The Indo-Asian collision caused uplift of the Himalayan orogen, growth of the Tibetan plateau, a ~70-km-thick continental crust, and large amounts of materials from the Tibetan plateau escaping towards east, southeast and west along large scale strike-slip faults. How the Indo-Asian collision controlled tectonic transition from compression to strike slip in the convergent boundary is critical for our understanding of deformation mechanisms of the continental lithosphere. Based on structural, metamorphic and magmatic records in the Himalayan orogen and SE Tibet since 55 Ma, we established a 3D kinematic extrusion model of the Greater Himalayan Complex. Extrusion of the Greater Himalayan Complex was triggered by partial melting of the middle and lower crust of the Himalayan orogen in the Eocene, and accommodated by coeval southward thrusting and orogen-parallel ductile extension since the Oligocene. Since the late Eocene, lithospheric bending around the eastern Indian indenter and mid-crustal decoupling occurred to allow southeastward escape and clockwise rotation of the continental blocks (i.e., the Lhasa terrane, the Qiangtang terrane). Combined with data of plate reconstruction in Southeast Asia, we propose that the tectonic transition from compression in the Indo-Asian collision zone to strike slip in SE Tibet was related to the transition from the Indo-Asian “continent-continent collision” to the Indian Ocean-SE Asian “oceanic-continental subduction”.