測定、残尿測定を行う。症状の評価には排尿日記、尿失禁がある患者には国際尿失禁スコアの利用が有用である。尿意切迫感（突然、強い尿意が出現し、尿が漏れそうになる）と頻尿（昼間8回以上、夜間1回以上）の存在が確認され、過活動膀胱（症）の診断が確定した場合には、膀胱内圧測定による involuntary detrusor contractions の有無を確認しないで治療に移行する。治療は行動療法（患者教育、時間排尿、排尿の我慢、骨盤底筋体操、再教育）、薬物療法、行動療法と薬物療法の併用が一般的である。薬物療法は抗ムスカリン薬が主に用いられているが、本邦における市販薬としてはオキシブチニン、プロピペリン、フラボキサートなどである。期待される効果は膀胱容量の増加と involuntary detrusor contractions の抑制とが挙げられる。今後の見通しとして諸外国を大幅に上回る速さで一層の高齢化が進むことが予測される本邦においては、全人口に占める65歳以上の割合が2005年（平成17年）には19.6%に、さらに2025年（平成37年）には27.4%にまで増大すると推計されている。過活動膀胱（症）が高齢者に多いことは周知の事実であることから、過活動膀胱（症）の診断と治療法の確立は急務の課題である。