

Parameters before chemotherapy

Case 372

1. A, B 2. A, C 3. A, D 4. C, D

【Progress】

He received chemotherapy with a combination of anti PD-L1 antibody and platinum formulation. The regime is scheduled to be continued because this combination is considered to be effective.

【Discussion】

Various anticancer drugs are used in patients with advanced gastric cancer that indicates difficulty to be controlled by surgical resection alone because of distant metastases, diffuse tumor intraperitoneal dissemination or others. They are largely categorized as DNA replication inhibitors, cellular receptor inhibitors. As DNA replication inhibitors, fluorouracil inhibitors cisplatin (bridging formation of DNA two chains), irinotecan (that inhibits enzyme from two DNA chains to single DNA chain) and paclitaxel (depolymerization of tubulin necessitated in DNA replication) are listed. As cellular receptor inhibitors, immune checkpoint inhibitors and human epithelial receptor (HER) inhibitors are listed.

Immune checkpoints usually come from the effector cytotoxic T cell itself. As time went by, two minute dents emerge; a new receptor called CTLA-4 to dendritic cell: another receptor called PD-1 to PD-L1 coming from body cell or tumor cell, inducing atrophy of function of cytotoxic T cell. Check point inhibitors of antiCTLA-4 and anti PD-1 induce to return momentum of cytotoxic effector cell (1-3). When tumor antigen manifests on tumor surface, check point inhibitors make its responses of anti-tumor enhance (4).

Human DNA has microsatellite phenomenon that imply repetition of the same DNA arrangement. It is known that the site of microsatellite tends to misread DNA arrangement and repair of DNA misarrangement is required (4). In case of tumor emergence, repair potency is believed to be lowered (microsatellite insufficiency MRI), indicative of tumor antigen on cell surface being enhanced and of being susceptible of immune cell attack and resulting in effectiveness of check points inhibitors

HER is one of tyrosine kinase family that allow hormone, cytokine and enzyme to pass through cell membrane easily by phosphorylation from ATP. HER can penetrate cell membrane without existence of legand and functions to promote proliferation and differentiation (5, 6). In some tumors, HER abnormal function is considered to stimulate tumor proliferation. Anti HER body called Herceptin is effective to control HER-positive tumor of breast cancer or gastric cancer (5, 6).

Then, before initiation of anti-cancer drugs administration, first of all laboratory test of HER is required. If positive, Herceptin is included to the first line medicines. Second, the presence or absence of microsatellite is investigated. If positive, anti-PD-1 body (pembrolizumab) is added as one of the second line of anticancer drugs.

【Summary】

We presented a sixty-seven-year-old male who underwent chemotherapy because laparotomy revealed liver metastases and peritoneal tumor dissemination. It is borne in mind that before chemotherapy it is imperative to receive tests of HER (human epithelium receptor) that accommodate growth and proliferation of epithelium, and microsatellite insufficiency that indicates less repair potency of misread arrangement of DNA. In case of positive HER and high microsatellite insufficiency, anti-HER body (Herceptin) and anti-PD-1 body (nivolumab Opdivo) are administered simultaneously with DNA replication inhibitors.

【References】

1. Hamid, O et al. "Safety and tumor responses with lambrolizumab (anti-PD-1) in melanoma". New England Journal of Medicine 2013 369 (2): 134-44
2. Pardoll, DM (Mar 22, 2012). "The blockade of immune checkpoints in cancer immunotherapy.". Nature reviews. Cancer 12 (4): 252–64.
3. Receptor tyrosine kinase signaling as a target for cancer intervention strategies". Endocrine-Related Cancer 8 (3): 161–73.
4. Stephen K H Li et al. Mismatch Repair and Colon Cancer: Mechanisms and Therapies Explored. Trends Mol Med 2016 Apr;22(4):274-289.
5. Slamon DJ, et al. "Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene." Science, Vol.235, No.4785, 1987, p.p. 177-182.
6. ^ American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer. Wolff AC, Hammond ME, Schwartz JN, Hagerty KL, Allred DC, Cote RJ, Dowsett M, Fitzgibbons PL, Hanna WM, Langer A, McShane LM, Paik S, Pegram MD, Perez EA, Press MF, Rhodes A, Sturgeon C, Taube SE, Tubbs R, Vance GH, van de Vijver M, Wheeler TM, Hayes DF; American Society of Clinical Oncology/College of American Pathologists. Arch Pathol Lab Med. 2007;131(1):18-43.

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