Septic arthritis

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Joint infection, particularly when it occurs in patients already suffering from rheumatoid arthritis, may present problems in diagnosis and management. This paper describes our experience during the last 10 years.

Patients

All patients admitted between January 31, 1960, and February 1, 1970, with a bacterial arthritis or in whom it developed during their admission have been included in this review. They were subdivided into two groups depending upon whether or not they had pre-existing rheumatoid arthritis.

GROUP A (11)

Eleven patients were admitted with septic arthritis which had arisen in apparently normal joints.

GROUP B (17)

Fifteen patients with adult rheumatoid arthritis had their disease complicated by the development of infection in one or more joints as had two cases with Still's disease.

The patients in Group A were aged from 9 months to 61 years (mean 22 years).

In Group B the mean age of the fifteen patients with adult rheumatoid arthritis was 61 years (range 44 to 78). The mean duration of the preceding rheumatoid arthritis was 28 years (range 1½ to 50); only one patient had had the disease for less than 14 years. The two children were aged 7 and 9 years and had had Still's disease for 5 and 8 years respectively: both were receiving corticosteroid therapy as were nine of the adults. One of the latter was also taking chlorambucil therapy at the time of the infection but had a normal white blood count.

Diagnosis

The diagnosis of infection was suspected on the clinical grounds of heat and swelling of one or more joints in a generally ill patient who was usually febrile and often had rigors. It was confirmed in a total of 22 by the results of joint aspiration (Table I). The reasons for considering the remaining six to have septic arthritis are detailed.

Of Group A, in five patients it was not possible to grow an organism from the joint, but three of these patients had positive blood cultures. In one other (Case 6), who had received penicillin before admission, an organism was later grown from the bone at operation. The fifth patient (Case 11) was a 9-month-old child in whom sterile pus was removed from the ankle joint and the blood cultures were negative. However, in this case too penicillin had been administered before admission; in view of the clinical features suggesting an infectious arthritis occurring in a child with no previous or subsequent joint disease, a diagnosis of septic arthritis was accepted. In the patient with meningococcaemia, the organism was isolated from the CSF as well as the blood but synovial fluid microscopy and cultures were persistently negative. Thus, altogether in this group, the organism was isolated from the blood only on three occasions, and from the joint only on three occasions; and in the remainder from more than one site in all except the one detailed above.

In Group B, the patients suffering from rheumatoid arthritis, the organism was found in the purulent synovial fluid in all but one (Case 28), a woman who had had antibiotics administered before referral. In view of the clinical findings of fever to 103°F, a red, hot, acutely swollen joint, and a purulent synovial fluid when the joint was aspirated, a diagnosis of infection was accepted. Organisms were cultured from fifteen of seventeen joints in Group B and the Gram stain was positive in fourteen; in the sixteenth case the smear of the synovial fluid demonstrated Grampositive cocci and although no growth was obtained on culture, β -haemolytic streptococci group G were isolated both from blood and from a necrotic lesion on the back. In a total of five of the rheumatoid arthritic patients blood cultures were also positive. In addition swabs were examined from any ulcerated areas or any other possible source of infection together with the nose. The erythrocyte sedimentation rate and the total white blood count with differential were also performed.

Organisms isolated

Staphylococcus aureus was the organism most commonly isolated in both groups (Table I). These were penicillin sensitive in 50 per cent. In Group A, there was frequently no obvious source of infection. The one patient with pneumococcal arthritis had an antecedent but untreated left lower lobar pneumonia, and two patients with staphylococcal infection had had frequent boils. In Group B, six patients developed an infection which was thought to stem from an ulcerating area of skin. In all of these the same organism was isolated from the ulcer as from the joints. A further four patients had a discharging

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Table I Organisms isolated and site

Group	Patient no.	Age (yrs)	Organism isolated	Site		
				Joint	Blood	Other
A	1	61	Staph. aureus*	+		
Non-	2	18	Staph. aureus†	+	+	
rheumatoid	3	18	N. meningitidis	<u>.</u>	+	+
	4	46	Strep. pneumoniae	+	·	+
	5	6	M. tuberculosis	+		
	6	13	Staph. aureus*	_	_	+
	7	22	Strept. group A	+	_	·
	8	53	Staph. aureus*	_	+	
	9	$2\frac{1}{2}$	Non-haem, streptococci	_	+	
	10	6	Strept. group A	+	+	
	11	9 mths	Nil	_	_	
В	12	78	Staph, aureus*	+		+
Rheumatoid	13	60	Staph. aureus*	+	_	+
Kilouillatola	14	65	Staph. aureus*	+	+	Т-
	15	66	Staph. aureus*	+	<u> </u>	+
	16	44	Staph. aureus†	+	_	т-
	17	63	Staph. aureus*	<u> </u>	_	
	18	63	Strept. group A	<u>.</u>	+	
	iğ	46	Staph. aureus†	+	<u>'</u>	+
	20	77	Staph. aureus†	+	+	+
	21	58	Fusiformis	+	_	-
	22	56	Proteus vulgaris	+		+
	23	57	Staph. aureus*	+	_	+
	24	63	Strept, group G	<u>+</u> ‡	+	+
	25	7	Staph. aureus†	+	_	-
	26	ģ	Staph. aureus†	+		
	27	52	Staph. aureus*	+	+	+
	28	55	Nil	<u>'</u>	<u>'</u>	<u>.</u>

Penicillin sensitive strain.

paronychia and one other an infected knee arthroplasty; here the organism was a penicillin sensitive Staph. aureus.

Duration of infection before diagnosis

The mean duration of joint infection before diagnosis was 4 days in Group A, excluding the patient with tuberculous arthritis, in whom joint swelling had been present for 2 years. In Group B the mean duration was 9 days. Three patients from this group developed the infection while in hospital and the diagnosis was made within 24 hours, but in three others there was a delay of over 2 weeks between the onset of symptoms and presentation at hospital. Two of these latter patients were amongst the three with recurrences.

Number and type of joints involved

The knee was the most commonly affected joint in both groups, with the elbows, shoulders, and wrists all being less frequently involved (Table II). In Group A (i.e., without underlying rheumatoid arthritis), five of the eleven patients had more than one joint involved, and in Group B, five of the seventeen patients had more than one joint involved; the maximum number, in one patient in each group, was five (Table III).

Table II Joints involved in each group

Joints involved	Group	Group			
	(B) Rheumatoid (17)	(A) Non- rheumatoid (11)			
Knee	8	11			
Elbow	2	6			
Shoulder		5			
Wrist	2 3 3	4			
Ankle	3	i			
Hip		Ī			
Sacroiliac	1	_			
Metacarpophalar	ngeal 2	_			
Total	21	28			

Table III Number of joints involved in each group

Group	No. o	Total				
	1	2	3	4	5	
A	6	3		1	- 1	11
В	12	2	1	1	1	17

[†] Penicillin resistant strain. ‡ Positive Gram stain but no growth.

Management

If the synovial fluid was obviously purulent, treatment with penicillin was started immediately. Once the nature and the sensitivity of the cultured organism was known, treatment was suitably modified. In the first two patients in the rheumatoid arthritis group, antibiotic therapy was of short duration. In the first case penicillin was given for only 10 days concurrently with streptomycin for 7 days, and in the second, therapy with methicillin was given for 10 days and then sulphonamides for a further 4 weeks. Subsequently, the next nine patients all received a minimum of 4 weeks' therapy. Since 1965 the initial treatment has been penicillin 12 mega units daily, and since 1968 with Cloxacillin 8 g. daily intravenously, until such time as the nature and sensitivity of the organisms are known. Intravenous antibiotic therapy was continued for 2 weeks, followed by oral therapy for a minimum of 6 weeks. In the three most recent patients or al therapy was continued for a total of 3 months. Allergy to penicillin required a change of drug in two patients.

The involved joint or joints were splinted with plaster of Paris in the optimal position. As long as the joints were becoming distended with pus, repeated aspiration was performed every 24 to 48 hrs; usually no more than three aspirations were required. Although all these cases were seen in consultation with our orthopaedic department, on two occasions only was surgical therapy considered necessary. One patient had osteomyelitis which required drainage of bone and removal of sequestra, and the other (Case 21) was a patient with rheumatoid arthritis who had had a recurrence of infection in the same joint 1 year later. One patient (Case 22) was moribund, with marked muscle wasting, multiple skin ulcerations, and pneumonia; the septic arthritis developed pre-terminally and no active management was undertaken.

Results

Of the eleven patients with septic arthritis in Group A, all but one recovered completely with no residual deformity. This patient's arthritis appears to have been secondary to osteomyelitis which required surgical intervention with removal of sesquestra. There were no deaths and no recurrence of infection in this group.

In Group B, the two earliest patients with rheumatoid arthritis both had a recurrence in the same joint 2 weeks after cessation of therapy. These had both received antibiotic therapy for very short periods by present standards. One other patient with rheumatoid arthritis had a recurrent infection in the same joint 1 year later despite 3 months of chemotherapy initially. There were two fatalities in this series, one patient with renal failure (Case 20) who died 3 days after admission and the patient who was moribund from her rheumatoid arthritis when septic arthritis developed preterminally. One of the patients who had a recurrence of infection, subsequently required surgical arthrodesis of the damaged knee. In none of the others did ankylosis develop and in only two was there significant deterioration in function.

Discussion

It is interesting to compare our findings with those given in the last review of joint infections from England; Kellgren, Ball, Fairbrother, and Barnes (1958) reported eleven patients with joint infection associated with rheumatoid arthritis of whom two died, while over a similar period thirteen patients with suppurative arthritis alone were seen. All except one of these, in which the diagnosis was not made until post mortem, survived. They found predominant infection with Staph. aureis, this organism being present in nine out of eleven infected joints of patients with rheumatoid arthritis, but of these seven were penicillin resistant. The main infectious agent in our Groups A and B was still Staph. aureus, but this organism was much more prominent in the patients with rheumatoid arthritis—14/17 (cf. 4/11 of Group B). Of three infections in the rheumatoid patients which developed in hospital, two were with this organism; both were penicillin sensitive strains. Rimoin and Wennberg (1966) found five out of five positive isolates to be Staph. aureus, four of which were penicillin resistant. In the patients described by Meyers, Miller, and Pinals (1969), twelve out of sixteen infections were due to Staph. aureus, but only three could be treated by penicillin. Karten (1969) found only two out of five patients to have a staphylococcal infection but his patients appear to have been more severely ill before the infection than ours, and two of his five died. Only two of our seventeen rheumatoid patients were in this state with multiple decubitus ulcers and gross muscle wasting. One of these patients developed joint infection with *Proteus* vulgaris while moribund, the other with betahaemolytic streptococcus Group G and recovered. However, in all, eleven of the seventeen patients in Group B had an obvious source of infection; in six an ulcerating area, and in one an infected prosthesis, in four a paronychia. The common occurrence of these infected lesions in patients with rheumatoid arthritis seems to be a major factor in predisposing them to joint infection. In no instance did infection follow recent aspiration or injection of a joint. Nevertheless, this can occur not infrequently (Kelly, Martin, and Coventry, 1970) and it is essential that full sterile techniques continue to be used.

Ten out of eleven of the rheumatoid patients with septic arthritis described by Kellgren and others (1958) had more than one joint involved. This compares with five out of seventeen of our patients and two out of sixteen described by Meyers and others (1969).

Multiple joint involvement in septic arthritis alone is not common (Kellgren and others, 1958; Baitch, 1962) although in the very young it is not as unusual as in the adult (Nelson and Koontz, 1966) and one of our patients aged $2\frac{1}{2}$ years had four involved joints.

Our patients represent a relatively selected population as some were referred to the unit with an initial diagnosis of rheumatic fever. This factor may account for the high incidence of multiple joint involvement seen in Group A. Argen, Wilson, and Wood (1966) had 24 per cent. of patients with more than one joint involved but these included a number of patients with rheumatoid arthritis on steroids as well as some diabetics and alcoholics. Our patient with meningococcal septicaemia had the characteristic purpuric rash and positive CSF and blood cultures as well as pericarditis, a persistent purulent arthritis of both elbows, a knee, ankle, and shoulder. This multiple joint involvement has been described previously and the inability to isolate the organism from the joint is a frequent finding (Pinals and Ropes, 1964). In this country at present, though not in less developed ones (Greenwood, 1970), tuberculous involvement of more than one joint is extremely uncommon.

At the time of diagnosis most of the rheumatoid patients could be suspected of harbouring infection somewhere, as judged by a deterioration in general health, fever, and leucocytosis, but, as has been pointed out previously (Kellgren and others, 1958; Karten, 1969), patients with rheumatoid arthritis may show only minimal increase in pain and swelling of the infected joint and it can be difficult to be certain of the diagnosis before aspiration. Although only three of the rheumatoid patients did not have a fever, nine had relatively uninflamed joints. This may have borne some relation to corticosteroid therapy as seven out of ten rheumatoids on prednisone did not have a hot red infected joint as compared with only two out of seven not taking corticosteroids. The three afebrile patients also had a maximum white blood count of under 8,000 cells/cu. mm. as did two others in Group B. Only one patient in Group A had a maximum white blood count under this level. The erythrocyte sedimentation rate was raised in all the patients and was over 100 mm./hr. in nine of Group B and three of Group A. This was not, however, a useful indicator in Group B except where a recent marked rise could be documented.

The two patients who had a definite recurrence of infection in the joint both had Staph. aureus isolated and by current standards the duration of antibiotic therapy was inadequate. Meyers and others (1969) found nine out of twelve staphylococcal infections recurred, but many of these cases had also received

antibiotics for only 30 days or less. In addition, at least three of these patients presented 3 weeks or more after the onset of infection. The one other patient, who had a recurrence 1 year later, had had the infection 1 month before presentation initially, and although treated for 3 months it is possible that a nidus remained in a large Baker's cyst which finally required surgical incision and drainage.

The use of local antibiotics is still controversial, but there is no evidence from our series or those of other authors that this practice has any effect in preventing recurrences. All previous studies indicate that antibiotics pass very freely into synovial fluid from the blood stream easily achieving therapeutic levels (Rapp, Griffith, and Hebble, 1966; Drutz, Schaffner, Hillman, and Koenig, 1967; Gump and Lipson, 1968; Nelson, 1971; Parker and Schmid, 1971) and there would seem now to be no good reason for continuing this practice.

Summary

Septic arthritis either presenting de novo or arising in patients with rheumatoid arthritis may give rise to difficulty in diagnosis, particularly if more than one joint is involved. This was so in four of eleven patients with simple septic arthritis and in five of seventeen patients with rheumatoid arthritis and joint infection. Diagnosis should always be suspected in the case of an ill patient with fever, particularly if this is accompanied by rigors and when a joint appears hot and swollen. It is particularly important to bear this in mind in patients with rheumatoid arthritis when one or two joints appear to be much more seriously affected than others. Even in the absence of corticosteroid therapy, it is not always easy to diagnose infection. Because of this, aspiration and culture of joints should be undertaken when any possibility of infection is present; remembering that the presence of skin ulceration, paronychia, etc., markedly increases the predisposition to infection. The importance of early diagnosis is stressed because it contributes markedly to complete recovery. Intensive and longterm antibiotic therapy appear essential if recurrence of infection is to be prevented. Provided early diagnosis is made and the joint is amenable to needle aspiration, septic arthritis, even when complicating rheumatoid arthritis, can usually be managed without surgical intervention.

References

ARGEN, R. J., WILSON, C. H., AND WOOD, P. (1966) Arch. intern. Med., 117, 661 (Suppurative arthritis) BAITCH, A. (1962) Clin. Orthop., no. 22, p. 157 (Recent observations of acute suppurative arthritis) DRUTZ, D. J., SCHAFFNER, W., HILLMAN, J. W., AND KOENIG, M. G. (1967) J. Bone Jt Surg., 49A, 1415 (The penetration of penicillin and other antimicrobials into joint fluid: three case reports with a reappraisal of the

Greenwood, B. M. (1970) Ann. rheum. Dis., 29, 56 (Polyarthritis in Western Nigeria. III. Other forms of polyarthritis)

- GUMP, D. W., AND LIPSON, R. L. (1968) Curr. Ther. Res., 10, 583 (The penetration of cephalothin into synovial and other body fluids)
- KARTEN, I. (1969) Ann. intern. Med., 70, 1147 (Septic arthritis complicating rheumatoid arthritis)
- KELLGREN, J. H., BALL, J., FAIRBROTHER, R. W., AND BARNES, K. L. (1958) Brit. med. J., 1, 1193 (Suppurative arthritis complicating rheumatoid arthritis)
- KELLY, P. J., MARTIN, W. J., COVENTRY, M. B. (1970) J. Bone Jt Surg., 52A, 1595 (Bacterial (suppurative) arthritis in the adult)
- MYERS, A. R., MILLER, L. M., AND PINALS, R. S. (1969) Lancet, 2, 714 (Pyarthrosis complicating rheumatoid arthritis)
- NELSON, J. D. (1971) New Engl. J. Med., 284, 349 (Antibiotic concentrations in septic joint effusions)
- —— AND KOONTZ, W. C. (1966) *Pediatrics*, 38, 966 (Septic arthritis in infants and children: a review of 117 cases) PARKER, R. H., AND SCHMID, F. R. (1971) *Arthr. and Rheum.*, 14, 96 (Antibacterial activity of synovial fluid during
- therapy of septic arthritis)
- PINALS, R. S., AND ROPES, M. W. (1964) Ibid., 7, 241 (Meningococcal arthritis)
- RAPP, G. F., GRIFFITH, R. S., AND HEBBLE, W. M. (1966) J. Bone Jt Surg., 48A, 1534 (The permeability of traumatically inflamed synovial membrane to commonly used antibiotics)
- RIMOIN, D. L., AND WENNBERG, J. E. (1966) J. Amer. med. Ass., 196, 617 (Acute septic arthritis complicating chronic rheumatoid arthritis)