Recurrent Stevens-Johnson syndrome

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Stevens-Johnson (erythema multiforme with severe mucous membrane involvement) is a serious illness as a single episode but when the condition is recurrent, it represents a grave hazard to the long-term health and even the life of the patient. It is considered an immune response to a wide variety of antigenic stimuli, so that prevention of recurrent attacks depends on identifying the cause in an individual attack, and choosing an appropriate prophylactic treatment is a difficult clinical problem.

Case report

An 11-year-old boy has had four attacks of Stevens-Johnson syndrome in the last 18 months, of such severity that prevention of further episodes is urgent. He presented initially with a 10-day history of cough, fever and malaise with progressive, painful blistering of the lips and mouth, and target lesions on his arms and body. He had been previously healthy and had been on no medication. Mycoplasma pneumonia was diagnosed on the basis of atypical chest X-ray shadowing and greatly raised mycoplasma titres and cold agglutinins. He was treated with intravenous erythromycin, topical steroid and antiseptic creams and opiate analgesia, and made a full recovery, leaving hospital 10 days later. Interestingly, his brother had been discharged only 2 weeks before, also with mycoplasma pneumonia and Stevens-Johnson syndrome.

Over the next 18 months the patient had three further attacks of Stevens-Johnson of increasing severity involving his mouth, skin, eyes, genitalia and anus, lasting 2-3 weeks. Each was preceded by a mild pharyngitis with no further evidence of mycoplasma. He required nasogastric feeding, sedation and strong analgesia. Trials of intravenous hydrocortisone, erythromycin and acyclovir at a dose of 17 mg/kg/day (250 mg three times a day intravenously) (in case of subclinical herpes simplex infection) did not alleviate his symptoms.

In order to prevent further occurrences evidence was sought of a possible association with mycoplasma, adenovirus, drugs, immunodeficiency and herpes simplex virus (HSV). Evidence that mycoplasma played a role included the fact that both the patient and his brother presented with mycoplasma pneumonia followed by Stevens-Johnson syndrome. As shown in Table 1 the role of mycoplasma was confirmed by raised titres and cold agglutinins on the first attack. Subsequent titres were either falling or not significant. Adenovirus was suggested as a cause by raised titres on the third attack, an attack preceded by a mild pharyngitis. It is doubtful whether raised titres on the fourth occasion represented a new adenovirus attack. Drugs were discounted as a cause as the patient was not on any medication before an attack. His immunocompetence was thoroughly investigated (complement, autoantibodies, immunoglobulins, immune complexes and T-cell subsets) and no abnormality was found. HSV has been implicated in recurrent Stevens-Johnson. We were repeatedly unable to isolate, culture, or even find raised titres of HSV antibodies.

Discussion

In the literature there is extensive evidence favouring the association of HSV and recurrent erythema multiforme (EM) from the clinical history, viral isolation studies, genetic marker studies and therapeutic trials. A history of herpes labialis has been obtained in 65% of cases[1]; HSV antigen has been found in circulating immune complexes[2] and in target lesions[3] in a high percentage of cases; and HSV DNA has been demonstrated in target lesions by the polymerase chain reaction[4].

The HLA type DQw3 occurred in 77.4% of patients with EM compared with 41.2% in the control group[5]; the frequency was 88.8% in HSV associated EM and 100% in recurrent EM. This suggests that recurrent EM represents a distinct entity associated with HSV infection. In keeping with this it was found that both the patient and his brother had this same HLA type.

Acyclovir given prophylactically suppressed the condition in 22 of the 32 cases even where there was no clinical evidence of HSV[6]. This suggests that some patients with recurrent EM are subjected to triggering by subclinical HSV infection.

In case the patient falls into such a group he has been started empirically on prophylactic oral acyclovir at a dose of 200 mg twice a day to try to prevent further debilitating attacks.

References

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Table 1. Serological changes during attacks

	1st attack 9-31/3/87		*2nd attack 12-19/7/88*		*3rd attack 20-31/3/89*		*4th attack 3-16/10/89*	
Mycoplasma	640	160	80	80	5	20	40	10
Cold agglutinins								
Anti-I	4000				32		2	
Anti-i	512				<4		neat	
Adenovirus CFT	<5	<5	<5	<5	320	160	40	160
Herpes simplex CFT	<5	<5	<5	<5	<5	<5	<5	<5

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