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LETTER

Vitamin B_{12}: An underestimated cause of acneiform drug eruption

Dear Editor,

Acneiform drug eruption is a type of adverse drug reaction characterized by monomorphic papulopustular lesions. There are a limited number of studies focusing on vitamin B_{12}-induced acneiform eruption (BIAE) in the relevant literature.[1,2] In this study, we retrospectively analyzed the clinical characteristics of BIAE in a consecutive series of 32 patients who were admitted to the dermatology departments of Ahi Evran University and Kozan State Hospital over the last 3 years. Collected demographic and clinical data for each patient included age, sex, history of medication, previous experience with vitamin B_{12}, symptoms, morphology, distribution and duration of the eruption, and the treatment used. Causality assessment between vitamin B_{12} intake and BIAE was mainly based on the diagnostic criteria for drug reactions that have been originally proposed by Naranjo et al[3] For the selection of the 32 patients, the inclusion criteria were as follows:

1. The eruption occurred suddenly within days to weeks following vitamin B_{12} administration.
2. The eruption disappeared after vitamin B_{12} was discontinued.
3. The eruption consisted of monomorphous papular, pustular, or papulopustular rashes without comedones and cystic lesions (Figure 1).

Patients who used additional medication or had another possible cause for acneiform eruption were excluded. The study was approved by Ahi Evran University Institutional Review Board.

A total of 32 patients were enrolled in the study. The majority of the subjects were female (n = 20, 62.5%) and the mean age was 28 ± 11 years. Intramuscular (IM) administration was associated with a statistically significant ($P < .05$) shorter time intervals between the first vitamin B_{12} intake and onset of the eruption. The mean time intervals between drug discontinuation and considerable improvement of the eruption showed no statistically significant difference between the IM and oral groups ($P > .05$). There was also no statistically significant difference between the total dose taken or treatment duration and the distribution of the lesions ($P > .05$).

Most of the patients were asymptomatic. There were mild itching and burning sensation in 12 (37.5%) and 4 (15.3%) patients, respectively. Asymptomatic cases were followed up without treatment while symptomatic cases were managed with topical clindamycin, and topical benzoyl peroxide-erythromycin combination, respectively. There was no statistically significant difference ($P > .05$) between the symptomatic and asymptomatic groups in terms of the recovery time. The demographic and clinical features of the patients are summarized in Table 1.

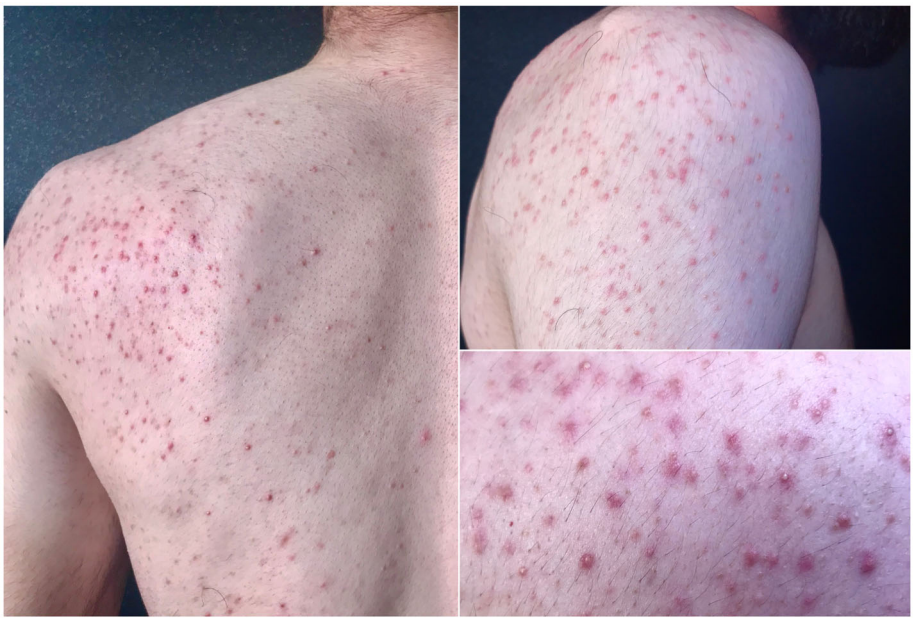

FIGURE 1 Vitamin B_{12}-induced acneiform eruption characterized by monomorphic papulopustular lesions on the back and shoulders in a young male patient

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TABLE 1 The demographic and clinical features of the patients with vitamin B_{12}-induced acneiform eruption

Variable	Result
Gender	20 (62.5%) female, 12 (37.5%) male
Age (mean ± SD) (year)	28 ± 11
Pharmaceutical preparations	Intramuscular vitamin B_{12} (1 mg); (n = 18, 56.25%) Oral combination of vitamin B_1 (thiamine hydrochloride) (250 mg), B_6 (pyridoxine hydrochloride) (250 mg), and B_{12} (cyanocobalamin) (1 mg); (n = 14, 43.75%)
Total dose taken	The mean total dose of vitamin B_{12} for intramuscular group: 1.6 ± 1.2 mg The mean total dose of vitamin B_{12} for oral combined group: 7.1 ± 2.6 mg
Previous acneiform eruption history with vitamin B	4 (12.5%)
The mean time interval between the first drug intake and symptom onset	11 ± 6 days (ranging from 1 to 30 days)
The mean time interval between drug discontinuation and considerable improvement of the eruption	7 ± 3 days (ranging from 4 to 15 days)
Distribution of eruption	Generalized involvement of face, neck, chest, and back (n = 8, 25%); limited to neck and chest (n = 13, 40.6%); limited to neck, chest, and back (n = 8, 25%); limited to face (n = 3, 9.3%)

Although the exact pathogenesis of BIAE is unknown, several immunological, endocrine, and vascular factors have been implicated. It has been shown that the anaerobic metabolism of *Propionibacterium acnes* is vitamin B_{12} dependent.[2] Kang et al found that vitamin B_{12} supplementation altered the transcriptome of *P acnes* in the skin microbiota.[4] It has also been suggested that BIAE may be associated with iodine, which is used for the extraction of vitamin B_{12}.[2]

BIAE is typically characterized by a sudden onset, within days to weeks following vitamin B_{12} administration.[2] In the present study, the mean time interval between the first drug intake and onset of the eruption was 11 ± 6 days. The time interval between vitamin B_{12} withdrawal and the spontaneous disappearance of the eruption has been reported to be 1 to 8 weeks. We detected that the average time needed for a considerable improvement after drug discontinuation was 7 ± 3 days.

The main limitation of this study is the relatively high proportion of the patients who took a combination of vitamin B_1, B_6, and B_{12} (43.75%). So, it was not possible to be sure whether vitamin B_{12} was the main culprit of the eruption for this group of patients. On the other hand, 18 patients had pure vitamin B_{12}-related eruption. Although this is a relatively small number, to the best of our knowledge, the largest series of vitamin B_{12}-related acneiform eruption reported in the relevant literature included only five cases, and of these five cases, only three received pure vitamin B_{12}.[2]

Given the limited number of studies focusing on the subject, vitamin B_{12} seems to be an underestimated cause of acneiform drug eruptions. We would encourage placebo-controlled studies with larger sample sizes to empower conclusions deduced in the present study.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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