Melanoma subtype

Reason/Evidentiary Support:

The common subtypes listed (superficial spreading melanoma, nodular melanoma, and lentigo maligna melanoma), have little if any prognostic significance independent of tumour thickness, interpretation is subjective and prone to interobserver variation,1-5 and their use is principally for clinicopathological correlation. Nevertheless, the traditional (“Clark”) melanoma histogenetic classification highlights the myriad of clinical and histological guises of melanoma, which if not recognized by clinicians and pathologists will inevitably lead to a delay in diagnosis and a concomitant adverse clinical outcome.6 The traditional classification has been criticised because the criteria upon which it is based include clinical features (such as the site of the melanoma) and non-tumourous histopathological features (such as the character of the associated epidermis and the degree of solar elastosis) and also because of overlap in defining features, lack of an independent association with patient outcome and minimal relevance as a determinant of clinical management.

Epidemiological and molecular genetic evidence suggests that there are subgroups of melanoma that are associated with specific genetic alterations. The mutations identified in melanomas have included NRAS (15-20%), BRAF (50%), KIT (2%), and GNAQ/GNA11 (50% of uveal melanomas). There are associations between the presence of some mutations and the anatomical site of a melanoma and the degree of solar elastosis.7-8 A comparison of the traditional clinicopathological melanoma classification with a classification based on the somatic mutation status reveals remarkable similarities. For example, melanomas associated with prominent solar damage (lentigo maligna melanomas) commonly have NRAS and sometimes KIT mutations, whereas superficial spreading melanomas that arise in the skin of intermittently sun-exposed areas often have BRAF mutations. KIT mutated melanomas most often involve acral (acral lentiginous melanoma) and mucosal sites. Nevertheless, the degree of accuracy of melanoma histogenetic subtype (or histopathological assessment) for predicting the mutation status of a melanoma is not sufficient to replace mutation testing for the purposes of patient care.

References: