Genetic status (Recommended)

Reason/Evidentiary Support

It is estimated that approximately 10% of primary tubo-ovarian and peritoneal carcinomas have a genetic basis,[1] and recent data suggest that this figure may be as high as 17% for high-grade serous carcinomas specifically.[2] Germline mutations in *BRCA1* and *BRCA2* account for the majority of genetically related cases while up to 10% of such cases are related to Lynch syndrome (LS).

It is acknowledged that definitive genetic status is often not known or information about genetic status is not provided to the pathologist at the time of surgery. Moreover, this information is not essential for the histological assessment and routine reporting of these tumours. Nevertheless, it is recommended that available information on genetic status be recorded for the following reasons:

1. High-grade serous carcinomas associated with *BRCA* mutations (germline or somatic) more commonly show certain morphological features such as solid, endometrioid or transitional-like ('SET') architectural patterns, very marked nuclear atypia, and tumour-infiltrating lymphocytes.[1,3,4] Thus, pathologists may be able to correlate the histological findings with any genetic data provided, or raise the possibility of *BRCA* mutation in certain cases with implications regarding improved prognosis, better chemotherapy response, and consideration of specific therapeutic regimes such as those including PARP inhibitors.[1,2,5] Patients with suspected germline *BRCA* mutations and their relatives, may also be referred for genetic testing and counselling in regard to appropriate screening for *BRCA*-related neoplasia.

2. Knowledge of proven or potential hereditary gynaecological cancer predisposition will affect pathological sampling of macroscopically normal tissues. This is most evident in the setting of prophylactic 'risk reduction surgery', especially in patients with known *BRCA1* or *BRCA2* mutation, where complete examination of tubal and ovarian tissues is mandatory.[1] The identification of small, macroscopically occult tubal carcinomas, and their *in situ* precursor serous tubal intraepithelial carcinoma (STIC) is much more likely in this setting.

Approximately 2% of all ovarian cancers are associated with LS due to a germline mutation in one of the genes encoding the DNA mismatch repair (MMR) proteins. In approximately 60% of women with LS, a gynaecological tumour (endometrial or ovarian) will represent the sentinel cancer.[6] Endometrioid and clear cell carcinomas occur more frequently in LS and therefore immunohistochemical analysis of MMR proteins or molecular testing for microsatellite instability may be considered in these tumour subtypes, or if there is relevant personal or family history of additional LS-related neoplasia. Similar studies may be considered in those patients with synchronous primary ovarian and endometrial endometrioid carcinomas although most such cases are not associated with LS.[7] It has been suggested that in a women with an endometrial carcinoma, the presence of a synchronous ovarian clear cell carcinoma may be an indicator of LS.[8]

References:

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