URTICARIA IN MALARIA FOLLOWED BY HERPES SIMPLEX

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Summary

In a short span of 8 weeks, several patients applied for treatment with glaring clinical manifestations having almost similar sequence of events, namely urticaria with malaria followed by herpes simplex. Seven of these form the subject of the present text.

Case Reports

All the seven cases started with generalized urticaria, which was followed by fever after two days. They had already been treated with corticosteroids and antihistamines, but there was no clinical response. The doses of these drugs, however, could not be ascertained.

Examination of the blood film in all the cases revealed the presence of malarial parasite and thus treatment with chloroquine diphosphate led to the disappearance of fever and urticaria within two days. The chloroquine was continued for a total of 3 days, each patient receiving 10 tablets (1500 mg. chloroquine base). Within a few days 5 of the cases developed an eruption of vesicular lesions of the face. In 4 cases, the lesions were located around the lips, while in the 5th they were periorbital. In all cases the lesions were profuse, extensive and bilateral. Culture from the lesions on *vero cells* was positive for herpes simplex virus in all the cases. Typing of the virus isolates by indirect haemagglutination inhibition test revealed the virus to be HSV_1 in 4 cases and HSV_2 in 1. The titres of antibodies to HSV_1 and HSV_2 in the blood of these patients, estimated by the indirect haemagglutination test (unpublished data) are shown in the table. The relative activity of serum to HSV_1 and HSV_2 index

$$= \frac{\text{antibody titre to } HSV_2 \times 100}{\text{antibody titre to } HSV_1}$$

An index value of 85 or less was considered to be positive for antibodies to HSV_1 and index value of 86 or higher indicated the presence of HSV_2 antibodies. This criterion was earlier established by one of us (P.S.) on patients with primary and recurrent HSV_1 and HSV_2 infections (unpublished data). Two patients had II/I indices less than 85, and in three the indices were more than 86.

Four of the five cases were treated with local applications of anaesthetic

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TABLE

Case No.	Virus isolated from the lesion	Titre (in log) of serum antibody to HSV				Type of virus indicated by the index
		Date of collecting the specimen	Type 1	Type 2	II/0 index	
1.	HSV_1	(a) 1st day	2.80	2.80	100	HSV_2
		(b) 4th day	3.10	3.20	103	
		(c) 14th day	2.65	2.35	89	
2.	HSV_1	(a) 1st day	3.10	2.20	71	HSV_1
		(b) 4th day	3.40	2.68	79	
3.	HSV_1	1st day	3.20	2.05	64	HSV_1
4.	HSV_2	1st day	2.50	2.50	100	HSV_2
5.	HSV_1	1st day	2.50	2.50	100	HSV_2

ether for 5 minutes on two consecutive days[2]. The lesions healed in the course of 3-4 days.

Discussion

Since urticaria in all these cases occurred along with fever and disappeared following treatment with chloroquine, it seems worthwhile to consider if malaria was responsible for urticaria. To the best of our knowledge, malaria parasite has only infrequently been associated with urticaria. To see if chloroquine could have produced a non-specific suppressive action on urticaria, 5 other patients having urticaria of unknown aetiology were treated with chloroquine in comparable doses, but none of them showed any significant response.

The second interesting feature in these cases was the occurrence of herpes simplex in 5 of the 7 cases, which is a known fact[3]. However, herpes simplex in these cases appeared after chloroquine therapy when malaria had already been controlled. Although there is no report indicating that chloroquine can precipitate an attack of herpes simplex, yet several conflicting reports[4,5,6], thus far available indicate that chloroquine may interfere with the immune responses of the body. It seems likely that in our cases chloroquine may have led to the activation of the virus and thus clinical sequence of events. To see if chloroquine could precipitate an attack of herpes simplex, 2 of these cases were readministered 6 tablets (900 mg.) of chloroquine, 1 and 2 weeks respectively after the herpetic lesions had disappeared, but there was no recurrence.

The third unusual feature was that the lesions of herpes simplex were quite extensive and bilateral in all the cases even when all the patients were adults. There was no history of previous clinical infection with herpes simplex virus in any of the cases. The index of antibody titres to HSV_1 and HSV_2 indicated the infection to be due to HSV_2 in 3 cases, while in 2 of these 3 cases the virus isolated from the lesions was HSV_1. Such discrepancies, however, are well known and are usually seen in patients with dual HSV infections. Moreover, even when the lesions were located on the face in all the cases, the virus isolated from the lesions in one case was HSV_2. Isolation of HSV_2 from an occasional patient with oral and perioral herpetic lesions has also been well documented[7].

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