Evaluation of a possible link between immunotherapy (IO) and acute vascular events


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Background: IO has become one of the major pillars of anti-cancer therapy. A range of immune-related adverse events (IRAE) are recognized within various organs. Acute vascular events (AVE) are generally not considered IRAE. Considering the role of inflammation in acute ischemic cardiovascular events, we assumed such events can be triggered by IO. We aimed to evaluate the frequency and nature of AVEs occurring shortly after the initiation of IO.

Methods: Computerized search of Sheba medical center (SMC) electronic medical records was done for patients (pts) that received IO (any of: pembrolizumab, nivolumab, atezolizumab, ipilimumab). Out of those, we searched for cases with a diagnosis of AVE within 1 month after initiation of IO. Search was for the diagnoses: cerebrovascular accident (CVA), transient ischemic attack (TIA), myocardial infarct (MI), non-ST-elevation MI, ST-elevation MI, embolic event, pulmonary emboli (PE) and deep vein thrombosis (DVT). We excluded cases with AVE within a year prior to the initiation of therapy, concomitant chemotherapy, and cases of a single-site DVT.

Results: Between 1st January 2015 and 14th March 2018, 1396 pts received IO in SMC. 14 pts were identified in the computerized search. Excluded: 4 with a single site DVT, 1 with a prior cardiovascular event within a year prior to initiation of IO, 1 with concomitant chemotherapy, 3 excluded due to AVE not definitely diagnosed, leaving 5 pts not excluded. 8 additional pts were identified by reports of physicians aware of this project, of these 2 were also identified by the computerized search, thus a total of 11 pts fit our study criteria. Events were: multiple CVA (3), PE (2), sudden cardiac death (2), bilateral DVT (1), CVA (1), TIA (1), MI (1). In one pt marantic endocarditis was suspected. 7 pts had diabetes, 7 pts had hypertension, 2 pts had a body mass index > 30, 3 were smoking within < 10 years ago, none had a family history of cardiovascular disease. 9 of the pts were treated in SMC, constituting a frequency of 0.6%.

Conclusions: AVEs occur at a low frequency shortly after initiation of IO. Initiation of IO may be the triggering event of those events. Further retrospective studies and analyses of clinical trials data are required to evaluate whether this is a random association or a true IRAE.

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