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Septic Gonococcal Dermatitis

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Summary

The overall incidence in gonorrhoea of septic gonococcal dermatitis was found to be 1.9% (3% for the females and 0.7% for the males). In 23 patients the common presenting symptoms were arthritis or arthralgia and bouts of fever, but the characteristic skin lesions served as an early clue to the diagnosis, and *Neisseria gonorrhoeae* was isolated from the genitourinary tract or from the blood. With the use of immunofluorescent techniques gonococci were also found in smears prepared from the skin lesions. An immune response to gonococci was found with the complement fixation technique in 90% of the patients. The response to treatment with penicillin was prompt, with complete relief from joint pains and fever, usually within two to seven days. The skin lesions faded within a few days, but scars could be observed for up to four weeks.

Introduction

Skin lesions and arthritis in gonorrhoea were described as early as 1893 by Vidal. The syndrome of fever, arthritis, and cutaneous manifestations in association with gonococcaemia was noted by Silvestrini (1903). Several reports of this syndrome appeared in the pre-antibiotic era and two clinical forms were distinguished—one relatively benign, the other fulminant with fatal endocarditis (Cohn, 1936; Levin and Silvers, 1937; Lichterman, 1937; Keil, 1938; Reitzel and Kohl, 1938).

After the advent of penicillin there were no reports of this type of complication of gonorrhoea until that of Abu-Nassar *et al.* (1963). Since then several authors have drawn attention to this syndrome (Kvorning, 1963; O'Sullivan, 1964; Ackerman *et al.*, 1965; Fred *et al.*, 1965; Björnberg and Gisslén, 1966; Danielsson and Michaëlsson, 1966; Wolff *et al.*, 1970). Septic gonococcal dermatitis is a more relevant name, since it has been shown with cultural methods and fluorescent antibody techniques that the cutaneous manifestations are due to the embolization of gonococci with a genitourinary gonorrhoea as the primary focus (Kahn and Danielsson, 1969).

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Most patients with septic gonococcal dermatitis have no symptoms indicating a venereal disease (Abu-Nassar *et al.*, 1963; Kvorning, 1963; O'Sullivan, 1964; Ackerman *et al.*, 1965), and it is certain that some are treated with penicillin or other antibiotics without a specific diagnosis but with prompt therapeutic response. It is also the experience of many authors that some patients recover without treatment. This type of complication of gonorrhoea is therefore easily overlooked, resulting in difficulties in getting information regarding its frequency and epidemiology.

Patients and Methods

PATIENTS AND PERIOD OF STUDY

Our attention was drawn to septic gonococcal dermatitis at the hospital in Örebro City in November 1968 when *Neisseria gonorrhoeae* was isolated from the blood of a man with fever, septic skin lesions, and minor joint affections. Since then 22 further patients with this disease have been seen at our hospital during a 20-month period. The monthly distribution of the cases is shown in Fig. 1. A presumptive diagnosis of septic gonococcal dermatitis was considered in patients presenting a history of moderate discomfort, with or without joint affections and bouts of fever, and with typical skin lesions similar to those described and excellently illustrated with colour prints by Abu-Nassar *et al.* (1963) and Ackerman *et al.* (1965). The diagnosis was considered to be conclusive when gonococci were found in skin lesions or isolated from the genitourinary tract or from the blood according to techniques described below. In one patient the diagnosis was based on the presence of skin lesions, arthritis, a high serum titre of gonococcal antibodies, and a prompt therapeutic response to penicillin therapy.

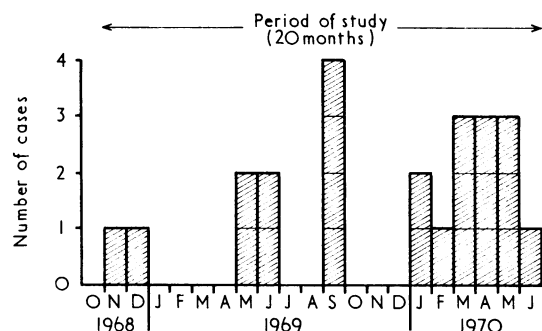


FIG. 1—Monthly distribution of patients with septic gonococcal dermatitis during a 20-month period.

BACTERIOLOGICAL EXAMINATIONS

Genitourinary specimens.—Charcoal-impregnated swabs were used to take specimens from the urethra in men and from the urethra, cervix, and rectum in women. The specimens were taken to the laboratory in modified Stuart transport medium (Gästrin and Kallings, 1968) and were inoculated on to gonococcal medium with or without antibiotics (Thayer and Martin, 1964; Martin *et al.*, 1967). The plates were incubated in 5-10% CO₂ at 35-36°C for two days. Suspicious colonies were subsequently identified as *N. gonorrhoeae* with immunofluorescent techniques (Danielsson, 1965) and tested for antibiotic sensitivity with the disc method (Ericsson, 1960).

Blood Cultures.—Five to 10 ml of blood was taken and injected into bottles containing a chocolate agar slant and enrichment broth with added penicillinase and *p*-aminobenzoic acid. The bottles were incubated at 35-36°C, inspected daily, and discarded after 10 days. Isolated bacteria were identified as *N. gonorrhoeae* with oxidase test, Gram stain, immunofluorescent tests, and fermentation tests, and they were examined for antibiotic sensitivity as described above.

Skin Lesions.—Direct smears were made from skin lesions by scraping off exudate with a finger-tip lancet or with the corner of a cover-glass from a blood-counting chamber. *N. gonorrhoeae* present in the smears was identified with immunofluorescent techniques (Danielsson, 1965).

SEROLOGICAL EXAMINATIONS

Serum specimens were obtained from 21 out of the 23 patients examined and were tested for gonococcal antibodies with the complement fixation technique (Magnusson and Kjellander, 1965). Two or more serum specimens were obtained from 18 patients and single serum specimens from three.

Syphilis serology was performed on all serum specimens with the use of standard reaginic tests (Kline's and Meinicke's reactions). The results were negative.

Results and Comments

The clinical manifestations and laboratory findings of the 23 patients with septic gonococcal dermatitis are summarized in

the Table. The female to male ratio was 4.75:1. Most of the patients were unmarried adults aged 18 to 30; the youngest was a 16-year-old girl. It should be noted, however, that three patients, two women and one man, were 44, 51, and 52 years old respectively.

The duration of symptoms was usually short. Eighteen patients had had bouts of fever, and all except two had had symptoms in one or more joints. Seventeen had had objective joint affections with swelling, sometimes redness, and very often non-pitting oedema of the periarticular tissues. Joint effusions were slight or absent. Pain was the only joint symptom in seven patients. One patient (Case 15) with no subjective or objective joint affections had a one-day episode of myalgia nuchae on his right side at the time he had his bouts of fever and his skin lesions appeared.

SKIN LESIONS

As a rule it was painful joint affections or bouts of fever rather than skin lesions that brought the patient to the hospital. From our point of view, however, the typical skin lesions were the most important diagnostic sign. The cutaneous manifestations appeared in various stages of development, from discrete violaceous maculopapules and vesiculopustules about 1-5 mm in diameter to haemorrhagic papules and vesiculopustules about 4-20 mm in diameter, often surrounded by an erythematous zone. Two patients presented pea-sized subcutaneous nodules which were painful and appeared with a bluish or violaceous colour reminding one of erythema nodosum. The number of skin lesions varied from one to more than 10; in three patients 25 to 40 lesions were observed. The lesions were unevenly distributed, with a certain predominance in the extremities and periarticular regions. A few patients had skin lesions similar to those seen in varicella; but, in contrast to this disease, lesions were never observed on the oral mucosae or on the scalp.

A few of the women had noted a somewhat increased vaginal discharge, but this was so slight that they had not suspected a venereal disease. It is noteworthy that three of the men (Cases 1, 13, and 22) did not have the slightest symptoms of a urethritis though gonococci were isolated from the urethra in two of them (Cases 13 and 22). When gonococci were isolated from the blood of Case 1 he had received penicillin for six days, and subsequent cultures from the urethra were negative for gonococci. The fourth man (Case

Summary of Clinical Manifestations and Laboratory Findings in Patients with Septic Gonococcal Dermatitis

Case No.	Sex and Age	Duration of Symptoms (Days) before Admission	Temperature in °C	Discharge	No. of Skin Lesions	No. of Joints Involved †	E.S.R. (mm)	Gonococcal Culture of Specimens from				IFL of Smears from Skin Lesions	C.F. Tests for Gonococcal Antibodies		Disappearance of Symptoms (Days) after Treatment
								Urethra	Cervix	Rectum	Blood		Max. Serum Titre	Change of Serum Titre	
1	M.36	14	40	—	2	(4) 0	22	N.D.	—	—	+	N.D.	1:10	N.A.	14
2	F.18	1	37	—	5	(0) 1	83	+	+	—	—	N.D.	1:80	Yes (8-fold)	7
3	F.20	1	39	+	15	(0) 1	14	+	+	+	—	+	1:10	Yes (4-fold)	3
4	F.*44	1	39	—	4	(N.A.) 0	22	—	+	—	—	N.D.	<1:5	N.A.	3
5	F.*26	1	N.A.	—	2	(0) 1	18	+	+	+	N.D.	N.D.	N.A.	N.A.	N.A.
6	F.20	30	38	+	3	(0) 1	83	+	—	—	—	N.D.	1:160	Yes (16-fold)	14
7	F.19	2	N.A.	—	1	(0) 1	77	+	+	N.D.	—	+	1:80	Yes (16-fold)	3
8	F.24	1	39	—	4	(5) 0	17	N.D.	N.D.	N.D.	+	+	<1:5	No	4
9	F.23	N.A.	N.A.	+	7	(N.A.) 1	N.D.	+	+	—	N.D.	N.D.	N.A.	N.A.	N.A.
10	F.*27	1	39	—	10	(1) 1	91	+	+	—	—	+	1:5	Yes (2-fold)	2
11	F.*51	3	39	—	10	(0) 1	55	N.D.	N.D.	N.D.	+	—	1:80	Yes (32-fold)	3
12	F.22	3	39	(+)	10	(6) 0	N.D.	+	+	—	—	(+)	1:10	Yes (4-fold)	5
13	M.*52	6	38	—	>30	(2) 3	86	+	+	—	—	+	1:20	Yes (8-fold)	2
14	F.18	6	39	—	6	(N.A.) 2	27	+	+	—	—	+	1:20	Yes (4-fold)	3
15	M.20	5	40	(+)	5	(0) 0	N.D.	+	+	—	N.D.	N.D.	1:5	Yes (2-fold)	7
16	F.*29	5	38	(+)	3	(0) 1	120	+	+	—	—	—	1:20	Yes (8-fold)	3
17	F.33	3	39	+	10	(2) 3	45	+	+	—	—	—	1:10	Yes (4-fold)	3
18	F.29	1	39	(+)	40	(2) 0	20	+	+	+	—	+	1:5	Yes (2-fold)	2
19	F.26	4	39	+	25	(0) 3	60	+	+	—	—	+	1:80	Yes (32-fold)	1
20	F.28	1	38	—	7	(0) 1	20	+	+	N.D.	—	+	<1:5	No	1
21	F.16	2	38	—	5	(0) 1	26	+	+	N.D.	—	+	1:10	Yes (4-fold)	2
22	M.28	7	N.A.	—	2	(0) 2	22	+	+	—	N.D.	(+)	1:5	Yes (2-fold)	7
23	F.*27	1	39	+	10	(5) 1	22	+	+	—	—	(+)	<1:5	N.A.	3

*Married.

† Figures in parentheses indicate number of joints presenting subjective symptoms, the other figures indicate objective symptoms.

E.S.R. = Erythrocyte sedimentation rate. IFL = Immunofluorescence.

N.A. = No information available. N.D. = Not done.

15) had slight symptoms of an untreated urethritis for six weeks. He was the partner of Case 14.

LABORATORY FINDINGS

As shown in the Table *N. gonorrhoeae* was isolated from all the patients but one; from urethral specimens in three of the men, and from one or more of the specimens from the genitourinary tract in 17 of the women. Specimens from the urethra or the genitourinary tract were not taken from three of the patients, one man and two women, before treatment with penicillin was initiated. Gonococci were, however, isolated from the blood of these patients. Blood cultures from another 16 patients gave negative results.

All the isolated gonococcal strains were sensitive to penicillin, with a minimum inhibitory concentration of less than 0.1 unit of penicillin per ml. The isolated strains were also sensitive to streptomycin and tetracycline.

Attempts to isolate gonococci by culture of material obtained from skin lesions were made in eight patients, but no growth of gonococci was obtained. With the use of immunofluorescent techniques, however, *N. gonorrhoeae* was detected in the smears of skin lesions in 14 out of 16 patients examined. In this way a diagnosis of septic gonococcal dermatitis was arrived at in two patients (Cases 7 and 17) within two hours after their admission to hospital. In three patients a reservation of the results of the immunofluorescent tests was made because the morphology of the "supposedly" observed gonococcal organisms was strongly distorted.

With the use of the complement fixation technique, antibodies to *N. gonorrhoeae* were found in serum specimens from 17 out of 21 patients examined. Only acute-phase sera were obtained from two (Cases 4 and 23), and they were negative in the complement fixation test. Serum specimens were obtained from 18 patients both in the acute and/or in the early and late convalescent phases of their disease, and 16 of them developed gonococcal antibodies as demonstrated with a two-fold to 32-fold increase or change of the antibody titres. Representative results of these tests in three of the patients—two women and one man—are given in Fig. 2.

THERAPY

As we regarded the disease as a septicaemia our policy was to treat these patients with parenteral penicillin G in a dose of 4.5 megaunits daily for two days followed by oral penicillin V in daily doses of 3 to 4 megaunits for 10 days. The therapeutic response was prompt—almost a diagnostic criterion—with complete relief from joint pains and fever generally within two to seven days (see last column of Table). The skin

lesions faded away within a few days, but scars could be observed for up to four weeks. Three patients were treated at the outpatient clinic for venereal diseases with 1 g of ampicillin followed by the same dose five hours later (Groth and Hallqvist, 1970) with apparently good clinical results and with no known relapse of the symptoms. Some of the patients showed a tendency to recover spontaneously before penicillin therapy was begun.

EPIDEMIOLOGICAL SITUATION AND INCIDENCE

The hospital in Örebro City, one of the seven so-called regional hospitals in Sweden, has a dual function: (1) as a reference hospital for selected cases from a region with 1.3 million inhabitants, and (2) as a local hospital serving a local district with 120,000 out of the 260,000 inhabitants of Örebro County. During the 20-month period of our study 914 men and 831 women were reported and treated for gonorrhoea within Örebro County. This would make the incidence of septic gonococcal dermatitis as a complication to gonorrhoea 2.3% for the females and 0.4% for the males. The more relevant figures, however, are provided by the local district, where 542 men and 523 women were reported and treated for gonorrhoea during the period of our study and where 16 women and 4 men were found to have septic gonococcal dermatitis. This makes the incidence 3.0% for the females and 0.7% for the males. These should be the minimal figures for septic gonococcal dermatitis as a complication of gonorrhoea since some cases within our county are treated by other colleagues. We have not included these cases in the present report as we were not able to collect enough clinical and laboratory data about them.

Discussion

Skin lesions associated with gonococcaemia were recognized in the pre-antibiotic era, but this type of complication of genitourinary gonorrhoea was then considered extremely rare and there were figures of only 0.2-0.3 per 1,000 (Neumann and Bingenheimer, 1937; Stertz, 1940). Since Abu-Nassar *et al.* (1963) reviewed 14 cases it has been widely reported that this characteristic syndrome, with typical skin lesions, intermittent fever and with or without arthralgia and arthritis in combination with genitourinary gonorrhoea is more common than is usually thought (Abu-Nassar *et al.*, 1963; Kvorning 1963; O'Sullivan 1964; Ackerman *et al.*, 1965; Fred *et al.*, 1965; Björnberg and Gisslén, 1966; Danielsson, and Michaëlsson, 1966; Kahn and Danielsson, 1969; Wolff *et al.*, 1970). Keiser *et al.* (1968) reported an incidence of approximately 0.4%. In the present report we have found an overall incidence of 1.9%.

These figures should mean about 650-700 cases of septic gonococcal dermatitis in Sweden a year. Nothing like that number are reported. Several authors have emphasized that if the doctor is not familiar with this type of gonorrhoeal complication it is prone to be dismissed under labels such as "benign bacteraemia of unknown aetiology," "allergic rash," "virus infection," or "benign rheumatic fever." The common use or misuse of penicillin and other antibiotics to treat patients with fever and joint symptoms may successfully mask the true aetiology of this syndrome, as may also the tendency to spontaneous remission in some of the patients observed in this report and also by others (Abu-Nassar *et al.*, 1963).

As skin lesions, joint pains, and fever are the predominant symptoms it is understandable that these patients are not seen initially by venereologists. The first eight cases in our series reported to the infectious disease unit were diagnosed through consultation with colleagues at the departments of infectious diseases or clinical bacteriology. After discussion of the syndrome at one of our regular staff meetings cases came

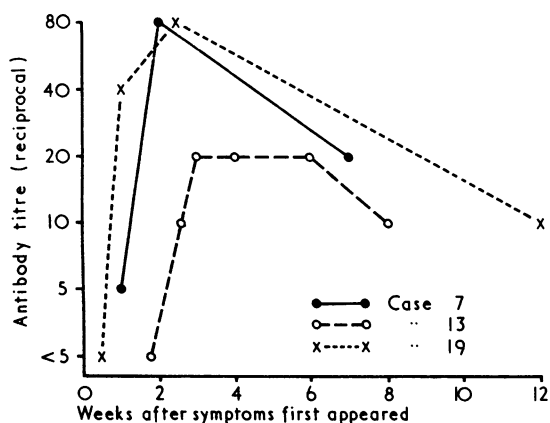


FIG. 2.—Appearance of gonococcal antibodies in three patients with septic gonococcal dermatitis.

from all parts of the hospital—the orthopaedic clinic (1 case), the surgical outpatient clinic (2 cases), the department of gynaecology (2 cases), the medical outpatient clinic (1 case), the outpatient clinic for venereal diseases, and the department of dermatology (3 cases).

It was notable that 10 out of 23 patients with septic gonococcal dermatitis were admitted to hospital during the last four months of this study (Fig. 1). This clustering of cases suggest that some unidentified epidemiological or bacteriological factor may be involved. Only two of the patients were sexual partners, however, while available data did not indicate common male or female contacts for the others. None of the men had symptoms of a gonorrhoeal urethritis, and a further two male partners of two of the women with gonococcaemia were also symptom-free but harboured gonococci in their urethras. These observations direct attention to the significance of asymptomatic gonorrhoea and a carrier state in males as well as in females.

Wolff *et al.* (1970), in a review of literature, showed that gonococci were isolated from skin lesions in only 2 out of 41 patients. Like most others we were also unsuccessful in culturing gonococci from skin lesions. With the use of immunofluorescent techniques, however, we demonstrated gonococci in skin lesions in 14 out of 16 patients examined. These findings are in agreement with those of Danielsson and Michaëlsson (1966) and of Kahn and Danielsson (1969), and they clearly indicate that the skin lesions of the patients with this syndrome are due to a generalized infection. This is further supported by positive blood cultures in a few of the patients.

The present report also shows that a serological examination with the gonococcal complement fixation test may be of diagnostic value, but it should be stressed that serum specimens have to be taken and examined during the acute and convalescent phases of the disease. In this way an immune response to *N. gonorrhoeae* was found in nearly 90% of the patients. The specificity of the gonococcal complement fixation test has been questioned by some authors (Reyn, 1962), but in our mind a significant change of serum titres strongly supports the diagnosis. Preliminary results with the double diffusion-in-gel technique of the patient's sera have also confirmed recent observations on an antigenic factor of the gonococcus involved in the immune response (Danielsson *et al.*, 1969; Reising *et al.*, 1969).

The clinical picture of septic gonococcal dermatitis may

resemble chronic meningococcaemia (Ognibene and Dito, 1964) and the very rare type of septicaemia caused by *N. flavescens* (Wertlake and Williams, 1968). The bacteriological findings will, however, differentiate these diseases.

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