Case 365

3. Gastric cancer with disseminated invasion to transverse colon

【Progress】

She was treated with artificial anus formation and chemotherapy using PD-1 antibody, inducing soft edematous transverse colon and leading improvement of stool passage (Figs 3, 4).

【Discussion】

As every person has its own face, every cell has its own specific common face: concretely, every cell has a specific peptide riding on a recess of cell surface called major histocompatibility complex 1 (MHC1). If a cell whose MHC1 rode peptide different from the common peptide appeared, the cell would be attacked and cleared by immune cells (cytotoxic cells or killer cells). For instance, when a virus infected a cell, the cell would ride peptide of the virus at MHC1 and then it would be eliminated by killer cells. Placenta trophoblasts, red blood cells and central-peripheral nerve cells have no MHC1, indicative of no attack from immune cells (1-6).

Dendritic cell has two recesses at its own surface of MHC1 and MHC2.

They function phagocytosis of foreign body and/or carry antigens to immune cells (T cells). When dendric cells phagocyte foreign cells such as bacteria, virus or cancer cells, they rode their peptides on MHC1 and carry to naïve cytotoxic T cell, while they rode them on MHC2 to carry naïve helper T cell. It induces helper T cell to turn into effective helper T cell. Effective helper T cell stimulates naïve cytotoxic T cell turning into effective cytotoxic T cell (CD8, killer T cell). Effective cytotoxic T cell attacks cancer cells and eliminate them. The above indicates main immune system for attack to cancer. However, handling the antigen from dendritic cells to T cell is not sufficient to activate immune attack to cancer. Along with handling antigen to T cell, Go-sign from dendric cells is essential for activating immune system: B7 ligand (CD80/86) of dendric cells gives go-sign signal to CD28 receptor of T cell (1-7).

If this attack system continues, the immune system might give damages to healthy cell of body itself. Then, the repressing mechanism of Stop sign to curve attacking works; as time advance, CTLA-4 receptor taking place of CD28 receptor emerges. B7 ligand (CD80/86) connects to CTLA-4, inducing inhibition of T cell function: further, as time progress, PD-1 receptor emerges at the surface of T cell itself, PD-L1 from body cell connects PD-L1 of T cell, inducing hypofunction of immune attack (4-6).

The strategy of cancer growing is escaping from attack by immune cells. The first escape is no creation of MHC1 with peptide such as placenta trophoblasts, red blood cells and nerve cells. This is the clever trick that survive cancer cells without attack of immune cells. The second escape of curbing immune potency using hypo functioning mechanism using PD-L1 of cancer cells connecting to PD-1 of effector cytotoxic T cell. It leads least attack by immune cells to cancer. Further, vascular endothelial growth factor (VEGF) secreted from cancer cells that originally is considered a factor of neo-vascularization of tumor cells, functions the regression of dendric cell maturation. PD-L1 and VEGF by cancer cells work hypo functioning of cytotoxic cells and dendric cells (1-7). In other words, cancer cells use stop sign (check point) mechanism suppressing runaway of immune response originally present in host cells to survive themselves in host.

As checkpoints inhibitors, antibody for PD-1, antibody for PD-L1, antibody for CTLA-4, and antibody for VEGF are listed. Obdivo (Nivolumab) is antibody for PD-1 (4-7). In our case, Obdivo (Nivolumab) is used as checkpoint inhibitor for gastic cancer with invasion to transverse colon.

【Summary】

We presented a seventy-year-old female who suffered from advanced gastric cancer with invasion to transverse colon associated with intraperitoneal dissemination. She was treated with anti-check point inhibitor of Obdivo (nivolumab), inducing partial regression of the tumor. It is borne in mind that checkpoint, repression of immune activation emerges in two situations; one, dendric cells with B7 connected to T cell with CTLA-4; another, T cell with PD-1 connect to body cell with PD-L1. Using the latter mechanism, tumor with PD-L1 connect to body cell with PD-1, inducing to inhibit attack from cytotoxic T cell. As checkpoint inhibitors, antibody for PD-1 (Obdivo, Nivolumab), antibody for PD-1L and antibody for VEGF are listed.

【References】

1. Smith S.M., et al. Clinical cancer advances 2021: ASCO's Report on progress against cancer. J. Clin. Oncol. 2021;39:1165–1184.
2. Sadeghi Rad H. et al. Understanding the tumor microenvironment for effective immunotherapy. Med. Res. Rev. 2021;41:1474–1498.
3. Barbari C.,et al. Immunotherapies and Combination Strategies for Immuno-Oncology. Int. J. Mol. Sci. 2020;21:5009.
4. Seidel J.et al. Anti-PD-1 and Anti-CTLA-4 Therapies in Cancer: Mechanisms of Action, Efficacy, and Limitations. Front. Oncol. 2018;8:86.
5. Liebl M.C., et al. Identification of responders to immune checkpoint therapy: Which biomarkers have the highest value? J. Eur. Acad. Dermatol. Venereol. 2019;33:52–56.
6. Paucek R.D. et al. The Cellular Immunotherapy Revolution: Arming the Immune System for Precision Therapy. Trends Immunol. 2019;40:292–309
7. Basudan AM, et al. The Role of Immune Checkpoint Inhibitors in Cancer Therapy. Clin Pract. 2023 Feb; 13(1): 22–40.

back

2024.12.6