Novel Anti-Cancer Agents and Capillary Leak Syndrome

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ABSTRACT

The term capillary leak syndrome (CLS) results clinically in the typical triad of hypotension, edema, and elevated hematocrit. The more severe cases of CLS may present with cardiovascular collapse, shock, and death. Data on CLS associated with novel anti-cancer agents is insufficient.

We reviewed the FDA adverse event reporting system (FAERS) quarterly legacy data first quarter 2010 to 4th quarter 2021 for all recently commonly used targeted therapies and immune-checkpoint inhibitors (ICI). Well established chemotherapy agents such as gemcitabine, clofarabine, cyclophosphamide, platinum-based therapy, colony stimulating factors were excluded. CAR-T therapy is well known to cause CLS and hence was excluded. The adverse event terms queried were: capillary leak syndrome, capillary leak and cytokine storm. We reviewed the literature using PubMed, case reports, case series and the registrational studies of anti-cancer agents associated with CLS as well.

FAERS reporting system reported 22 cases of CLS in the last 11 years with novel anti-cancer agents. The most common class was anti CD20 (rituximab-9 cases), followed by ICIs (6) and then anti VEGF agents (4). Other meds (4) were mainly bortezomib and trastuzumab. The two reported ICIs were ipilimumab and nivolumab. The most common anti VEGF inhibitor was bevacizumab.

The literature search revealed anti CD20 (rituximab) being the most common agent with 19 cases reported followed by bortezomib (anti plasma cell agent) with 13 cases. Trastuzumab had 11 cases reported and other rare cases with alemtuzumab (6) and blinatumomab (3). Immune checkpoint inhibitors with specifically nivolumab, there were 4 cases reported.

CLS is rare in novel anti-cancer agents. Anti CD20 agents such as rituximab seem to be the most common cause of this rare side effect. Other agents such as bortezomib, anti VEGF agents, trastuzumab and ICIs (mainly nivolumab and ipilimumab) can also rarely cause CLS. Oncologists and nephrologists need to be mindful of this rare fatal side effect.