SEROUS ADENOCARCINOMA OF THE ENDOMETRIUM: COMPLETE CLINICAL RESPONSE UNDER IMMUNE CHECKPOINT INHIBITOR

Abstract :

Background : Complete clinicalresponseachievedwithimmunochemotherapy in the treatment of stage 4 endometrial cancer.

Summary: Immunochemotherapyis a relativelyrecentapproach in the treatment of advanced or recurrentendometrial cancer. Thesetherapiesaim to release the immune brake, allowing the immune system to betterrecognize and destroy cancer cells. We report a clinical case of completeresponsewith a combination of chemotherapy and immunotherapy in a patient with stage 4 endometrial cancer.

Conclusion: This case report demonstrates the significant contribution of immunotherapy in the management of endometrial cancer.

Keywords:endometrial cancer, immunotherapy, completeclinicalresponse.

INTRODUCTION:

Endometrial cancer is one of the few malignant conditions whose incidence and mortality are currently on the rise. By 2040, itisprojected to become the thirdmostcommon cancer and the fourthleading cause of cancer-relateddeaths in women. Itsprognosisis favorable whendetected at an early stage, but remainspoor in advanced (metastatic or recurrent) situations, with few therapeutic options available.

Metastatic or recurrentendometrial cancer thusremains a fairlycommon and serious condition requiringmultidisciplinary management. The combination of pembrolizumab and cytotoxicchemotherapy has led to clinicallysignificantimprovements in progression-free survival and overallsurvival in patients withvarioussolidtumors.

Here, wepresent the case of a 69-year-old patient with high-grade serousadenocarcinoma stage 4 endometrial cancer, in whomweachieved a completepathologicalresponsewithimmunotherapycombinedwithchemotherapy.

Case présentation :

PATIENT AND OBSERVATION:

This is a 69-year-old patient, hypertensive on triple therapy, type 2 diabetic on oral antidiabeticdrugs, dyslipidemia on atorvastatin, venousinsufficiency on treatment, and

transluminal angioplasty for 15 years, presentingwithepigastric pain, intermittent abdominal pain with transit disorders, and pelvic pain associatedwithmetrorrhagia, all evolving in the context of preservedgeneral condition.

As part of the etiologicalassessment, the patient underwent an Esophagogastroduodenoscopywhichrevealed no abnormalities. Hysteroscopyshowed the presence of 3 polyps in the uterinecavitywhichwereresected. Histologicalexamination of thisresectionrevealedmorphologicalfeatures consistent with high-grade invasive serouscarcinoma, Her2 negative (score 0), 50% positive estrogenreceptors, and immunohistochemistryshowing MSS profile and 100% positive P53.

As part of the stagingworkup, a thoracoabdominopelvic CT scan showedabundantperitoneal effusion without distant secondarylesions. An exploratorylaparoscopyrevealedcarcinomatosisinvolving the entireperitoneum. Several biopsies wereperformed, and the pathological report showedperitoneal and omental localization of a high-grade invasive adenocarcinoma consistent with the knownendometrialserousadenocarcinoma in the patient. Tumor marker levelswere as follows: CA125: 654 U/ml, CA19.9: 279 U/ml.

We are facedwith a 69-year-old patient withseveralcomorbiditiespresentingwith high-grade invasive serousendometrialcarcinoma, MSS profile, positive P53, positive ER, negative PR, and HER2 negative, at stage IV withperitoneal and omental metastases.

The decision for chemo-immunotherapy (pembrolizumab 200mg, paclitaxel 75 mg/m2, and carboplatin AUC2) was made in a multidisciplinary team meeting. The first and fourth cycles wereperformedwithout paclitaxel due to peripheralneuropathyrelated to herdiabetes.

The patient's follow-up wasmarked by clinicalintolerance to chemotherapyrequiringhospitalizations for profoundasthenia, anorexia, and isolatedfebrile syndrome (withoutclinical, biological, or radiologicalsigns of infectiousetiology) and necessitating dose reductions of chemotherapy.

Evaluation after the third cycle of treatmentshowedradiologicalstabilitywith persistent micronodularmesenteric infiltration and large omental infiltration withgallbladder macro lithiasis. Therefore, wedecided to administer the fourth cycle withcarboplatin AUC 1.5 and pembrolizumab due to persistent neuropathy, followed by maintenance therapywith pembrolizumab. The patient tolerated the maintenance treatmentwell.

A positron emissiontomographycomputedtomography (PET-CT) wasperformed as part of the evaluationafter the sixth cycle of pembrolizumab, showingcompletedisappearance of the previouslydescribedabdominopelvichypermetabolicfoci, indicating a completeresponse.

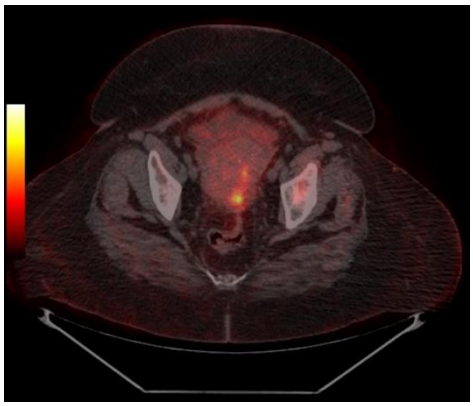

Fig1 : Posterioruterinehypermetabolism

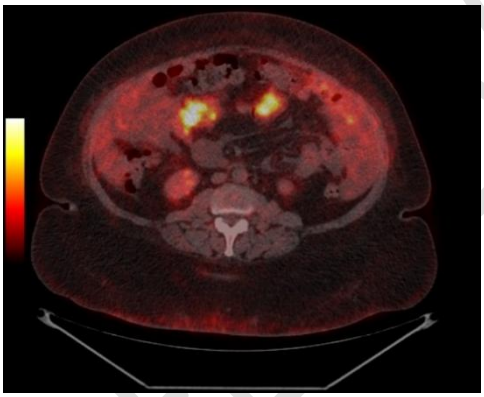

Fig2 :peritoneal effusion and peritonealcarcinomatosis

DISCUSSION:

Immunochemotherapyis a relativelyrecentapproach in the treatment of advanced or recurrentendometrial cancer, raising questions about treatmentmodalities and duration. The mostcommonlyusedimmunotherapies in endometrial cancer target immune checkpoint moleculessuch as anti-PD-1/PD-L1 and anti-CTLA-4 antibodies. Thesetherapiesaim to release the immune brake, allowing the immune system to betterrecognize and destroy cancer cells.

Several immune checkpoint inhibitors (ICI) currently have marketing authorization in advanced non-smallcelllung cancer (NSCLC): pembrolizumab, nivolumab, and atezolizumab. Thesetreatments have demonstratedefficacy in variousstudies, in first-line or beyond settings, with variable planned durations of immunotherapytreatment: Pembrolizumab wascontinued for up to a total of 35 cycles every 3 weeks (KEYNOTE 024, KEYNOTE 407, KEYNOTE 189) or 24 months (KEYNOTE 010).

An earlier trial comparing the addition of pembrolizumab to paclitaxel/carboplatin versus placebo and paclitaxel/carboplatinshowedthatincorporatingimmunotherapyinto first-line treatment for patients withadvanced or recurrentendometrial cancer resulted in betteroncologicaloutcomes, regardless of PD-L1 status or histologicalfindings.

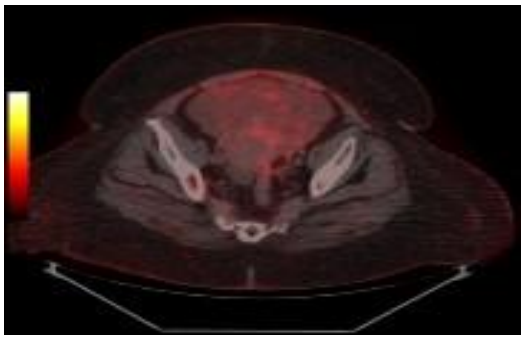

Fig 3: Complete disappearance of uterinehypermetabolism.

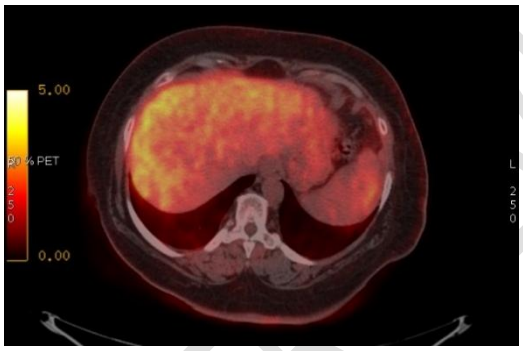

Fig 4 : Complete disappearance of peritonealcarcinomatosis and pleural effusion.

CONCLUSION:

The prognosis of advanced stage endometrial cancer continues to improve due to bettermultidisciplinary management and access to new innovative strategies. In patients withadvanced or recurrentendometrial cancer, the addition of pembrolizumab to standard chemotherapy has resulted in significantly longer progression-free survivalthanchemotherapyalone. However, the optimal duration of treatmentremains a subject of consideration.

ABREVIATIONS :

AUC : Area Under The Curve.

CTLA-4 : Cytotoxic T-Lymphocyte Antigen-4.

HER2 : Human EpidermalGrowth Factor Receptor2 .

ICI : Immune Checkpoint Inhibitors.

NSCLC:Non-Small Cell Lung Cancer

MSS : MicroSatelliteStability.

PD-1 : Programmed Death-1.

PD-L1 : ProgrammedDeath-Ligant 1.

RE : EstrogenReceptors.

RP : ProgesteroneReceptors.

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