STEVENS-JOHNSON SYNDROME: A STUDY OF 17 CASES

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Summary

Seventeen cases of Stevens-Johnson syndrome are reported. Clinical manifestations and laboratory findings have been described. Only 5 cases had classical triad of conjunctivitis, stomatitis and urethritis with skin lesions. Four patients had corneal ulcerations. There were 3 deaths. Sulfonamides, acetylsalicylic acid, thiacetazone, isoniazide, phenylbutazone, oxyphenbutazone and strepto-penicillin were the responsible drugs for the development of Stevens-Johnson syndrome in 11 cases, whereas, no cause could be ascertained in 6 cases.

Introduction

Stevens-Johnson Syndrome is a symptom complex consisting of conjunctivitis, stomatistis, urethritis and generalised bullous skin eruptions. Alibert (cited by Sainani and Balsara, 1970[1]) in 1828 first described this clinical entity and Hebra[2] labelled it as erythema multiforme exudativum. This condition came to be more generally recognised when Stevens and Johnson in 1922[3] reported two children with fever, multiple cutaneous eruptions, stomatitis and opthalmia. Since then their names have been associated with this condition. Few cases of this syndrome have been reported from time to time[4-18]. Ashby and Lazer[19] reviewed 77 cases from literature and added four cases of their own. Claxton[20] reviewed 31 cases from Australia. Thirty cases of Stevens-Johnson Syndrome following the use of long acting sulphonamide therapy were reviewed in B.M.J.-Editorial[21]. Soll (cited by Ashby and Lazer,[19]) reported a series of 20 personal cases of this syndrome. Recently Sarkari et al[22] reported 20 cases from India. The present paper is an analysis of 17 cases of Stevens-Johnson Syndrome.

Material and Methods

Material of this paper consists of 17 cases of Stevens-Johnson Syndrome admitted to the Irwin Group of Hospitals, Jamnagar, from June, 1970 to December, 1974. A careful history of recent ingestion of drugs was obtained. All the patients were subjected to complete clinical examination with particular emphasis on type of the skin and mucous membrane lesions. An attempt was made to detect any involvement of cornea.

Routine investigations like total and differential leucocytic count, haemoglobin, erythrocyte sedimentation rate, bleeding and clotting time, platelet count, urine analysis, stool examination, fluoroscopy and/or skiagram of the chest were carried out. A bacteriological smear examination and culture studies from skin, mouth, eyes and urethra were

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routinely done. Cold agglutination test was performed in all the cases.

All the patients received good nursing care and supportive treatment. Intragastric and/or parenteral feeding were carried out as and when required. Systemic steroid therapy (prednisolone) was given to all the cases ; the dosage varying from 20 to 40 mg. daily in divided doses depending upon the sevcrity of the disease. Steroid therapy was gradually tapered and eventually stopped as the condition of the patients improved. Parenteral steroid therapy was used when patients were not able to swallow and the disease was severe. Prophylactic systemic antibiotics were given to all the cases. Patients with involvement of the eyes were treated in consultation with ophthalmologist.

Observation

Seventeen cases of Stevens-Johnson Syndrome were included in the present study. There were 12 males and 5 females with ages ranging from 10 to 60 years, the mean age being 27.2 years. Ten patients were below 30 years of age. Table 1 shows the clinical details of these cases. Classical triad of conjunctivitis, stomatitis and urethritis with skin lesions were seen only in 5 cases. Ten patients had pyrexia. Involvement of the conjunctivae and mouth was present in all the cases. Lesions of the mouth varied in the extent of involvement from scanty isolated lesions to widespread lesions of buccal mucosa, pharynx, tongue, gums and lips. Mucopurulent conjunctivitis was seen in all cases. Corneal ulcers were present in 4 cases. Five cases had only macular erythematous skin lesions while remaining 12 cases had bullous eruptions with or without haemorrhagic fluid. Crusting and fissuring particularly over the lips were seen in 5 cases.

Conjunctival smears were examined bacteriologically but no organisms could be demonstrated. Bacterial culture from the conjunctivae revealed staphylococcus aureus in 5 cases and streptococcus haemolyticus in 2 cases. The culture study from the skin lesions were negative in 14 cases while staphylococcus aureus was cultured in 3 cases. Culture from the mouth revealed staphylococcus aureus and β streptococcus haemolyticus in 4 and 3 cases respectively. Total leucocytic count was more than 12,000/cmm. in 5 cases. Bleeding time, clotting time and platelet count were normal in all the cases. Cold agglutinin test was negative in all the cases.

Three patients died out of which 1 had pulmonary tuberculosis; remaining 2 cases were admitted late in poor general condition and expired within 24 hours of hospitalisation as a result of peripheral circulatory failure and toxemia. Autopsy could not be performed. As seen in Table 1, three cases had received sulfonamides, 3 received acetyl salicylic acid, 2 thiacetazone and isoniazide, 1 oxyphenbutazone, 1 phenylbutazone and 1 streptomycin and penicillin.

Discussion

Different names have been given to this syndrome by various workers at different times. These are ectoderma erosiva pleuriorificialis[23], erythema multiforme exudativum[16], erythema multiforme bullosum, erythema multiforme iris[24] and new eruptive fever[3]. Although of historical importance, these different names offer no advantage and some of these placed too much emphasis on a single morphological feature. Stevens-Johnson syndrome is now the most commonly used term. This syndrome includes conjunctivitis, stomatitis, urethritis and skin lesions. All of these or a combination of some of them may be seen in one patient. (Gwannu, Williams, 1963[8].)

TABLE 1

Showing details of clinical features and investigations : Stevens-Johnson syndrome—Shah et al

S. No.	Age	Sex	Mouth Lesions	Conjuc-tivities	Corneal ulcer	Urogenital lesions	Skin Lesions	Pyrexia	Responsible drugs	Culture studies		
										Conjuc-tive	Skin	Mouth
1.	14	M	Stomatitis Glossitis	+	—	Balanitis	Macular	—	—	Staph Aure	—	Strept Haem
2.	19	M	Stomatitis glossitis crusts and fissures on lips	+	—	Urethritis	Bullous	—	Sulfonamide	—	—	Staph Aure
3.	45	M	Stomatitis glossitis oedema lips	+	+	Balanitis	Bullous	+	—	Strept Haem B	—	Staph Aure
4.	18	M	Stomatitis glossitis	+	—	Urethritis	Bullous Haemorrhagic	—	Oxyphenbuta-zone	Staph Aure	—	—
5.	60	F	Stomatitis glossitis crusts and fissures on lips	+	—	Labial ulceration	Macular	—	Acetyl salicylic acid	Staph Aure	—	Staph Aure
6.	31	M	Stomatitis glossitis crusts and fissures on lips	+	—	Extensive denudation of scrotal skin	Bullous	+	Sulfonamide	—	Staph Aure	—
7.	19	F	Stomatitis ulcers on pharynx	+	+	Urethritis	Bullous Haemorrhagic	+	Phenylbuta-zone	—	—	Staph Aure
8.	17	M	Stomatitis, glossitis, fissure-crusts on lips	+	+	Urethritis	Bullous Haemorrhagic	+	Phenyl-butazone	Staph Aure	—	β Strept Haem

S. No.	Age	Sex	Mouth Lesions	Conjunctivities	Corneal ulcer	Urogenital lesions	Skin Lesions	Pyrexia	Responsible drugs	Culture studies		
										Conjunctive	Skin	Mouth
9.	35	M	Stomatitis, glossitis, oedema over lips	+	—	—	Bullous	+	—	—	Staph aur	—
10.	36	F	Glossitis	+	—	—	Bullous	—	—	Staph aure	—	—
11.	32	F	Glossitis, stomatitis oedema lips	+	—	—	Macular	+	—	—	—	β Stre haem
12.	25	F	Stomatitis, glossitis, ulcers over pharynx with slough	+	—	Labial ulceration, vaginitis	Bullous haemorrhagic	+	Acetyl salicylic acid	—	—	—
13.	42	M	Stomatitis, glossitis	+	—	urethritis	Bullous haemorrhagic	+	Thiacetazone Isoniazide	—	Staph aure	—
14.	10	M	Stomatitis, glossitis	+	—	—	Macular	+	Sulfonamide	β Strep haem	—	—
15.	22	M	Stomatitis, glossitis, fissurecrusts on lips	+	+	—	Macular	—	Strepto-penicillin	—	—	—
16.	20	M	Stomatitis, glossitis	+	—	—	Bullous	—	Acetyl salicylic acid	—	—	—
17.	18	M	Stomatitis, glossitis	+	—	—	Bullous	+	Thiacetazone Isoniazide	—	—	—

N.B. Case No. 8, 13 and 15 died.

The disease usually starts as a febrile illness followed by mucocutaneous eruptions which may take a vesiculobullous form with exfoliations. Ulcers may develop on various mucous membranes so that patients may present themselves with stomatitis, conjunctivitis, urethritis and/or balanitis. Only 5 of our cases had classical triad of stomatitis, conjuntivitis and urethritis with skin lesions. Ocular manifestations are reported to be present in 50 to 80% of the cases[18]; these include conjunctivitis of various types, iritis, iridocyclitis, corneal ulcerations and perforation. Conjunctivitis was seen in all the cases reported by Sarkari et al[22] and the same was true in the present series. Four of our cases had corneal ulceration.

The disease is usually self limiting though it can be fatal. Greenberg and Messer[5] observed a fatal case following the administration of sulfadiazine. Similarly fatal cases have been reported by Rafetto & Nichols[25], Dardinski[6] and Salvaggio & Gonzalez[26]. Out of 30 reviewed cases of Stevens-Johnson syndrome due to long acting sulfonamides, 8 were fatal[21]. Sarkari et al[22] reported 3 deaths among their 30 cases. Three of our cases succumbed to the disease. Out of 77 reviewed cases, Ashby & Lazer[19] reported 8 deaths. Necropsy was performed in 6 of these cases. The main cause of death was lung involvement.

No laboratory test is specific for the diagnosis of Stevens-Johnson syndrome and hence the diagnosis is mostly clinical. Some degree of leucocytosis is common although the leucocytic count may be normal or decreased. Singer et al[16] reported 2 cases with leukemoid reaction. Leucocytosis was seen in 6 of our cases. Culture studies from skin, conjunctivae, oral cavity and urethra are generally negative or exhibit contaminants or secondary invaders. Similar was our experience, as well as that of Sarkari et al[22].

There exists certain disagreement as to whether Stevens-Johnson syndrome is a separate clinical entity. Klauder[23] and Keil[27] were of the opinion that this condition is a variant of erythema multiforme while Stevens-Johnson[3] and Ginandes[28] presented arguments in favour of the syndrome as a separate disease. The pathogenesis of the disease is not understood. It has been assumed to result from some infection[10],[29] or as an hypersensitive or allergic reaction to some drugs. A large number of drugs which have been incriminated to cause this syndrome are: long and short acting sulphonamides,[3],[5],[6],[8],[12],[30],[31], salicylates[1], thiacetazone and other antituberculous drugs[4],[11],[13],[18],[22],[32], oxyphenbutazone[1], phenylbutazone[22], penicillin[15], antiepileptic drugs[33], etc. In the present study definite history of drug consumption was obtained in 8 cases. Sulphonamides, acetyle salicylic acid, thiacetazone, isoniazide phenylbutazone, oxyphenbutazone and streptopenicillin were responsible for the development of this syndrome in 3,3,2, 1 and 1 cases respectively. Ludlam et al[10] have shown relationship between this syndrome and mycoplasma pneumoniae by the presence of cold agglutinin in the blood. This observation is interesting. In all of our cases cold haemagglutinin test was negative.

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