Articular and cutaneous manifestations of gonorrhoea

Review of sixteen cases

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The incidence of gonococcal infection of the urogenital tract has risen steeply throughout the world in the past few years. With this rise has re-emerged a benign syndrome of gonorrhoea associated with acute polyarthritis and characteristic vesiculo-pustular skin lesions.

This syndrome was first described by Vidal (1893), and a year later Hewes (1894) isolated Gram-negative organisms from the blood of these patients. Before the advent of antibiotics these complications were reported rarely (Irons, 1909), and Abu-Nassar, Hill, Fred, and Yow (1963) were the first for 20 years to draw attention to the illness. Since then it has been well documented in the United States (Ackerman, Miller, and Shapiro, 1965; Partain, Cathcart, and Cohen, 1968; Keiser, Ruben, Wolinsky, and Kushner, 1968; Wheeler, Heffron, and Williams, 1970; Holmes, Counts, and Beaty, 1971; Cooke, Owen, Irby, and Toone, 1971, and also in Europe (Kvörning, 1963; Danielsson and Michaelsson, 1966; Björnberg, 1970; Barr and Danielsson, 1971).

Three cases were reported by Wolff, Goodman, and Vahrman (1970), and five by Harris, McCann, and Mahoney (1973), but no large series of similar patients has been presented from Great Britain.

This paper describes the presentation, diagnosis, and treatment of sixteen patients with systemic manifestations of gonorrhoea seen in the last 2 years at St. Thomas' Hospital, London.

Patients and methods

Of the sixteen patients, thirteen were women (Cases 12 and 14 negro and the rest caucasian). The age range was 17 to 43 years (mean 25). There was one married couple, all the others being single or separated. Only three patients were seen initially in the Department of Venereal Diseases; the others presented to general physicians, rheumatologists, or dermatologists.

The typical picture was that of a mild systemic illness, with pyrexia, polyarthritis or arthralgia, sometimes migratory, and typical vesiculo-pustular skin lesions often

occurring in crops. Gonococci were always isolated from the urogenital tract, blood, or joint effusion fluid, and there was a dramatic response to antibiotic treatment.

JOINTS

Arthritis was present in all patients and was recognized if a joint was painful on movement, or showed tenderness, effusion, or marked soft tissue swelling. The arthritis was acute in onset, asymmetrical, and sometimes migratory. Affected joints could be exquisitely painful both on passive movement and at rest, even if not obviously swollen. Tenosynovitis and sacroiliac pain were recorded, but monarticular involvement was not. Some patients complained of generalised aches and pains in their joints at the onset of their illness. Definite gonococcal arthritis was diagnosed only if gonococci could be recovered from a joint, but was thought to be probable if polyarthritis associated with gonococcal infection elsewhere responded dramatically to antibiotic treatment.

SKIN

Cutaneous lesions were found in fourteen patients, and always appeared within a week of the joint symptoms. They were often found near affected joints. The rash was characteristic (Figs 1, 2, and 3) and occurred usually on the extremities, four to five lesions being the average number, though it could be widespread. No lesions affected the scalp or mucous membranes. The lesions were often painful, and cropping occurred, each crop being preceded by a rise in temperature. Lesions started as a red macule or purpuric spot, and proceeded to papule, vesicle, and finally to pustule. Haemorrhage was common in both large and small lesions. The lesions faded in a few days to leave small scars.

UROGENITAL SYSTEM

All three men had a urethral discharge, although this was not a symptom in two. One of the women presented with a vaginal discharge, which was found to be due to co-incident trichomonal vaginitis (present in six others), but none of the other women had any urogenital symptoms, and examination of the urogenital tract was unremarkable. Six patients had had previous episodes of gonorrhoea and three had subsequent attacks, but none had any systemic manifestations.

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FIG. 2 Early skin lesion, macular and purpuric

LABORATORY TESTS

Smears and cultures were taken from the urethra in men, and from the urethra, cervix, and rectum in women, on one or more occasions. Blood cultures were taken after pelvic examination and these, together with synovial fluid specimens, were cultured immediately. Air-dried smears were stained by Gram's method and examined immediately. Cultures were plated onto VCNT medium as described by Phillips, Humphrey, Middleton, and Nicol (1972), and incubated at 37°C. in candle-extinction jars. The plates were examined after 18 hrs and any growth identified by immunofluorescence microscopy, using a fluorescein-labelled rabbit anti-gonococcal antiserum (Difco Labs.). Plates were kept for a further 24 hrs, and examined in the same way.

The joint fluid was examined in five patients and skin biopsies in four. Skin sections were examined histo-

FIG. 2 Large pustule

logically, and part of the biopsy tissue was cultured for gonococci. Direct immunofluorescence microscopy was performed in three cases, as described previously. Routine seriological and haematological tests were taken.

Results

In thirteen of the sixteen patients, reliable information was obtained to establish a presumed date of infection (Table I, overleaf). Most of the patients contracted the infection about 2 weeks before the onset of symptoms. No patient gave a history of more than 21 days symptoms.

An accurate menstrual history was obtained in eleven of the thirteen female patients: seven of these had had a menstrual period within a week of the

FIG. 3 Large vesico-pustule

Table I *Clinical particulars of sixteen patients*

Case no.	Sex	Age (yrs)	Marital status	Pre-vious gonor-rhoea	Last inter-course before symp-toms (days)	Last men-strual period (days before onset)	Skin les-ions	No. of joints in-volved	Body tempera-ture (°F.)	Interval from arth-ralgia to skin lesions (days)	Evidence of pelvic inflam-mation	Reso-lution of symp-toms (days after inter-course)	Presenting feature
1	M	43	M	+	15?	0	+	4	104	2*	0	1	Symptoms of septicaemia
2	F	21	S	—	5?	0	+	2	0	7	—	3	Arthritis + skin lesions
3	F	26	Div.	—	Not known	19	+	3	101	2*	—	3	Arthritis + skin lesions
4	F	43	Div.	—	49	10	+	3	102	7	—	2	Arthritis
5	F	19	S	+	14	23	+	4	99.4	2*	—	1	Arthritis + skin lesions
6	F	42	M (Wife of case 1)	—	15	21	+	2	98.4	1	—	1	Known gonorrhoea contact
7	F	17	S	—	16	22	+	2	102	7	—	1	Arthritis + skin lesions
8	F	22	Sep.	+	7	Not known	+	5	100	7	—	—	Contact of case 1
9	M	18	S	+	14	0	+	7	102	3	0	—	Skin lesions + arthritis
10	M	28	S	+	14	0	+	4	99.8	1	0	6	Known gonorrhoea contact
11	F	21	S	—	14	Not known	+	3	0	7	—	—	Arthritis + skin lesions
12	F	29	S	—	Not known	38–52	—	5	101	—	—	—	Arthritis + skin lesions
13	F	20	S	—	21	Pregnant 28+	+	3	98.4	2*	—	5	Arthritis
14	F	18	S	—	7	2	—	2	99.4	—	—	5	Gonorrhoea contact
15	F	19	S	—	8	4	+	5	99	1*	—	4	Arthritis
16	F	25	Sep.	—	21	77 Not pregnant	+	4	98.4	1	—	2	Arthritis + skin lesions

* Indicates skin lesions preceded arthritis
0 = not done, or not asked

onset of symptoms, and one was 38 weeks pregnant. The results of the laboratory tests are given in Table II (opposite). *Neisseria gonorrhoeae* was isolated from the urogenital tract in thirteen cases, from the blood in six cases, and from the joint fluid in only one of the five aspirates examined, although many polymorpho-nuclear leucocytes were found in the others.

Examination of the skin biopsy specimens by Gram stain and culture yielded no gonococci. Histology of the skin lesions was the same in all

specimens, and showed a small vessel vasculitis in the dermis and sub-cutis, and marked fibrinoid change. Surrounding each vessel was a dense aggre-gate of mononuclear and polymorphonuclear cells. Leucocytoclasia was a prominent feature of all speci-mens, and evidence of haemorrhage was always found (Figs 4 and 5, overleaf). Immunofluorescent-stained sections were examined by three observers: many solitary or oval fluorescent bodies were seen scattered throughout the dermis. These did not have

Table II *Investigations in sixteen patients with gonococcaemia*

Case no.	Neisseria gonorrhoeae isolated from:					Hb (g/100 ml.)	Total white blood count/mm ³	Erythrocyte sedimentation rate (Westergren) (mm. in 1st hr)	Gonococcal complement-fixation test	Gonococcal complement haemagglutination antibody test
	Urethra	Cervix	Rectum	Blood	Joint fluid					
1	+	0	0	+	0	16	12,400	50	+	1:256
2	+	+	0	0	0	0	0	0	—	0
3	—	—	—	+	0	13.8	6,800	41	—	1:128
4	—	—	—	—	+	13.3	11,000	70	+	1:32
5	+	+	—	+	0	10.2	7,700	63	+	1:512
6	+	+	+	—	0	12.6	7,400	25	0	1:64
7	+	+	—	—	0	13.6	6,700	27	—	0
8	+	+	0	—	—	13.0	13,000	25	—	1:256
9	+	0	0	—	—	14.7	6,800	44	0	1:128
10	+	0	0	0	0	0	0	0	0	0
11	+	+	0	—	0	13.4	12,300	35	0	0
12	+	+	0	—	—	12.5	4,400	58	+	1:128
13	+	+	—	+	0	12.4	9,100	18	—	1:32
14	+	+	—	—	—	12.1	9,100	82	+	1:32
15	+	+	+	+	0	13.5	8,300	42	+	1:32
16	—	—	—	+	0	14.0	5,300	53	0	1:256

0 = not done

the characteristic appearance of gonococci seen in smears and cultures from the urogenital tract, and could not be positively identified as gonococci, but such bodies were not seen in similarly stained sections of normal skin.

The knee was the joint most commonly involved, followed by the wrist, metacarpophalangeal joints, shoulder, elbow, and ankle. One patient had severe sacroiliac pain (which resolved quickly when antibiotic treatment was started), and in three patients tenosynovitis was found in association with the wrist.

Routine tests for syphilis were negative in all patients. The gonococcal complement-fixation test was positive in five of eleven patients tested, and the gonococcal complement haemagglutinating antibody test showed a significantly high titre in only four out of twelve patients when first seen.

Six patients had positive blood cultures. None of these had a significant leucocytosis, and only two had a significant pyrexia (above 100°F.) at any time during observation.

All patients had a raised erythrocyte sedimentation rate (18 to 82 mm. in the first hour (Westergren) mean 45). Four patients had a total blood leucocyte count of more than 10,000/mm. when first seen.

The radiological appearances of the joints in all patients were normal. None had any residual joint damage.

Immunoglobulin levels were normal in the 4 patients tested.

Treatment

In the first thirteen patients penicillin was used. Probenecid 1 g. orally was followed after 20 minutes by intramuscular soluble penicillin 5 m.u. (3 g.), and then 1 m.u. (0.6 g.) soluble penicillin 6-hrly for 7 to 10 days. Patients were initially confined to bed.

In three patients a regime of Ampicillin capsules 1 g. plus probenecid tablets 1 g. given together immediately, followed by 0.5 g. of each 6-hrly for 7 to 10 days, was a successful alternative treatment.

The response to this treatment was prompt, and signs and symptoms abated within 24 to 48 hrs.

Discussion

The patients we have described had a benign illness. There was not the severe morbidity common before the advent of antibiotics when cardiac manifestations (Keefer and Myers, 1934; Keil, 1938; Williams, 1938), meningitis (Branham, Mitchell, and Brainin, 1938), and myositis and purulent arthritis (Linnér, 1943) were reported. In a recent report of 42 patients, however, Holmes and others (1971) described ten patients who had either myocarditis or pericarditis, and two who had endocarditis. One of these died, and the

FIG. 4 *General view showing blister. Fibronoid change is visible in the vessels, and these are numerous cells around the vessels.*

other required a valve replacement; two others had meningitis. The possibilities of these more serious consequences should not be overlooked.

The confusion in the past between patients with Reiter's disease and those with gonococcal arthritis caused an artificially high reported incidence of the latter in males (Keefer and Myers, 1934). However, a retrospective study by Wright (1963) of patients seen at the Johns Hopkins Hospital showed that 51 of 152 patients previously thought to have gonococcal arthritis had in fact Reiter's disease, and that very few of these were female. In our patients the sex incidence, the acuteness of the arthritis, the typical skin lesions, and the response to penicillin treatment made confusion unlikely. Recent series confirm our finding of an 80 per cent. female incidence (Keiser and others, 1968; Holmes and others, 1971; Cooke and others, 1971).

Partain and others (1968) found an average time interval of ten days between infection and the first systemic manifestations. In our patients the interval was 12 days. The high incidence of complications occurring around a menstrual period or in pregnancy has been reported before (Keiser and others, 1968).

FIG. 5 *Leucocytoclasia (Fragmentation of the polymorphs)*

None of our patients complained of menstrual irregularities, nor had any of them had any recent surgical interference with the urogenital tract, and there was no clinical evidence of pelvic inflammation in any of them.

The distribution of the arthritis in our patients is similar to that in other series (Partain and others, 1968; Cooke and others, 1971).

The morphology and development of the skin rash and its histopathology are characteristic but not diagnostic of gonococcal septicaemia. The main differential diagnosis is that of chronic meningococcal septicaemia. Stott and Copeman (1940) described very similar clinical features and Hill and Kinney (1947) described leucocytoclastic angiitis as the histological feature of chronic meningococcal septicaemia. Their patients, however, tended to be more ill, with a more widespread rash which rarely became pustular. The onset was characteristically sudden. Schönlein-Henoch purpura has a similar histology but a different distribution, being most profuse on the extensor aspects of the limbs and buttocks, and around the knees, ankles, and elbows. Again, these lesions do not usually become pustular.

In most series of patients with benign gonococcaemia, the gonococci can be recovered from the blood in 20 to 30 per cent. of cases. It is unusual, however, to recover them from the skin lesions. Kahn and Danielsson (1969) observed that the gonococci occasionally seen in histological sections were disintegrating, and hence no longer viable. Ward, Glynn, and Watt (1972) have shown that once the gonococci are phagocytosed they are no longer viable even if morphologically intact, and degenerate within 30 to 60 minutes. It is possible that this is why it has proved difficult to recover gonococci from the lesions.

It has been estimated (Barr and Danielsson, 1971) that the overall incidence in gonorrhoea of systemic manifestations is 1.9 per cent. As there were approximately 56,000 reported cases of post-pubertal gonorrhoea in England and Wales in 1971 (Registrar General's Statistics) one could predict that over a thousand such cases should have been seen in this country in that year. The appearance of a few vesiculo-pustular lesions on the extremities in a patient with pyrexia and polyarthritides or arthralgia should lead to a very thorough search for the gonococcus. This should include the examination of pharyngeal specimens in passive homosexuals and in females practising fellatio. In our series only two patients presented with symptoms of the venereal

diseases department. Twelve of the thirteen women had no urogenital symptoms, and none had any clinical evidence of pelvic inflammation.

The lack of urogenital symptoms makes it very important for this syndrome to be recognized by rheumatologists, dermatologists, and general physicians as these patients are likely to present to them.

Summary

The details of sixteen patients with systemic manifestations of gonorrhoea are presented and discussed. It is emphasized that these patients do not usually have symptoms referable to the genitourinary tract and so it is important that the characteristic skin lesions associated with polyarthralgia prompt a careful search for evidence of gonorrhoea. The dramatic response to treatment is mentioned and the literature is reviewed.

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