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Pt. Age:	39	Gender:	Female	Received date:	2025-12-30
Referred By:	د/ احمد فؤاد		Reported date:	2026-01-10	

PATHOLOGY REPORT

Clinical Information.	Referred paraffin block of gastric mass, endoscopic biopsy diagnosed as signet ring cell carcinoma, requested for MMR, PDL1, PD1, and HER2/neu immunostaining.
Nature of specimen.	Referred block.

GROSS:

-MMR:

The protein under study is considered intact (positive) if unequivocal nuclear staining of any intensity above background is seen in at least 90% of tumor cells. It is considered as lost (negative) if there is absence of any detectable nuclear staining or pale grey/tan staining in tumor cells. MMR is reported as showing heterogeneous staining if 10% or more of tumor area showing loss of expression of an MMR protein.

- PD-L1:

in gastric signet-ring cell carcinoma, PD-L1 positivity is assessed using the Combined Positive Score (CPS) and is considered positive when CPS ≥ 1 , with CPS ≥ 10 representing high expression.

- PD-1:

PD-1 expression is evaluated in tumour-infiltrating lymphocytes and is reported descriptively as absent, focal, moderate, or dense.

- HER2/neu:

HER2 immunohistochemistry is interpreted as negative when scored as 0 or 1+, defined by absent (0) or faint/barely perceptible membranous staining (1+) in tumour cells. A score of 2+ is considered equivocal, characterized by weak to moderate complete, basolateral, or lateral membranous staining, and requires reflex in situ hybridization for confirmation of HER2 gene amplification. A score of 3+ is considered positive, defined by strong complete, basolateral, or lateral membranous staining in tumour cells.

MICROSCOPIC:

MLH1: Intact, nuclear expression in $>90\%$ of tumor cells.

PMS2: Heterogeneous, nuclear expression in 40% of tumor cells.

MSH2: Intact, nuclear expression in $>90\%$ of tumor cells.

MSH6: Intact, nuclear expression in $>90\%$ of tumor cells.

PD-L1: Immunohistochemistry demonstrates high expression with a Combined Positive Score (CPS) =25, showing staining in both tumour cells and associated immune cells.

PD-1: Immunostaining highlights a moderate population of tumour-infiltrating lymphocytes.

HER2/neu: Negative score 0

DIAGNOSIS:

Referred paraffin block of gastric mass, endoscopic biopsy:

- MMR immunostaining: Heterogeneous expression due to focal loss of PMS2; MLH1, MSH2, and MSH6 intact.
- PD-L1 positive (CPS = 25); PD-1 demonstrates moderate expression in tumour-infiltrating lymphocytes.
- HER2/neu negative score 0

COMMENT:

The tumor demonstrates heterogeneous expression of PMS2, with intact MLH1, MSH2, and MSH6. This pattern suggests possible subclonal mismatch repair deficiency. While most tumor cells retain PMS2 expression, focal loss may have clinical significance. Recommend confirmatory testing for microsatellite instability (MSI) or molecular analysis to clarify MMR status, as heterogeneous staining can be associated with Lynch syndrome or influence immunotherapy eligibility.

High PD-L1 expression (CPS ?10) has been associated with an increased likelihood of response to PD-1/PD-L1 immune checkpoint inhibitors in gastric and gastro-oesophageal adenocarcinoma in appropriate clinical settings.

Pathologist

Prof. Dr. Neveen Tahoun, MD, PhD
10-01-2026

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