Ancillary studies (Non-core)

Recent publications have highlighted the most common diagnostic errors in trophoblastic lesions as follows:[1,2]

1. Misinterpretation of early complete hydatidiform mole as partial mole.
2. Overdiagnosis of hydatidiform mole in tubal pregnancy because of florid appearance of normal early first-trimester trophoblastic proliferation.
3. Misdiagnosis of exaggerated implantation site associated with hydatidiform mole or non-molar gestation as placental site trophoblastic tumour (PSTT) or choriocarcinoma.
4. Misinterpretation of non-gestational (germ cell or somatic) choriocarcinoma as gestational choriocarcinoma.
5. Errors in assignment of incorrect antecedent gestation to gestational trophoblastic neoplasia (GTN).

DNA genotyping is performed for diagnosis to separate gestational trophoblastic tumours from non-gestational trophoblastic tumours. DNA genotyping is also performed for risk score assessment to determine the nature of the antecedent/causative gestation and the time interval between the causative gestation and the onset of tumour.[3]

Choriocarcinoma can be either gestational or non-gestational in origin. Those arising from a complete hydatidiform mole are purely androgenetic, whereas the intraplacental (non-molar) form of gestational choriocarcinoma is biparental. The rare non-gestational choriocarcinoma is unrelated to pregnancy and can be of germ cell origin or somatic (genetically related to the patient (tumour DNA matching patient DNA)), arising as a component of a carcinoma. Gestational and non-gestational choriocarcinomas have distinct clinical behavior, sensitivity to chemotherapy, and prognosis. Gestational choriocarcinoma has a favorable prognosis when appropriately treated, whereas non-gestational choriocarcinoma is less sensitive to chemotherapy and has a poor prognosis. Two of the factors used to determine the World Health Organization (WHO)/ International Federation of Gynecology and Obstetrics (FIGO)[4,5] prognostic score for patients with gestational choriocarcinoma are the type of antecedent pregnancy and the time interval from the index pregnancy. Gestational choriocarcinoma related to a molar pregnancy has a lower risk than that related to a non-molar abortion or a term pregnancy, and a shorter time interval since the index pregnancy. However, the immediate antecedent or concurrent pregnancy is not always the causative pregnancy of a gestational choriocarcinoma. In addition, patient age, menstrual status, pregnancy history, and tumour location are not necessarily reliable for determining the gestational versus non-gestational nature of a choriocarcinoma. Genetic analysis, in particular DNA-based genotyping via short tandem repeat (STR) analysis performed on formalin-fixed paraffin-embedded tissues, can distinguish gestational and non-gestational choriocarcinomas, determine the molar versus non-molar nature of the gestational tumours, and can identify the causative pregnancy for the gestational tumours when material is available for comparative analysis. Genotyping can also be applied to other trophoblastic neoplasms, including PSTT and epithelioid trophoblastic tumour (ETT), to distinguish them from rare non-gestational variants of either germ cell or somatic origin.[6]

PD-L1 is commonly expressed in GTN and testing for PD-L1 expression by immunohistochemistry may guide potential immunotherapy for patients with chemoresistant tumour recurrence.[7]

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