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1839 | Successful one-bag desensitization protocol in a patient with pembrolizumab hypersensitivity

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Case report:

Background: Pembrolizumab is a humanized monoclonal IgG4 kappa anti-PD1 antibody approved as a treatment for several cancers (advanced melanoma, non-small cell lung cancer, Hodgkin disease...). We report a case of a successful pembrolizumab desensitization. A 58-year-old man was referred for an anaphylactic reaction to pembrolizumab. This immunotherapy was proposed as first-line therapy (200 mg every three weeks without premedication) for a bronchial adenocarcinoma. During the 9th cure, five minutes after the end of the infusion, the patient presented with shivers without eruption, chest tightness, drop of the blood pressure to 60/30 mmHg, tachycardia, and hypoxemia (SatO₂: 63%). He was treated with IV isotonic saline volume expansion, oxygenotherapy, dexchlorpheniramine and

methylprednisolone. Other differential diagnoses (pulmonary embolism, myocardial ischemia, ...) were ruled out by the usual investigations. The diagnosis of anaphylaxis was confirmed by the tryptase level raising to 118 µg/L during the reaction while the level was normal (8.11 µg/L) two months later.

Methods: Skin testing was performed 7 weeks after the reaction. The prick tests (PT) with pembrolizumab 25 mg/mL and polysorbate 80 were negative. The intradermal test (IDT) with pembrolizumab were performed at 0.25, 2.5 and 25 mg/mL. All initial IDT diameters measured 4 mm. Twenty minutes later, the diameter of the papula an erythema raised to 4/0, 4/12 and 6/17 mm respectively. were IDT with saline and PT with histamine were performed as negative and positive controls.

As the patient was a good responder to this immune checkpoint inhibition therapy, a desensitization to pembrolizumab was performed using a one bag-protocol with 4 steps at the concentration of 1 mg/mL (Table 1) with a premedication combining acetaminophen, dexchlorpheniramine and methylprednisolone.

Results: To date, the desensitization protocol on this patient was completed at least two times without any allergic reactions. According to the French national pharmacovigilance database 7 cases of hypotensive shocks (4 without cutaneous symptoms) have been reported but none of these cases reported tryptase or histamine measure. To our knowledge, there is only one previous report desensitization to pembrolizumab using a 3 bags-desensitization protocol (1).

References: Isabwe et al. J Allergy Clin Immunol 2018; 142(1) : 159-70

TABLE 1 One bag-desensitization protocol to Pembrolizumab (1 mg/mL)

Step	Flow (ml/h)	Duration (min)	Dose (mg)	Cumulated dose (mg)
1	1	15	0.25	0.25
2	3	15	0.75	1
3	10	15	2.5	3.5
4	30	30	15	18.5
5	50	215	179.2	197.7