■ Sat-465 ■

Successful rapid desensitization for obinutuzumab-induced anaphylaxis: A case report

[1]서울대학교 의과대학 내과학교실, [2]서울대학교병원 약물유해반응관리센터, [3]서울대학교 의학연구원 알레르기 및 임상면역연구소

*김광우[1], 정수지[1], 강혜련[1,2,3]

Obinutuzumab is a humanized, type II, anti-CD20 monoclonal antibody that recently demonstrated an overall survival advantage compared with rituximab, when combined with chemotherapy in previously untreated older patients with chronic lymphocytic leukemia (CLL) and comorbidities. Infusion related reaction (IRR) is the most common toxicity of obinutuzumab and can be fatal in severe form such as anaphylaxis. However, there is no report of desensitization for obinutuzumab hypersensitivity. Therefore, we present a 16-step intravenous desensitization procedure, which was successfully carried out in the general ward setting. A 71-year old man with CLL was admitted for obinutuzumab/chlorambucil treatment. Despite premedication was done with chlorpheniramine 4 mg, dexamethasone 20 mg, and acetaminophen 650 mg, the abrupt development of chest/abdominal discomfort, and sore throat occurred in one hour during infusion of obinutuzumab solution (100 mg in normal saline 100 mL) in a rate of 25 mL/hr. Infusion was resumed on the next day by a 12-step desensitization protocol with premedication of chlorpheniramine 4 mg, methylprednisolone 40 mg, propacetamol 1 g. Infusion started in a rate of 0.10 mL/hr and doubled per 15 minutes. However, in spite of desensitization, breakthrough reaction (BTR) such as high fever, dyspnea, chest discomfort, stridor, and desaturation (about SpO2 85%, at room air) occurred when infused at 0.4 mL/hr. The desensitization protocol was mitigated into 18 steps with slower incremental infusion rate of 1.6 times per 15 minutes in total of 18-incremental steps and the patient finally received the end target dose without any symptoms suggesting BTR. In summary, we report the first case of successful obinutuzumab desensitization carried out in a patient who had presented obinutuzumab-induced anaphylaxis by using a mitigated desensitization protocol with 1.6 time increment between steps.

Table 1. Obinutuzumab desensitization protocol (18-step protocol)

1st bag : Obinutuzumab 100 mg in 100 mL of 0.9% normal saline

Step	Rate (mL/hr)	Time (min)	Administered dose (mg)	Administered volume (mL)	Cumulative dose (mg)	Cumulative volume (mL)
1	0.1	15	0.0240	0.025	0.0240	0.025
2	0.2	15	0.0481	0.05	0.0721	0.075
3	0.3	15	0.0721	0.08	0.1442	0.15
4	0.5	15	0.1202	0.13	0.2644	0.275
5	0.8	15	0.1923	0.20	0.4567	0.475
6	1.3	15	0.3125	0.33	0.5048	0.8
7	2.1	15	0.5048	0.5	1.2740	1.325
8	3.4	15	0.8173	0.85	2.0913	2.175
9	5.5	15	1.3221	1.38	3.4135	3.55
10	8.9	15	2.1394	2.23	5.5529	5.775
11	14.4	15	3.4615	3.60	9.0144	9.375
12	23.3	15	5.6010	5.83	14.6514	15.2
13	37.8	15	9.0865	9.45	23.7019	24.65
14	61	15	14.7356	15.3	38.4375	39.975
15	99	15	23.7981	24.8	62.2356	64.7
16	160	14.7	37.7644	39.3	100.0	104.0
		224.7	100.0	104.0	100.0	104.0

2nd bag : Obinutuzumab 900 mg in 250 mL of 0.9% normal saline

Step	Rate (mL/hr)	Time (min)	Administered dose (mg)	Administered volume (mL)	Cumulative dose (mg)	Cumulative volume (mL)
17	80	15	62.9371	20.0	62.9371	20.0
18	130	122.8	837.0629	266.0	900.00	286.0
		137.8	900.0	286.0	900.00	286.0

■ Sat-466 ■

A case of acute localized exanthematous pustulosis involving unusual site of body

[1]차의과학대학교 분당차병원, [2]차의과학대학교 분당차병원

*이혜연[1], 김미애[2]

Acute localized exanthematous pustulosis (ALEP) is a localized form of acute generalized exanthematous pustulosis (AGEP), characterized by acute onset of multiple nonfollicular, pin-head-sized, sterile pustules following drug administration, usually antibiotics such as β-lactams. Until 2017, 25 cases were reported as ALEP and a case summary was published analyzing these cases. Among them, most common culprit drugs were amoxicillin and ampicillin, following NSAID, and other antibiotics. Common involving sites of ALEP were face and trunk, following neck, limbs, and abdomen. Here, we experienced a case of ALEP involving unusual site of body, unilateral side of buttock. A 46 year-old female patient, admitted in infectious disease department because of fever, was consulted to allergy department because of abnormal skin finding. There were multiple pin-head-sized pustules with erythema affecting only on her right side of buttock. She does not have any medical history of allergic or dermatologic diseases, including drug hypersensitivity. Her skin symptoms were started 3 days after ceftriaxone injections. White blood cell count was 13,890/μL and differential count was abnormal (Seg 89.1%,lym 8.8 %,mono 1.9%,Eo 0 %). Blood and urine culture studies were all negative and there were no significant findings regarding various virus antigens. Pustule culture showed no-microorganisms growth. The skin lesion was a typical finding of AGEP but we still had a doubt because its distribution was localized, while AGEP usually involving whole body. After searching medical literatures, we suspected her as ALEP to ceftriaxone, based on temporal relationship of drug administration and skin lesion, and previous reports about culprit drugs for ALEP, although unilateral side of buttock was not reported before. Ceftriaxone was withdrawn immediately and systemic steroid was started. After steroid treatment, her skin symptoms got better without fever and she could be discharged. **Conclusion:** Physicians should be aware that exathematous pustulosis could be developed as not only generalized form but also localized dstribution in any site of body.