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Opinion
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Immunotherapy: A New Challenge for Supportive Care

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Opinion

Supportive care in cancer medicine is primarily devoted to improve the quality of life of cancer patients, namely by minimizing the adverse effects of cancer therapy, such as, among many others, infections related to neutropenia and nausea/vomiting caused by chemotherapeutic agents.

The recent and dramatic development of new immunotherapy's, especially those using the "checkpoint inhibitors", represents a new challenge for supportive care, similar but probably more important than that posed by the introduction of "targeted therapies". In both cases, the difficulty for the clinician results from the observation that these new side-effects are very different from those we learnt to control in chemotherapy-treated patients; these side-effects are also less predictable and require a delicate differential diagnosis, namely with potential infectious diseases.

It is also important to stress that we know these side-effects from large controlled studies that have established the efficacy of these new "immunotherapies"; however, there is very limited information about their incidence and clinical course in unselected patient populations which are representative of common practice.

As far as these side-effects consist of, the most frequent manifestation is fatigue (50%), various skin lesions (20%)-which appearance might be a positive predictor of clinical response-and diarrhea (20%) among toxicities involving specific organs or systems (25%), one has to mention colitis, pneumonitis and various endocrinopathies (hyper and/or hypothyroidism, adrenal failure and hypophysitis), which pathogenic mechanism is probably immunologic. However, almost any organ or system within the body can be targeted by these agents: many "rare" side-effects have been reported (ophthalmological, cardiac, neurological, etc.) and it can be suspected that the list is not complete yet. Although, the frequency and the severity of these adverse reactions clearly increases when the immunotherapeutic agents are used in combination, overall these complications are usually not severe and respond to the discontinuation of immunotherapy and/or corticoids. However, there are many reports contradicting this optimistic point of view: fatal outcomes are regularly reported.

Another aspects which makes the approach of immunotherapy-induced side-effects difficult is that sometimes immunotherapy induces "pseudo-progressions" (that are followed by remission) or "hyper-progression" (that represent true acceleration of the tumor growth); both situations pose the differential diagnosis of tumor progression or side-effects.

Thus, with the introduction of new "immunotherapies", the oncologist is confronted to new aspects of clinical medicine that he has to learn and master. A high degree of suspicion of these new side-effects allows for early detection but requires a very high surveillance of the patients. Only such an approach can lead to early discontinuation of the offending "immunotherapy" (that can be transitory or definitive) and the administration of effective therapy (corticoids and/or other immunosuppressive drugs).

In order to meet these challenges, additional training of the oncologists will be unescapable. Moreover, it will be mandatory to create a research activity to establish paradigms for the diagnosis and treatment of these new side-effects.

It will probably be necessary to implement whole teams and structure familiar with these complications in order to follow adequately the patients who are undergoing theses promising therapies, in order to provide maximal security and comfort to most of them [1-9].

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