CHAPTER 10

GERSTMANN-STRÄUSSLER-SCHEINKER DISEASE

Pawel P. Liberski
Department of Molecular Pathology and Neuropathology, Medical University Lodz, Lodz, Poland
Email: ppliber@csk.am.lodz.pl

Abstract: Gerstmann-Sträussler-Scheinker (GSS) is a slowly progressive hereditary autosomal dominant disease (OMIM: 137440) and the first human transmissible spongiform encephalopathy (TSE) in which a mutation in a gene encoding for prion protein (PrP) was discovered. The first “H” family had been known by the Viennese neuropsychiatrists since the XXth century and was reported by Gerstmann, Sträussler and Scheinker in 1936. In this chapter we present the clinical, neuropathological and molecular data on GSS with the mutations in the PRNP gene: at codons 102, 105, 117, 131, 145, 187, 198, 202, 212, 217 and 232. In several families with GSS the responsible mutations are unknown.

INTRODUCTION

Gerstmann-Sträussler-Scheinker (GSS) is a slowly progressive hereditary autosomal dominant neurodegenerative disease of the Central Nervous System (CNS) (OMIM: 137440) and the first human transmissible spongiform encephalopathy (TSE) in which a mutation in a gene encoding for prion protein (PrP) was discovered. The true prevalence is difficult to estimate but numbers in a range of 1-10/100 000 000 are quoted.1

According to Budka et al., GSS is defined as a neurodegenerative disease “in family with dominantly inherited progressive ataxia and/or dementia): encephalo(myelo)pathy with multicentric PrP plaques” (Figs. 1,2).

The first “H” family had been known by the Viennese neuropsychiatrists since the 20th century and was reported by Dimitz in 1913,3 then by Gerstmann in 1928 and again by Gerstmann, Sträussler and Scheinker in 1936.5 Later on Scheinker became an established neuropathologist and published, among other works, Neuropathology in Its Clinicopathologic Aspects.6

Neurodegenerative Diseases, edited by Shamim I. Ahmad.
Gerstmann in 1928 described a peculiar reflex, when a patient extended both arms in
front of the chest and then the head was turned to one side, both arms crossed moving to
the midline.\textsuperscript{6} The arm contralateral to direction of turning was placed above the other arm.
Subsequent members of the same family were described by von Braunm"uhl\textsuperscript{7} and Franz
Seitelberger, then director of the Obersteiner Institute, Vienna, Austria.\textsuperscript{8,9} Seitelberger, four
years before the discovery of the transmissible nature of kuru by Gajdusek et al\textsuperscript{10} stressed
the close neuropathological similarity (amyloid plaques—Figs. 1, 2) of these two diseases
and in a sense preconceived the transmissible nature of GSS.\textsuperscript{11} The history of original GSS
“H” family from Vienna is interesting. This family stems from a little rural town in the lower
Austria (Niederoestereich) and had been diagnosed by local physicians as suffering from a
form of hereditary neurosyphilis. As this diagnosis would stigmatize them, they decided to
hide from doctors. In 1990, one of us consulted on a female case suspected of CJD whose
father died with a diagnosis of “Friedreich ataxia”. The maiden name of this case “H” was the
name of the GSS family.\textsuperscript{12,13} This discovery enabled modern studies of that fascinating kindred.

In 1981 a seminal paper by Masters et al\textsuperscript{11} was published. In this paper, several GSS cases
were proved transmissible to nonhuman primates. The Fujisaki strain of GSS (codon 102
mutation) first isolated by Tateishi et al\textsuperscript{14} was passaged to mice, rats, guinea pigs and Squirrel
monkeys. Another case with the same mutation\textsuperscript{15} was passaged to Spider monkeys and to
Marmosets.\textsuperscript{16} To date, only inocula derived from 5 brains with 10\textsuperscript{2.46} could be transmitted.\textsuperscript{17,18}

Of note, in the 1981 paper, Masters et al mentioned the “CG” family described by
Worster-Drought et al.\textsuperscript{19-21} While phenotypically similar to GSS in regard to amyloid
plaques, this family had been later proved to represent Familial British Dementia with
genetic alteration obviously different from that in GSS.\textsuperscript{22}