Gonococcal arthritis – a common rarity

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Swediaur (1819) commented on the lack of previous mention of swelling of the knees as a consequence of 'blennorrhagia' and reported that he had personally attended several patients in whom the arthropathy started from the 8th to the 16th day of the illness; it was not until the turn of the century that gonococcal arthritis was eventually defined as a clinical entity in association with gonococcal septicaemia. Lindemann (1892) cultured the characteristic diplococci from a joint which became involved after ophthalmia neonatorum. Bacteriological proof of gonococcal septicaemia during life was reported from the Johns Hopkins Hospital by Thayer and Blumer (1896) and the occurrence of this septicaemia in association with arthritis and various types of skin lesions was reviewed by Buschke (1899).

In the pre-antibiotic era, gonococcal arthritis was described as a disease occurring more commonly in men than women (Wehrbein, 1929; Luys, 1922; Lees, 1932); it was regarded by some as the commonest cause of pyogenic arthritis requiring hospital admission (Cole, 1908). It was reported in infants and children in two large series by Holt (1905) and Cooperman (1927), and the well-known association with pregnancy was documented by Royston (1923).

The advent of therapy with sulphonamides (Colston, 1937; Parrish, Console, and Battaglia, 1940) and antibiotics (Hagemann, Hendin, Lurie, and Stein, 1952), and the wider recognition of Reiter's syndrome (Reiter, 1916) as a clinical entity resulted in a reappraisal of gonococcal arthritis. It was suggested that the term 'gonococcal arthritis' should be reserved for cases in which *Neisseria gonorrhoeae* was actually isolated from the joint fluid (*New Engl. J. Med.*, 1968; Partain, Cathcart, and Cohen, 1968)—the term 'presumptive gonococcal arthritis' being applied to cases with the typical clinical course and antibiotic response in which the gonococcus was cultured from some other site. Kirsner and Hess (1969) and other workers pointed out that with greater diagnostic accuracy linked to the awareness of Reiter's syndrome there has been a reduction in the frequency with which gonococcal arthritis is diagnosed in males, but how much of this is due to early cure of symptomatic urethral gonorrhoea in the heterosexual male is unknown. Pariser, Farmer, and Marino (1964),

Landman and Gelmi (1959), Bittiner and Horne (1955), and others have demonstrated that the asymptomatic male, the passive homosexual (Kirsner and Hess, 1969), and the asymptomatic female (Simpson and Brown, 1962; Brown, Brown, Walsh, and Pirkle, 1963; Dunlop, 1963) may receive no antibiotic therapy for long periods while the disease is unsuspected so that they have an increased potential to develop gonococcal arthritis.

In the series of Keiser, Ruben, Wolinsky, and Kushner (1968) and Goobar and Clarke (1964), over 80 per cent. of the patients with gonococcal arthritis were female, and Grabar, Sanford, and Ziff (1960), who first emphasized this alteration in sex incidence, also noticed that a relatively high proportion of the males who were affected were homosexual. Many of the female patients were either pregnant (Taylor, Bradford, and Patterson, 1966; Parker and Shingleton, 1967; Niles and Lowe, 1966) or were having a menstrual period at the time of the onset of the arthritis. Norris (1913) pointed out many years ago that the organism is disseminated *via* the blood stream to both tendon sheaths and joints. This bacteraemia is associated with systemic symptoms of chills, malaise, and fever (Johnson, 1970). Many patients with gonococcal septicaemia have skin lesions and certain of these are secondary to gonococcal embolization (Danielsson and Michaëlsson, 1966; Fred, Eiband, Martincheck, and Yow, 1965). The cutaneous manifestations of gonococcal septicaemia were reviewed by Abu-Nasser, Hill, Fred, and Yow (1963) from Houston and Kvorning (1963) reported a similar syndrome in the same year from Denmark. The lesions present during pyrexial episodes as erythematous macules and papules, some of which develop into tender necrotic vesicular, pustular, or rarely haemorrhagic lesions (Ackerman, 1970), mainly at the peripheries; the haemorrhagic lesions slowly discolour to a dark brown. A migratory polyarthropathy follows generalized arthralgia although on occasions only one joint is involved. Poske, Montgomery, Libnoch, and Pilz (1969) and others stated that tenosynovitis occurred in 50 per cent. of patients and is an invaluable diagnostic sign. Vietzke (1966) reviewed the occurrence of pericarditis as an infrequent manifestation of gonococcal septicaemia and Altman (1969) emphasized that it was usually asymptomatic.

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That gonococcal arthritis and other metastatic complications are ceasing to be rare in Great Britain is illustrated by the five following cases which were diagnosed in the Venereological Department of the Royal Victoria Hospital, Belfast, between September, 1968, and September, 1971. During this time the total number of cases of bacteriologically-proven gonorrhoea diagnosed in Belfast was 1,198.

Case histories

Case 1, a 31-year old man, attended on September 20, 1968, suffering from a purulent urethral discharge with associated dysuria for 7 days; he had also noticed some stiffness of the left knee joint during the 24 hours before attending the clinic.

Examination

He at first denied any exposure to risk of infection, but eventually admitted exposure with an unknown person on September 9.

Neisseria gonorrhoeae was isolated and identified on Gram-staining and culture of the urethral discharge and he was treated with 900,000 u. procaine penicillin by intramuscular injection. At this time there was no clinically detectable abnormality of the locomotor system.

The urethral discharge still contained *Neisseria gonorrhoeae* 2 days later and there was now an effusion in the left knee joint which was warm and tender; the swelling in the knee had begun the evening before this second visit. The body temperature was 101·6°F. and the patient was in great pain. On examination in daylight he was noticed to have large numbers of erythematous macular lesions, approx. 0·2 to 0·5 cm. in size, on the lower parts of both legs, and the dorsa of the feet, and blotchy purplish lesions in relation to the swollen left knee joint. He also complained of tenderness over the left thenar eminence and, although there was no obvious abnormality of the joints nor any tenosynovitis in that region, several pustules with erythematous areolae were present.

Treatment

The knee joint was aspirated and, although gonococci were not cultured from it nor from blood cultures taken at the same time, the joint condition responded to treatment with 50,000 u. intra-articular crystalline penicillin followed by 500,000 u. intramuscularly 6-hrly for 14 days. The gonococcal complement-fixation test was initially negative but became positive after 20 days. The latex test for rheumatoid factor was negative. Serum uric acid levels were within normal limits. The erythrocyte sedimentation rate was 110 mm./1st hr. initially, but gradually fell during the 2 weeks' treatment to 18 mm./1st hr.

Case 2, a 45-year-old married woman, was admitted to Belfast City Hospital on July 5, 1970. She was on holiday in Northern Ireland and had been staying with relatives for one week. On July 1, 1970, she developed what she believed to be influenza with generalized aches and pains and loss of appetite. During the next few days she rested in bed. In the early morning of July 5, 1970,

she developed a localized pain in the region of the right knee and during the day, as the pain became more severe, swelling of the knee joint became noticeable. Towards evening she developed rigors.

Examination

She appeared to be very ill, with a fever of 101°F. The right knee was hot, swollen, and very tender, with associated soft tissue swelling, especially in the suprapatellar region. There was no rash. *Neisseria gonorrhoeae* was identified in smears from the urethra, cervix, and vagina, and cultured from specimens taken from all three sites. 35 ml. fluid containing 94,500 cells per cu. mm. were aspirated from the right knee joint, and Gram-negative intracellular diplococci were identified in two of the twenty smears made from this aspirate but culture was not successful. The gonococcal complement-fixation test, initially negative, became positive 10 days later. The latex test was negative. The erythrocyte sedimentation rate was 95 mm./1st hr.

Treatment

She was treated with intra-articular penicillin in a dosage of 50,000 u. on one occasion, and 500,000 u. intramuscular crystalline penicillin 6-hrly for 14 days, joint stabilization, and graduated physiotherapy. When discharged from hospital she had not regained full joint function.

Consort

Her husband had been abroad for 9 months and had returned home on June 11. She denied any extra-marital exposure while he had been away. He came over to Belfast to see her on July 19 and we saw him at the hospital on July 20. He had been asymptomatic but, as there had been extra-marital exposure abroad on June 4, he agreed to let us examine him. There was no evidence of urethral discharge, but gonococci were found not only in smears taken from the urethra but also in smears obtained by prostatic massage. In both instances the diagnosis was confirmed by culture. He was successfully treated with procaine penicillin, 900,000 u.

Case 3, a 23-year old man, was admitted to the Royal Victoria Hospital, Belfast, on September 26, 1970, having suffered from dysuria for 3 days. On September 24, he had noticed stiffness in both shoulders and the left elbow joint. On the evening before admission he had several rigors and became aware of swelling around his left wrist joint associated with severe pain on movement.

Examination

He had a fever of 100°F. and there was an effusion in the left wrist with associated soft tissue swelling. There was a mucopurulent urethral discharge. The erythrocyte sedimentation rate was 130 mm./1st hr. A provisional diagnosis of Reiter's syndrome was made.

Progress

Treatment was started with phenylbutazone, joint immobilization, and rest in bed. During the next 24 hours his condition deteriorated, the temperature rose to 102°F., with further rigors, and the joint involvement spread to the left second, third, and fourth metacarpophalangeal

and the first right metatarsophalangeal joints. All the affected joints were hot and tender, and contained effusions. The skin of the dorsum of the left hand was tense and had a mottled purplish appearance. This soft tissue swelling was recognized as tenosynovitis, and papules and macules, mostly of a brownish colour, were noticed over the dorsa of both hands and feet. Gonococci were found on Gram-staining and by culture of the urethral discharge and also in the pus aspirated from the left wrist joint; three slides out of ten and all five cultures were positive. The gonococcal complement-fixation test was negative.

The intense joint pain and pyrexia settled within 24 hours of starting treatment with intramuscular penicillin and joint aspiration, but the rash persisted for several days. Intramuscular crystalline penicillin (500,000 units) was given 6-hrly for 14 days. Full function was not regained at the left wrist joint for some weeks and the soft tissue swelling in relation to the tenosynovitis took 4 weeks to disperse completely.

Contact

We were unable to trace his contact, a married woman on holiday in Northern Ireland, with whom he had had intercourse on September 2, 1970.

Case 4, a 30-year old man, attended on May 6, 1971, complaining of a urethral discharge of over 4 weeks' duration.

Examination

He had a painful effusion in the proximal interphalangeal joint of the left middle finger with marked soft tissue swelling and an overlying erythema. This was associated with a tenosynovitis of the extensor tendon of the same finger. No distinct rash was observed. He was also found to have a minor degree of limitation of movement of the left knee with a painless slight effusion in that joint. The urethral discharge was found to be positive for gonococci on Gram-staining and culture, but *Neisseria* could not be isolated from the joint fluid in this instance.

Treatment

Both the urethral discharge and arthritis showed a dramatic and complete response within 72 hours of starting a course of trimethoprim-sulphamethoxazole therapy.

Case 5, a 21-year old nurse, attended on August 5, 1971, as one of the contacts of a man who had been treated for bacteriologically-proven gonococcal urethritis 3 weeks earlier. She volunteered the history that she was at that time undergoing investigation by a general physician for polyarthralgia of 2 weeks' duration. She also remarked that her left elbow had been stiff and painful for 2 days.

Examination

She was found to have positive results to smears and cultures for gonococci from both the cervix and the urethra. It was noted that there was a minimal effusion in the left elbow joint with associated limitation of movement and soft tissue swelling. Apart from the erythema

overlying the joint there were at least a dozen discrete macules on the inner aspect of the left forearm, and a few pustules with an erythematous margin in the same area. The latex test was negative and the serum uric acid within normal limits. LE-cells were not seen. The erythrocyte sedimentation rate was 56 mm./1st hr. No fluid could be aspirated from the elbow joint.

Treatment

She was given 500,000 u. crystalline penicillin 6-hrly for 7 days. There was complete resumption of joint function, and the rash disappeared after 2 days.

Discussion

None of these patients exhibited ocular, mucosal, or skin lesions characteristic of Reiter's disease, and none of the men developed circinate balanitis.

It will be noted that four of the five patients had initial malaise and generalized aches and pains for several days before the onset of arthralgia. Three of them had polyarticular involvement while the other two (Cases 1 and 2) had an effusion in one large joint only. Tenosynovitis was a marked feature in two of the five patients (Cases 3 and 4). Peripherally distributed erythematous macules occurred in Case 3 and pustules and macules in Cases 1 and 5; these lesions were more commonly found on extensor surfaces or over areas of tendon or joint involvement.

The intense joint pain that all patients experienced was relieved by penicillin therapy and joint aspiration, and the skin lesions usually cleared within 48 hours of starting treatment. Recovery of joint function was delayed.

The soft tissue swelling related to the tenosynovitis on the dorsum of the hand, which superficially resembled cellulitis in Case 3, took several weeks to regress. This association of tenosynovitis with polyarthropathy is considered, by workers in the southern United States at least, to be pathognomonic of gonococcal arthritis (Johnson, 1970); tenosynovitis occurring in Reiter's disease is most often associated with the Achilles tendon (Reynolds and Csonka, 1958; Wright, 1963). We emphasize that, although this particular group of patients all showed gonococcal arthropathy, this condition may be limited to arthralgia or to tenosynovitis; arthropathy is only one facet of gonococcal dissemination.

When gonorrhoea is considered as a cause of acute polyarthropathy or pyogenic arthritis, then obviously specimens of urogenital and rectal secretions must be taken before giving antibiotics (Schroeter and Pazin, 1970; Wilkinson, 1949; Nicol, 1948; Scott and Stone, 1966). Whenever possible, joint aspirate and material from skin lesions should be examined (Frichot and Everett, 1967; Ackerman, Miller, and Shapiro, 1965), but there is

little doubt that in *early* cases detection of gonococci at these sites is difficult. Several Gram-stained slides should be prepared from joint fluid, and specimens for culture should best be inoculated directly on to suitable media at the patient's bed-side but, if facilities are not appropriate, transport media can be employed. Although blood cultures were not taken from all the cases described above, this procedure may be of diagnostic value, as shown by Kirsner and Hess (1969). The conventional gonococcal complement-fixation test is of little value and at best gives only partial retrospective evidence in favour of gonorrhoea as a cause, in cases diagnosed by other means. Recent work using flocculation tests (Schmale, 1970) and indirect sero-immunofluorescent methods (Hess, Hunter, and Ziff, 1965) hold out hope for specific diagnosis in the future. Deacon, Peacock, Freeman, and Harris (1959) and Danielsson and Michaëlsson (1965) pointed out that fluorescent antibody techniques will be of diagnostic value, and Lucas, Price, Thayer, and Schroeter (1967) emphasized that this value would not have been impaired if antibiotic therapy had already been begun, since strong antibody staining has been observed *in vitro* 24 days after exposure to bactericidal concentrations of penicillin. The need to examine sexual contacts was stressed by Altman (1969).

Once the sulphonamides and then penicillin had become available, gonococcal arthritis seemed to become so rare in Great Britain that it could be termed a 'clinical curiosity' (King, 1964). Ford (1953), studying the records at the London Hospital, found only one case of proven gonococcal arthritis during the previous 15 years, and no other proven case occurred in that hospital in the succeeding decade (Hancock (1972) personal communication). This dearth of cases has been remarked upon by several other writers in Great Britain (King and Nicol, 1969; Catterall, 1970; Schofield, 1970; Wigfield, 1970). The position abroad was not clear cut; some countries reported a virtual absence of cases, for example, Hungary (Károlyi, Foldvári, and Kovacs, 1961), Finland (Olin, 1954), Sweden (Gisslén, Hellgren, and Starck, 1961), France (Durel, 1956), Chile (Coutts, Prats, Vargas-Zalazar, and Infante-Varas, 1956), and Canada, (Ford and Rasmussen, 1964), whereas numerous series were reported from North America (Sharp, Lidsky, and Riley, 1968; *J. infect. Dis.*, 1969; Eisenstadt, 1968; Grossman and Roos, 1968), South America (Losada, 1966), and Europe (Björnberg and Gisslén, 1965, 1966).

In Great Britain the lack of reports of cases has been consistent and the reason is difficult to pinpoint. Certainly, except for a short period in the

middle 1950s, there was an abundance of uncomplicated gonorrhoea. Symptomless infection is a well-recognized precursor (Spink and Keefer, 1937; Ackerman, 1966), and it could be argued that the scarcity of gonococcal arthritis was a feature of the virtual cessation of asymptomatic urethral infection in men (to the point that such cases came to be judged worthy of publication (Bittiner and Horne, 1955), but this was certainly not the case with infections in women, or with rectal infection in men. Until about 1957 almost all strains of gonococci in Great Britain were very sensitive to penicillin so that there was a strong possibility that asymptomatic infection in women would be 'accidentally' cured before the onset of complications, by modest doses of penicillin given for intercurrent infections, but this would have been a good deal less likely to have been the case in the last decade, when up to 40 per cent. of strains of gonococci are of lessened sensitivity.

In Great Britain, during this period, arthritis associated with sexually transmitted infection was almost without exception considered to be due to Reiter's disease, but it seems highly unlikely that if cases of gonococcal arthritis were still occurring they were being misdiagnosed by venereologists. The majority of first and early recurrent attacks of Reiter's disease associated with gonorrhoea present an easily recognized picture because of the associated ocular, mucosal, and penile lesions, and the lack of response of the major features of the syndrome to antibiotics curative in gonorrhoea. Furthermore, confusion between the two forms of arthritis would have been unlikely because those who were most influential in putting Reiter's disease 'on the map' (for example, Harkness, 1950; Levy, 1950; King, 1960) were men of abundant previous experience with genuine gonococcal arthritis of the preantibiotic era.

Cole (1908) stated that 'there are three forms of gonococcal arthritis—that seen by the genito-urinary specialist, that seen by the physician, and that seen by the surgeon'. The patient presenting with polyarthropathy, skin lesions and pyrexia is unlikely to be referred in the first place to a venereology unit, and it may be argued that, if gonococcal arthritis really was occurring in recent decades, it was not being diagnosed as such through the failure of physicians other than venereologists to recognize the condition. Certainly, the three reports by British authors in the last 15 years have come from Dermatological, Physical Medicine, and Infectious Diseases Units (O'Sullivan, 1964; Verbov, Boswell, and Featherstone, 1970; Wolff, Goodman, and Vahrman, 1970), but the total of cases amounted to only six. Rheumatologists also have recorded gonococcal arthritis as 'an increasing rarity' (Boyle and Buchanan, 1971). In an

investigation of all admissions to the Medical Research Council Rheumatism Research Unit between 1960 and 1970, Russell and Ansell (1972) found only 28 cases of bacterial arthritis, of which none was gonococcal; in two there had been previous treatment with penicillin but both patients were children. Failure to consider the possibility that arthritis may be associated with genital infection is certainly possible because of the reluctance of patients to discuss such matters except in Venereal Diseases clinics, but that such failure should be consistent over a long period of years would seem less likely, at least in those centres where the great interest in Reiter's disease in the 1950s and 1960s resulted in excellent co-operation between venereologists, rheumatologists, orthopaedic surgeons, ophthalmologists, and general physicians. Nevertheless, the clinical picture of rheumatic fever can be so closely simulated that some patients with gonococcal infection may well have been treated inadvertently. (It is of interest in this context that the two female contacts of two men whose gonorrhoea was recently treated by us had been treated as cases of rheumatic fever by their family doctors before we were able to trace them.)

Gisslén and others (1961), in Gothenberg, who surveyed the incidence of complications of gonorrhoea including in his survey patients from all departments in the hospital, found a higher incidence of gonococcal salpingitis than had been found in all other series published during the 10-year period before that date (WHO Expert Committee on Gonococcal Infection, 1963). It is suggested that, if the same principle were applied to the problem of septic arthritis and acute polyarthropathy with or without associated skin lesions in Great Britain, then the true incidence of gonococcal arthritis would be better appreciated.

In Great Britain the diagnostic pendulum may have over-swung from pre-antibiotic days when nearly all cases of arthropathy associated with urethral discharge were regarded as gonococcal arthritis, to the present situation when it is believed to be very rare. Almost certainly the true incidence lies between these two extremes and we would anticipate that with the present high incidence of gonorrhoea a prospective aetiological investigation of acute arthropathy organized on an interdepartmental basis might well demonstrate that gonococcal arthritis is now as frequent in Great Britain as elsewhere.

Summary

The literature relevant to gonococcal arthritis is reviewed and five patients with this condition are discussed. The numerous reports of cases of gonococcal arthritis seen in North America and Europe

during the past 15 years are contrasted with the virtual absence of reports from Great Britain during the same period. The fact that in 1969 and again in 1970 gonorrhoea was diagnosed in over 50,000 patients who attended venereology clinics in Great Britain shows the importance of a greater awareness of the occurrence of its complications. It is emphasized that the diagnosis of gonococcal arthritis will be made more frequently on a high index of suspicion, meticulous bacteriological technique, and improved communication between venereologists and specialists in other fields.

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Arthrite gonococcique—une rareté commune

On passe en revue la littérature concernant l'arthrite gonococcique et l'on discute de 5 malades qui en étaient atteints. Les nombreux cas d'arthrite gonococcique rapportés en Amérique du Nord et en Europe pendant les quinze dernières années contrastent avec l'absence virtuelle des cas rapportés en Grande Bretagne pendant la même période. Le fait qu'en 1969, de même qu'en 1970, la gonococcie fut diagnostiquée chez plus de 50.000 malades fréquentant les cliniques vénéréologiques en Grande Bretagne, montre l'importance de porter une plus grande attention à la survenue de ses complications. On insiste sur le fait que le diagnostic d'arthrite gonococcique serait porté plus fréquemment grâce à un indice plus élevé de suspicion, une technique bactériologique méticuleuse et de meilleurs contacts entre les vénéréologues et les spécialistes d'autre domaines.