Heightened incidence of sporadic Creutzfeldt-Jakob disease is associated with a shift in clinicopathological profiles

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M. Glatzel and A. Aguzzi coordinated the design and operation of the study. Katharina Stoeck and Klaus Hess were involved in clinical assessment of patients. M. Glatzel and Dieter Zimmermann were involved in assessment of specimen. All authors contributed to the manuscript and approved the final version. M. Glatzel and A. Aguzzi had full access to all data in the study and had final responsibility for the decision to submit for publication.

The study was performed according to established ethical guidelines

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Abstract Incidences of human transmissible spongiform encephalopathies are monitored by national registries in the majority of countries in Western Europe. During the past 13 years incidences for Creutzfeldt-Jakob disease (CJD) in Switzerland fluctuated between 0.4 and 2.63 cases/10^6 inhabitants. We have compared clinicopathological patient profiles including geographic and gender distribution, age at disease onset, duration of disease, clinical symptoms, and recognized or hypothetical risk factors for CJD, genetic risk factors, biochemical and histopathological data for two cohorts of Swiss sporadic CJD patients from years of regular sporadic CJD incidence (1996–2000, mean incidence 1.3 cases/10^6 inhabitants, n = 47) to Swiss sporadic CJD patients from years of elevated sporadic CJD incidence (2001–2004, mean incidence 2.3 cases/10^6 inhabitants, n = 73). Sporadic CJD patients from the cohort with elevated sporadic CJD incidence presented with a higher frequency of rare sporadic CJD subtypes. Patients of these subtypes were significantly older and showed a skewed male/female ratio when compared to published patients of identical sporadic CJD-types or to patients from the 1996–2000 cohort and indicates that improved detection of rare sporadic CJD subtypes may have contributed to increased incidence.

Key words Creutzfeldt-Jakob disease · prions · dementia · epidemiology
Introduction

Prion diseases or transmissible spongiform encephalopathies are fatal neurodegenerative diseases affecting both humans and animals [23]. Neuropathologically, they are characterized by spongiosis, gliosis, neuronal loss and the accumulation of an aberrantly folded isoform of the normal cellular prion protein, termed PrPSc, which is an essential component of the infectious agent [22]. The most common human prion disease, sporadic Creutzfeldt-Jakob disease (sCJD) comprises about 85% of all human prion diseases and is of unknown origin. sCJD may present with a marked clinical heterogeneity. By combining clinical features with histopathological analysis, the status of a polymorphism on the gene encoding the prion protein as well as biochemical analysis of PrPSc, several sCJD types may be differentiated [14, 19].

About 15% of human prion diseases are caused by known mutations in the prion protein gene (PRNP) and may be inherited as autosomal dominant traits [15]. A further subset of human prion diseases are acquired by exposure to infectious prions, in the framework of neurosurgical interventions or through hormone substitution, and are referred to as iatrogenic CJD [2]. A novel human prion disease, variant CJD (vCJD), is thought to be caused by exposure to BSE prions via uptake of BSE-contaminated material or by transfusion of vCJD-contaminated blood products [3, 13, 20, 29].

The appearance of vCJD and its development into an epidemic in the UK has led to the establishment of CJD surveillance centres among European countries which carry out active surveillance according to standardized protocols in order to identify and monitor the epidemiology of human prion diseases (http://www.eurocjd.ed.ac.uk/).

In 1995, the Swiss National Reference Centre of Prion Diseases (NRPE) was established and active CJD surveillance has been conducted since 1996. This includes clinical and epidemiological assessment of patients, genetic analysis, as well as pathological and biochemical analysis of tissue specimens [25].

From 1996 to 2000, sCJD affected between seven to 11 patients per year, corresponding to an annual incidence of 1.0 to 1.4 patients per million per year which is well in line with the presumed global incidence of sCJD, about one patient per million per year [11]. However, in 2001 the number of sCJD patients increased to 18, translating to an incidence of 2.5 patients per million per year [10]. In the subsequent three years, the incidence remained elevated, ranging from 1.4 to 2.0 per million per year (Fig. 1).

The aim of the present study was to compare clinical, genetic, biochemical and pathological features of sCJD in two cohorts of patients. The first cohort comprises patients from the years 1996 to 2000 with an average incidence of sCJD of 1.3 per million per year, whereas the second cohort comprises patients from the years 2001 to 2004 with an average incidence of sCJD of 2.3 per million per year.

Patients and methods

Patients

In this study, 120 sporadic CJD patients, who were reported to the Swiss National Reference Centre of Prion Diseases (NRPE) and to the Swiss Federal Office of Health between 1996 and 2004, were included. Clinical information including assessment was carried out according to standardized protocols. We collected tissues at necropsy from patients according to established safety and ethical guidelines [4]. The group comprises 109 'definite', neuropathologically-proven, and 11 'probable' CJD patients, corresponding to a proportion of 'definite