Objective: To evaluate clinical features of a ALS1 H46R after 15 years since the first report of 2002.

Patients and Methods / Material and Methods: We interviewed 15 Japanese cases including eight patients in five successive generation and conducted neurological examination in 2002. We found an A to G transition in exon 2 of the SOD1 gene that resulted in a H46R substitution. Affected 71 year-old female of clinical course of 47 years died of pneumonia and her neuropathological findings confirmed FALS. The disease duration of this family was 18.1±13.2 (M±SD) years with the age of onset in 2002. The initial sign was unilateral distal weakness of lower limb, extending to the other lower limb. A wheel chair became necessary at 9.8±3.2 years after the onset. Upper limb No patient had bulbar sign, extra ocular movements(EOMs) abnormality and respiratory failure except the autopsied case. Three affected sibling in this family(one female, two males) were enrolled in this study in 2017. The disease duration of them was 32.0±8.2 years and the age of onset was 44.0±10.1y/o. The clinical features of them were weakness and atrophy of extremities without bulbar sign, EOMs abnormality and respiratory failure.

Results: Result: The progression of ALS1 H46R is extremely slow. The initial sign appeared in the distal portion of unilateral lower limb.

Conclusion: Conclusion: ALS1 H46R has characteristic features.

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Background: Contacting site of endoplasmic reticulum (ER) and mitochondria, which called mitochondria-associated membrane (MAM), regulates various functions including calcium (Ca2+) transfer from ER to mitochondria. Sigma 1 receptor (Sig1R), a gene product of SIGMAR1, is a chaperone specifically localized in MAM. Recessive mutations for SIGMAR1 gene were causative for juvenile ALS, ALS16.

Objective: To clarify the role of the MAM in the pathomechanism for ALS.

Patients and Methods / Material and Methods: Whole exome sequencing was performed for juvenile ALS patient. Characterization of mutant Sig1R proteins was performed in cultured cells and Sig1R-deficient mice. The integrity and role of the MAM was examined in Sig1R-deficient mice and mutant Cu/Zn superoxide dismutase (SOD1) mice. Institutional Review Board / Animal Use Committee approval were obtained for this study.

Results: We identified a novel recessive mutation c.283dupC/p.L95fs in SIGMAR1 gene, which causes juvenile inherited ALS (ALS16). The mutant Sig1R proteins were unstable, and unable to regulate the intracellular Ca2+ flux. The loss of Sig1R function accelerated the disease onset by more than 20 % in mutant SOD1 mice. Moreover, collapse of the MAM structure was observed both in Sig1R deficient mice and mutant Cu/Zn superoxide dismutase (SOD1) mice. Institutional Review Board / Animal Use Committee approval were obtained for this study.

Conclusion: These results indicate that collapse of the MAM is a common pathomechanism in both Sig1R- and SOD1-linked ALS. Furthermore, our result of the selective enrichment of IP3R3 in mutant SOD1 mice suggests that integrity of the MAM is crucial for the selective vulnerability in ALS.

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Background: We recently identified pathogenic mutations in the coiled-coil-helix coiled-helix domain containing 2 (CHCHD2) gene from the patients with Parkinson’s disease (PD) with autosomal dominant inheritance. The homologous gene; CHCHD10 has been known the association among the patients with frontotemporal dementia and amyotrophic lateral sclerosis (ALS).

Objective: To elucidate the prevalence of the CHCHD2 variants or mutations in the patients with sporadic ALS.

Patients and Methods / Material and Methods: We obtained 944 DNAs of ALS, supported by Japanese Consortium for ALS Research. We screened entire exon and exon-intron boundaries in CHCHD2, using Sanger sequencing. We referred allele frequencies on the basis of bioinformatics data. We investigated the pathological findings of a brain, harboring novel variant, and the expression levels of CHCHD2 using real-time quantitative reverse transcriptase-PCR (RT-qPCR) and Western blotting.

Results: We identified one novel variant; -8T>G in the 5’ UTR region and three variants previously reported (-9T>G, 5C>T, and *125G>A), of which minor allele frequencies have no differences between patients with ALS and controls [p = 0.22, odd ratio (OR): 1.19; p = 0.99, OR: 1.00; p = 0.14, OR: 0.69, respectively]. We obtained the brain pathology harboring -8T>G, which revealed high amounts of TDP-43, along with moderate amount of Lewy bodies and neurofilibrillary tangles as Braak’s stage 3, and amyloid plaques as NIA-AA score A3. The expression analysis indicated the lower levels of CHCHD2 protein comparing to those of controls and PD.

Conclusion: CHCHD2 variant -8T>G probably relates to both synucleinopathies and tauopathies via suppressive regulation.
Background: Stroke remained a major public healthcare burden worldwide despite availability of modern acute treatment. For instance in ischemic stroke, results from clinical trials and routine clinical practices shows that patients who receive thrombolysis treatment within 3 hours from stroke onset are more likely to have minimal or no disability. In our previous study, we found < 1% of our ischemic stroke patient were eligible for thrombolysis treatment.

Objective: We aim to describe stroke patient characteristics and factors associated with delayed hospital admission.

Patients and Methods / Material and Methods: All stroke patient demographic and clinical data recorded in the National Neurology Registry (NNR) from July 29, 2009 to April 19, 2016 were extracted for analysis. Descriptive analysis was performed. Factors associated with delayed hospital admission were examined using logistic regression.

Results: A total of 9365 stroke patients from 15 public hospitals across the country were registered in the NNR. Of these, 26.6% arrived within 3 hours of symptoms onset with their own transport. After adjustment of confounding factor, Chinese ethnicity (age below 60 years), male gender, Chinese ethnicity, higher education level (> 12 years) arrived within 3 hours on symptoms onset with their own transport. After adjustment of confounding factor, Chinese ethnicity and higher education level remained to be positively associated with early hospital arrival. Stroke symptoms such as hemiparesis, speech disturbance and vertigo were not recognized as warning sign to seek immediate medical care.

Conclusion: Stroke symptom recognition and time from stroke onset to hospital arrival is critical in acute stroke management to reduce disability.

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Wcn17-2091
FREE PAPERS: STROKE 3
Clinico-radiological evaluation of intracranial venous sinus thrombosis in a large cohort from India
K.R. Naik, A.O. Saroja. aKLE University’s Jawaharlal Nehru Medical College, Neurology, Belagavi, India; bKLES Dr. Prabhakar Kore Hospital and MRC, Neurology, Belagavi, India

Background: Cerebral venous thrombosis affects all age groups and has multifactorial aetiology. Clinical syndrome is acute, subacute and chronic with features of intracranial hypertension, focal deficits, seizures and altered consciousness. Early diagnosis and anticoagulation results in good outcome.

Objective: To evaluate risk factors, clinical profile and outcome in a large cohort of cerebral venous thrombosis.

Patients and Methods / Material and Methods: Patients with radiologically proven CVT were evaluated both prospectively and retrospectively over a period of 16 years. Their clinical profile including symptom duration, risk factors and laboratory parameters were analysed. Outcome at discharge was assessed using modified Rankin score.

Results: There were 548 CVT patients (men 349, women 199) with mean age of 34.12 years (SD 11.62). Eighty-six percent had intracranial hypertension, 59.5% had seizures (6.7% of them with status epilepticus), 61% had focal neurological deficits and 45% had altered consciousness. Uncommon symptoms included aphasia, hemianopia and impaired vision. Single etiological factor was present in 39% and multiple in 61%. These included pregnancy (15.15%), anaemia (46.5%), polycythemia (16%), hyperhomocysteinemia (32.5%), tobacco chewing (12%), alcohol (20%), and hormonal preparation (15.5% of non-pregnant women). Other causes were malignancy, psoriasis, ulcerative colitis, retroviral disease and infections. Seventy-four had deep cerebral venous thrombosis and 11 had cerebellar infarction. Seventy percent had good outcome and mortality was 7.9%. Presence of infarction predicted poor outcome in men and non-pregnant women (P < 0.0001).

Conclusion: This is a large CVT cohort from a single center. Tobacco chewing and alcohol are preventable risk factors in men. Low admission Glasgow coma score and status epilepticus predicted poor outcome.

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Wcn17-2094
FREE PAPERS: STROKE 3
Cerebral venous thrombosis in older individuals: a hospital based retrospective study
N.M. Shah a, A.O. Saroja a,b, K.R. Naik a,b. aKLE University’s Jawaharlal Nehru Medical College, Neurology, Belagavi, India; bKLES Dr. Prabhakar Kore Hospital and MRC, Neurology, Belagavi, India

Background: Cerebral venous thrombosis (CVT) is common in younger individuals. Older individuals are more prone for arterial ischemic strokes and haemorrhages whereas venous thrombosis is uncommon. The literature on cerebral venous thrombosis in older individuals is sparse.

Objective: To evaluate clinical profile, etiology and outcome of CVT in older individuals.

Patients and Methods / Material and Methods: Patients above 44 years with radiologically proven CVT from 2006 to 2016 were included. Clinical data, imaging and laboratory parameters were obtained from their case records. Outcome at discharge was assessed using modified Rankin score (mRS).

Results: There were 115 patients whose age was 52.54 ± 7.96 years (range 45 to 84, median 50 years) with male : female ratio of 2:4:1. Eighty-five percent were below 60 years. Symptomatology included intracranial hypertension (79%), seizures (53%), hemiparesis (57%) and altered consciousness (45%). Comorbidities were diabetes and hypertension. Risk factors were anemia (40%), hyperhomocysteinemia (42%), polycythemia (19%) and alcohol (12%). Other causes were hormonal preparations, tobacco, malignancy, dehydration, infection, inherited prothrombotic state and sepsis. Imaging revealed cerebral infarction in 86.9%. Multiple sinuses were involved in 63.5% and single sinus in 36.5%. Five patients had cavernous sinus thrombosis. In-hospital mortality was 13% and good outcome was seen in 61.7%. Conclusion: Elevated blood sugars, dehydration and increasing age were associated with poor outcome and mortality. The presence of parenchymal lesions or sinuses involved did not affect the outcome.

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Wcn17-2140
FREE PAPERS: STROKE 3
Expression of sphingosine-1-phosphate receptor 1 in leptomeningeal arteries is upregulated and its agonist improves neurological outcome in ischemic stroke in mice
E. Iwasawa a, F. Li a, S. Ishibashi a, M. Ichijo b, K. Miki b, T. Yokota b. aTokyo Medical and Dental University, Department of Neurology and...