＜シンポジウム 9―3＞前頭側頭型認知症（FTD）をめぐる基礎と臨床の最前線

FTD（前頭・側頭型認知症）神経病理学的研究の最前線

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Key words：ピック病，タウ，TDP43，意味性認知症，進行性非流暢性失語

FTD は，前頭・側頭葉性萎縮（FTLD），言語障害・認知症を呈する，Pick により報告された Pick 症候群の中核症状である．Pick 症候群は，I 型：（Pick 球をともなう）Pick 病，II 型：皮質基底核変性症（CBD），III 型：認知症をともなう筋萎縮性側索硬化症（ALSD）・ユビキチン陽性封入体をともなう FTLD（FTLD-U）に分類される．FTD は「我が道を往く症候群」と呼ばれ，意味性認知症（semantic dementia），進行性非流暢性失語（progressive non-fluent aphasia）とともに，FTLD を構成し，鑑別上，アルツハイマー病，進行性核上性麻痺，嗜銀顆粒性認知症が問題となる．タウは微小管結合部位の数で，3 リピートタウ，4 リピートタウの isoform よりなるが，Pick 病は 3 リピートタウオパチー，CBD は 4 リピートタウオパチーに分類される．FTD の表現型は，タウ遺伝子変異による，第 17 番染色体にリンクした，パーキンソン症状をともなう前頭側頭型認知症（frontotemporal dementia with parkinsonism＝linked to chromosome 17：FTDP-17）でもおきる．ALSD/FTLD-U は，リン酸化，ユビキチン化を受けた TDP-43 が蓄積し，TDP-43 遺伝子異常により同一表現型がえられることより，TDP-43 proteinopathy と最近命名された．

しかし臨床病型と病理型が一致しない点が大きな問題である．臨床病型はケアの点で重要であり，病理型は根本療法のためには必須である．今後後者のためのサロゲートバイオマーカーの確立がきわめて重要である．

Abstract

Neuropathology of frontotemporal dementia

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Frontotemporal dementia (FTD) is a clinical phenotype of dementia, characterized by complex of clinical symptoms, including disinhibition, character change, increased appetite, sexual misconduct and language problems. Frontotemporal lobar degeneration (FTLD) is a pathological classification of neurodegenerative disorder and its core consists of Pick's disease (PiD). Historically, PiD was morphologically subclassified into three types, but recent immunocytochemical investigations defined type I as PiD with Pick bodies (three repeat tauopathy), type II as corticobasal degeneration (CBD, four repeat tauopathy) and type III as FTLD with ubiquitinated inclusions (FTLD-U). The recent progress provided an evidence that the majority of FTLD-U represented primary TDP 43 proteionopathy. Three major clinical phenotypes of FTLD consist of FTD, semantic dementia (SD) and progressive non-fluent aphasia (PNFA). Clinical and pathological correlative studies demonstrated that majority of the background pathology of FTD is PiD with Pick bodies, that of SD is FTLD-U and that of PNFA is CBD, although there are too many exceptions. Although FTD is one of the major clinical manifestations of FTLD, the most frequent pathological background of FTD is Alzheimer disease (AD). The degenerative processes causing FTD symptoms include dementia with Lewy bodies (DLB), progressive supranuclear palsy (PSP) and argyrophilic grain disease. Moreover, vascular process such as Binswanger disease and inflammatory process such as neurosyphilis could also present with FTD symptoms. Since FTD requires special clinical care distinct from AD, clinical diagnosis of FTD is quite important. But for the fundamental treatment based on background pathological processes, surrogate biomarkers, including structural and functional neuroimages and findings of cerebrospinal fluid, blood and urine, should be pursued for future progress in FTD research.

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Key words: Pick disease, tau, TDP43, semantic dementia, progressive non-fluent aphaisa

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