Tamponade during immune checkpoint inhibitors therapy in lung cancer: case-reports and systematic review of the literature

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Introduction: Immune therapy is a new option that has revolutionized cancer therapy. Immune checkpoint inhibitors target mostly either PD-1 (Pembrolizumab, Nivolumab) or PD-L1 (Durvalumab). Immune-related cardiotoxic side effects, among them, tamponade, initially thought to be rare, seem to be increasingly cited in the literature. Moreover, tobacco smoking is linked to 80% of lung cancers. Smoking during cancer therapy may influence on radiotherapy and chemotherapy outcomes but little is known on immunotherapy.

Purpose: We aimed to review all the published cases of tamponade during immune therapy for lung cancer and to report all the cases that occurred in the University Hospital Ambroise Paré. We also wanted to highlight the possible impact of tobacco on immunotherapy.

Methods: We conducted a literature review in the PubMED database, from database inception up to 02/14/2020, with a combination of the following terms: "tamponade AND ((immune checkpoint inhibitors) OR (PD-1) OR (PD-L1))". We also reported all the tamponade cases occurred in our hospital from the beginning of immune checkpoint inhibitors therapy existence up to 02/14/2020.

Results: Seventeen cases citing tamponade were identified in the literature to which we added 3 cases from our hospital. Mortality rate at 1 month was of 20%. Nivolumab was involved in 80%, Pembrolizumab in 10% and Durvalumab in 10%. In 75%, lung cancer was with a stage IV. Men accounted for 85% and mean age was of 62 years. Active smokers represented 85% and passive smokers existed in 5%, after diagnosis, smoking cessation was done in 10%. Tamponade occurred either shortly after the first administrations but also after several doses. Pericardial fluid cytology revealed malignant cells in half of the cases and microbiology was always negative. For all the cases, excepted for one who was directly considered as palliative, an evacuation of the pericardial fluid was done. In 45% a corticotherapy was initiated. Two cases quickly worsened after pericardial evacuation by unmasking a probable myocarditis with cardiogenic shock which needed the use of a veno-arterial extracorporeal membrane oxygenation.

Conclusions: Tamponade under immune checkpoint inhibitors therapy appears less rare than initially thought and mortality rate at one month was not negligible. The use of regular echocardiography during this immune therapy may be crucial in detecting early stages of the disease process and smoking cessation should also be advised for these patients. The prevalence of complications among all the patients both exposed to immune therapy and tobacco could not be calculated in this work (case-reports), but some recent studies may indicate survival gains of smoking cessation. Further research establishing more specific guidelines is naturally necessary in dealing with this potentially fatal effect but also in establishing the possibly additional role of smoking in the cardiotoxicity of immunotherapy.