Targeting c-KIT, PDGFR in cancer of unknown primary: a screening study for molecular markers of benefit.

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Source

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Abstract

AIMS:

In view of available targeted therapies, we investigated the presence of c-kit, PDGFR gene mutations and protein expression in cancer of unknown primary (CUP) in order to study their contribution in pathogenesis, their prognostic value and potential as therapeutic targets.

METHODS:

Mutations in hot spots c-kit exon 11 and PDGFR exons 12 and 18 were studied in paraffin-embedded tumour samples from 50 patients with CUP by means of PCR-based single-strand conformational polymorphism and protein expression by means of streptavidin-biotin immunoperoxidase assays. Molecular markers were screened for possible correlations with patient outcome.

RESULTS:

No shifted band was detected in any of the polyacrylamide gel electrophoreses, indicating absence of c-kit exon 11 and PDGFR exon 12, 18 mutations. Immunohistochemical analysis in 37 tumours revealed positive membranous CD117 expression in 30 samples (81%) of which five exhibited strong (+3), four moderate (+2) and 21 weak (+1) staining. PDGFRa protein staining was seen in 15 out of 30 (50%) cases, mostly weak (13) and rarely moderate (1) or strong (1). The expression of KIT or PDGFRa protein did not correlate with the clinical outcome of the patients in our cohort.

CONCLUSIONS:

In a moderate-sized CUP patient cohort, KIT or PDGFRa protein overexpression is rare, does not have gross prognostic significance for survival and is not associated with presence of activating mutations.