those of the later, definitive state of the skin. Furthermore, the marked ultrastructural abnormality of the upper stratum corneum, found in neonatal collodion skin of lamellar ichthyosis, was not observed in the self-healing collodion baby. These results should encourage early microscopic examination and follow-up of all types of collodion babies, such data being needed to elaborate reliable, early diagnostic and prognostic criteria.

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Stevens-Johnson Syndrome Associated with Intrahepatic Cholestasis and Respiratory Disease: A Case Report

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Abstract. In an 8-year-old boy, the Stevens-Johnson syndrome (SJS) was associated with protracted intrahepatic cholestasis and ultimately fatal respiratory disease. No precipitating factors of SJS were identified, but a *Mycoplasma pneumoniae* infection was suspected. The appearance of jaundice on the seventh day of illness was preceded by the prescription of erythromycin ethyl succinate, but intrahepatic cholestasis has never before been associated with this derivative of erythromycin. It is suggested that there may exist a subtype of SJS with severe hepato-pulmonary pathology.

Key words: Stevens-Johnson syndrome; Intrahepatic cholestasis; Bronchiolitis; Pneumomediastinum; Erythromycin ethyl succinate

Stevens-Johnson syndrome (SJS) is an acute clinical entity which encompasses fever, exanthema, and inflammation of the orifices of the body (10). SJS may involve internal organs, especially the respiratory and the alimentary tracts (1). There are only occasional reports on liver pathology in association with SJS. We report a unique case of SJS associated with intrahepatic cholestasis and fatal respiratory disease.

CASE REPORT

An 8-year-old boy had suffered from a scaling dermatitis since early childhood. The patient had no record of adverse drug reactions or earlier treatment with erythromycin.

On March 5, 1979, the patient fell ill, with a temperature rising to 40°C. During the next 24 hours he developed an unproductive cough, a red non-vesicular exanthema, conjunctivitis, and erosions of the lips and mouth, glans penis and anus. He was admitted on March 8, the temperature then being 40.4°C, and a generalized purple macular exanthema was found with isolated bullae on the cheeks and extensive ulcerous lesions of the orifices of the body, which led to the immediate diagnosis of SJS.

Examinations on admission. The hemoglobin was 13.7 g/dl, the erythrocyte sedimentation rate 24 mm/h, the leukocyte count 7800/μl with normal distribution. The chest X-ray appeared normal except from subsegmental atelectases of the left inferior lobe.

Treatment. Mycoplasma infections were prevalent in our area at that time, and an underlying infection with this microorganism was suspected (8, 10). Erythromycin ethyl succinate (Abboticin®, Abbott), 300 mg four times a day, was started on March 8 and given for 11 days. The patient's weight was 27 kg.

Topical treatment was given, i.e. prednisolone and chloramphenicol for the eyes, diluted potassium permanganate for the mouth, ointment with silver nitrate for the lips, and mucilago borica for the genital and anal erosions.

Clinical course. The general condition of the patient improved parallel with lytic defervescence within 2 weeks of admission, and the mucocutaneous lesions gradually healed. Mild respiratory discomfort with a productive cough persisted. Jaundice was observed on the fourth day of hospitalization, and it took a protracted course (further details below and in Fig. 1). On April 5, the liver disease prompted a therapeutic trial with prednisone, 40 mg per day, withdrawn over a period of 12 days, but no immediate response was observed.

On April 8, the patient developed stridor with pneumomediastinum and interstitial emphysema, which

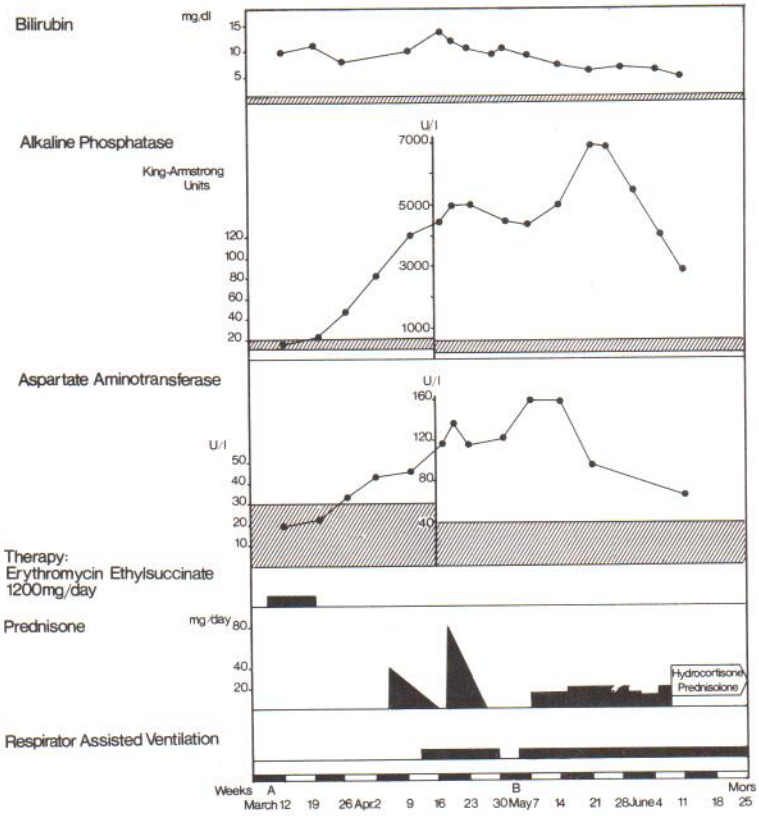

Fig. 1. Liver function tests and therapy in a case of Stevens-Johnson syndrome. The patient was transferred to an intensive care unit, which created confusion of some of the observations. The enzyme activities are not fully compatible. *A*, Admission; *B*, liver biopsy. Normal range of serum bilirubin, alkaline phosphatase and aspartate aminotransferase indicated by hatching.

progressed to the face and the entire trunk. Moderate left pneumothorax was demonstrated on April 11. A tracheostomy was performed, and because of respiratory distress mechanical ventilatory assistance was instituted. The pneumomediastinum and interstitial emphysema abated in 3 weeks but recurred temporarily in the middle of May. Concurrently, there were signs of bronchiolar obstruction, which progressed despite reinstitution of prednisone from April 18, and treatment with theophylamine, sympathicomimetica, and parasympathicolytica. Attempts to wean the patient from the respirator was frustrated by severe respiratory acidosis, which was not alleviated by mechanically assisted ventilation, even with high inspiratory pressure and increased minute volume. From June 16 the patient was kept completely sedated and relaxed. Paradoxically, at that time the liver disease showed definite signs of resolution (Fig. 1). On June 25 death ensued from rapidly developed cor pulmonale. The family was against a post-mortem examination.

The liver disease. The serum levels of bilirubin, alkaline phosphatase, and aspartate aminotransferase (GOT) are shown in Fig. 1. The high level of alkaline phosphatase was attributed to hepatic isoenzymes. Part of the alkaline phosphatase activity was found in association with exceedingly high levels of lipoprotein X. Biochemically, there were no signs of liver insufficiency. A normal extrahepatic biliary tract was demonstrated by endoscopic retrograde cholangiography on April 19, but the intrahepatic branches were not visualized. On May 2, a percutaneous liver biopsy was performed. There was a pronounced centrilobular cholestasis; the distended portal areas were infiltrated by neutrophilic and eosinophilic leukocytes and a few mononuclear cells. The liver cells appeared normal except for a few 'foam cells', which were also present in the small biliary ducts.

The lung disease. Chest X-rays gave no evidence of pulmonary infiltration, but from early June numerous emphysematous bullae and signs of cor pulmonale were observed.

Bronchoscopy on April 11 and May 15 revealed diffuse inflammation with mucinous secretions, but the lumen of the central airways was patent. Cytologic, bacteriologic, and mycologic examinations of the bronchial secretions were unrewarding. A lung scintigram by inhalation of ^{133}Xe failed to reveal the source of the air leakage into the mediastinum and interstitial tissues.

Serology. The following serological tests were negative: Hepatitis B surface antigen, Paul-Bunnell, leptospirosis, cytomegalovirus, herpes virus, and mycoplasma complement binding titres. Within 2 weeks of admission there was a rise in the titre of cold hemagglutinins from 32 or below to 64 or above; no exact titration was carried out, however.

Other investigations. Alfa-1-antitrypsin was within normal limits. In peripheral blood the percentage and the total number of thymus-derived (T) lymphocytes and

lymphocytes with complement receptors were within the normal range. No eosinophilia was present. There was no evidence of hemolysis.

DISCUSSION

The etiology of the SJS reported here remained enigmatic. Respiratory disease has been recognized as one of the main causes of mortality in SJS (1). Earlier reports have pointed to the association of SJS with pneumomediastinum and pneumothorax (4, 5). The fatal respiratory distress was most likely due to severely destructive bronchiolitis, which has been demonstrated in autopsy studies in SJS (1, 3).

Liver disease in association with SJS seems rare. In most reported cases a variety of drugs had been administered before involvement of the liver was diagnosed (7, 9). Cholestasis was demonstrated biochemically or histologically in most patients. The protracted intrahepatic cholestasis observed here might be related to SJS in some undefined way, but a cholestatic drug reaction must also be considered (12). Erythromycin ethyl succinate was the only drug given systemically before jaundice was observed, and therefore this drug is incriminated. To our knowledge, cholestatic reactions to erythromycin ethyl succinate have not been reported before, although the hepatotoxicity of other derivatives of the erythromycin base, i.e. the estolate, is well known (6, 11).

Severe hepato-pulmonary pathology equal to that described here has been reported in a 6-year-old girl with SJS (2). In both cases the prodromal period was short and no systemic therapy preceded the development of SJS. The unique features of these cases may constitute a hitherto unrecognized subtype of SJS.

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Acute Diffuse Scleroderma

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Abstract. A case of acute diffuse scleroderma without contemporaneous visceral involvement is described. Antibodies to endothelial cells have been found in the skin.

Key words: Acute scleroderma; Immunofluorescence

Acute diffuse scleroderma (ADS) or malignant scleroderma is an exceedingly rare kind of systemic sclerosis, with acute onset, involving the trunk, sparing face and hands, and without Raynaud's phenomenon (8). The involvement of