Hereditary spastic paraplegias (HSPs) comprise a group of genetically heterogeneous neurodegenerative disorders characterized by spastic weakness of the lower extremities. We have generated a *Drosophila* model for HSP type 10 (SPG10), caused by mutations in *KIF5A. KIF5A encodes* the heavy chain of kinesin-1, a neuronal microtubule motor*.* Our results imply that SPG10 is not caused by haploinsufficiency but by the loss of endogenous kinesin-1 function due to a selective dominant-negative action of mutant KIF5A on kinesin-1 complexes. We have not found any evidence for an additional, more generalized toxicity of mutant Kinesin heavy chain (Khc) or the affected kinesin-1 complexes. Ectopic expression of *Drosophila* Khc carrying a human mutation (N256S) is sufficient to disturb axonal transport and to induce motoneuron disease in *Drosophila*. Neurofilaments, which have been recently implicated in SPG10 disease manifestation, are absent in arthropods. Impairments in the transport of kinesin-1 cargos different from neurofilaments are thus sufficient to cause HSP-like pathological changes such as axonal swellings, altered structure and function of synapses, behavioral deficits and increased mortality.