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RESEARCH WATCH

Clonal hematopoiesis of indeterminate potential (CHIP): A potential contributor to atherlosclerotic cardio/cerebro-vascular diseases?

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Abstract At least 10% of the elderly population above the age of 70 carry a condition termed clonal hematopoiesis indeterminate potential (CHIP) due to oligoclonal expansion of mutated hematopoietic stem cells. Although CHIP is known to predispose patients to a higher risk of malignant blood disorders, the recent revelation of its association with higher morbidity and mortality of atherosclerotic cardiovascular disease and ischemic stroke is rather surprising. Two independent research groups published studies indicating that Tet2 mutated monocytes from mice modeling CHIP had a causal role in accelerating the growth of atherosclerotic lesions due to their pro-inflammation activities. This important discovery points to CHIP as a risk factor and raises the prospect of novel treatment to minimize the adverse cardio/cerebro-vascular events.

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Clonal hematopoiesis of indeterminate potential (CHIP) is a blood disorder more frequently associated with the elderly population.[1–3] According to an analysis published in 2014, at least 10% of the elderly subjects beyond the age of 70 were found to be affected by CHIP. The prevalence nearly doubles among those beyond the age of 90.[4] In CHIP patients a portion of genetically-mutated white blood cells, such as neutrophils and monocytes, persists in circulation due to oligoclonal expansion of mutated hematopoietic stem cells. Clinically most of these patients are otherwise healthy and can live with CHIP for years without any bone marrow pathology. Although CHIP is known to predispose patients to various malignant blood disorders, its associations with the heart attack and ischemic stroke are rather surprising.[4] These recent findings have raised the possibility of CHIP as a previously unknown risk factor for elderly patients and may help explain why a small group of elderly patients with coronary heart disease and stroke have no identifiable risk factors, such as high blood cholesterol, hypertension, smoking, and diabetic conditions, a phenomenon that has long baffled clinicians.[5] Tet2, a gene known to have a role in inflammation regulation,[6] is one of the few genes found to be frequently mutated in CHIP blood cells. To examine the link between CHIP and mortality among elderly patients from cardio/cerebro-vascular events, two independent research groups have recently presented their findings using *Tet2* genetically altered mice modeling CHIP.[7,8] Researchers found Tet2-deficient mouse monocytes to have a more active proinflammatory responses in the presence of low density lipoprotein (LDL) and endotoxin. Upon bone marrow transplantation into the atherosclerotic mice, the mutated monocytes infiltrated and accelerated the growth of vascular atherosclerotic lesions in contrast to control mice which received normal hematopoietic cells. This characterization of CHIP as a potential contributor to atherosclerotic cardio/cerebro-vascular diseases raises the promise of developing novel anti-inflammation agents targeting the "rogue" white blood cells. Since Tet2 is only one of several genes found to be frequently mutated in CHIP, further clinical and preclinical studies are warranted to examine the role of other genes involved in CHIP among patients with heart attack and ischemic stroke.

Conflict of interest

The authors declare that no conflict of interest exists.

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