Title	Ischaemic stroke related to branch artery disease: a missing link?
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Ischaemic stroke related to branch artery disease: a missing link?

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Introduction: Clinicians and researchers often classify atherosclerotic cerebral infarctions into large artery atherothrombotic disease (LAD) and small artery lacunar infarction (LACI), but this system of 'dichotomisation' cannot account for a substantial proportion of stroke cases. Twenty years ago, a third mechanism for cerebral infarction—branch artery disease (BAD)—was proposed. However, this concept was understudied and still remains an obscure entity.

Methods: Stroke patients admitted under the Neurology Unit of Queen Mary Hospital over a 24-month period were studied retrospectively. Patients with ischaemic stroke presumably due to atherosclerotic disease were classified according to their imaging +/– clinical findings into three groups: LAD, BAD, and LACI. Patients with BAD were further categorised into five BAD stroke syndromes based on radiological criteria. Clinical characteristics, vascular risk factors, results of vascular workup, and outcome among the various stroke subgroups were compared.

Results: A total of 720 patients with a diagnosis of stroke were admitted during the study period, including 123 LAD (17% of all stroke patients or 33% of all studied patients), 147 BAD (20% or 40%), and 102 LACI (14% or 27%). Among the BAD patients, the number of cases involving Heubner's artery, lenticulostriatal arteries, anterior choroidal artery, thalamoperforating/geniculate arteries or paramedian pontine infarction were 0, 47, 45, 15 or 40 (0, 32, 31, 10 or 27%), respectively. Patients with BAD were the youngest among the three groups. As compared to LAD patients, BAD patients had lower NIHSS scores, were less often diabetic, and carotid stenosis was less common, while stenosis of the intracranial arteries were more frequently seen in BAD as compared to LACI patients. Mean follow-up period was 1085 days, and outcome of BAD patients was intermediate between LAD and LACI. Comparison of variables among the BAD stroke syndromes showed that they were a homogenous group of conditions.

Conclusion: Despite being a rarely applied concept, BAD is the most prevalent subtype of ischaemic stroke in our study. The homogeneity among the BAD syndromes suggests they might represent a distinctive stroke entity. Although patients with BAD and LACI had similar degrees of neurological deficits on presentation, outcome in the former group was significantly worse than the latter.

Generation of human-induced pluripotent stem cells in feeder-independent, serum-free culture system with defined factors

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Introduction: Induced pluripotent stem cells generated from human adult somatic cells through reprogramming hold great promises for future regenerative medicine. However, exposure of human-induced pluripotent stem cells to animal feeder cells and serum in the process of their generation and maintenance imposes risk of transmitting animal pathogens to human subjects, thus hindering the potential therapeutic applications. Our aim was to generate patient-specific human-induced pluripotent stem cells in a feeder-independent culture system with defined factors.

Methods: Fresh human dermal fibroblasts obtained from two healthy volunteers were reprogrammed with a defined set of transcription factors using lentiviral vectors in a feeder-independent cell culture system with defined culture medium.

Results: Two new human-induced pluripotent stem cell lines were generated from dermal fibroblasts of the two subjects under feeder-independent culture system with defined factors. The resultant cells maintained normal karyotypes and expressed a panel of pluripotency markers including stage-specific embryonic antigen (SSEA)–4, tumour-rejection antigen (TRA)-1-60 and TRA-1-81, and alkaline phosphatase. In addition, these cells can be induced to differentiate along lineages representative of the three embryonic germ layers upon formation of embryoid bodies, indicating their pluripotency. Furthermore, subcutaneous transplantation of these cells into immunodeficient mice resulted in teratoma formation.

Conclusion: Our findings are an important step towards generating patient-specific human-induced pluripotent stem cells in a more clinically compliant manner by eliminating the needs of animal feeder cells.