Simple genetic diagnosis of hairy cell leukemia by sensitive detection of the *BRAF*-V600E mutation

Semplice diagnosi genetica di leucemia a cellule capellute mediante il rilevamento della mutazione BRAF-V600E.

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Abstract

Hairy cell leukemia (HCL) is a distinct clinicopathologic entity that responds well to purine analogs but is sometimes difficult to differentiate from HCL-like disorders (eg, splenic marginal zone lymphoma and HCL variant). We recently identified the *BRAF*-V600E mutation as the disease-defining genetic event in HCL. In this study, we describe a new, simple, and inexpensive test for genetics-based diagnosis of HCL in whole-blood samples that detects *BRAF*-V600E through a sensitive allele-specific PCR qualitative assay followed by agarose-gel electrophoresis. This approach detected *BRAF*-V600E in all 123 leukemic HCL samples investigated containing as few as 0.1% leukemic cells. *BRAF*-V600E was detected at different time points during the disease course, even after therapy, pointing to its pivotal role in HCL pathogenesis and maintenance of the leukemic clone. Conversely, 115 non-HCL chronic B-cell neoplasms, including 79 HCL-like disorders, were invariably negative for *BRAF*-V600E. This molecular assay is a powerful tool for improving the diagnostic accuracy in HCL.

Riassunto

La Leucemia a cellule capellute (HCL) è un'entità clinico-patologica distinta che risponde bene agli analoghi delle purine, ma a volte è difficile differenziare l' HCL da altre malattie (ad esempio, il linfoma della zona marginale splenica e variante HCL). Recentemente abbiamo identificato come evento genetico per definire la malattia HCL, la mutazione BRAF-V600E. In questo studio, descriviamo un nuovo test semplice e poco costoso per la diagnosi genetica di HCL su campioni di sangue intero che rileva la mutazione BRAF-V600E. Questo approccio ha rilevato la mutazione BRAF-V600E in tutti i 123 campioni leucemici HCL indagati contenenti da un minimo di 0,1% delle cellule leucemiche. BRAF-V600E è stato rilevato a tempi diversi durante il corso della malattia, anche dopo la terapia, indicando il suo ruolo chiave nella patogenesi HCL e manutenzione del clone leucemico. Al contrario, 115 neoplasie croniche a cellule B non-HCL, tra cui 79 con disturbi HCL, erano invariabilmente negativi per BRAF-V600E. Questo saggio molecolare è un potente strumento per migliorare l'accuratezza diagnostica in HCL.

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