

EPIDEMIC ORCHITIS

A Report with Biopsy Studies of an Outbreak of Twenty-one Cases Occurring in Gold Coast Negro Troops

BY

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A MINOR epidemic of an inflammatory disease affecting mainly the testicles occurred in the Accra area of the Gold Coast District at the end of 1948. The patients were all Gold Coast native troops from both Southern and Northern territories and were admitted to the 37 (Accra) W.A. Military Hospital Special Treatment Department. A total of 21 cases were seen: 1 in June, 2 in September, 1 in October, 10 in November, 6 in December and 1 in January. 3 more doubtful cases were seen and 2 more occurred in the period February–May which have not been included in the averages. Examination of the records over a three-year period from June 1946 to May 1949 reveals no comparable outbreak although there is a small number of cases recorded as having been diagnosed simply as orchitis. There are 31 cases in this period which appear from their notes to be very similar to and may be identical with the disease at present under review. 7 of these occurred in January 1947 and 5 in June of that year but in no other month were there more than 2 cases. Over the same period cases of true gonococcal epididymitis occurred at a steady rate showing no comparable variation.

It appears probable, therefore, that there is in this area an endemic testicular inflammation with a slight tendency to minor epidemic outbursts. The following description of the disease as it was seen in these 21 cases is given, together with an attempt to elucidate its aetiology.

GENERAL DESCRIPTION

The disease is very painful causing the patients to report sick very soon after the onset of symptoms (average 2·1 days). They were all admitted to hospital on the following day, the common complaint was that pain was experienced first and that subsequently the swelling was discovered. A characteristic attitude was adopted with the knee on the affected side slightly flexed with slight lateral flexion of the spine to the same side. All except three also complained of "pain in the waist" (87 per cent) but there were no physical signs of any local lesion to account for this. The affected testicle was enlarged to about three times the normal bulk and was exquisitely tender; 2 cases of extreme enlargement occurred with scrotal circumferences

of 29 and 31 cm. A small hydrocele was present in 8 cases (38 per cent) containing from 8 to 38 ml. of clear fluid. The epididymis was involved in 10 cases (47 per cent) but in all the enlargement was much less than that of the testicle and much later in onset (average seven days). The enlargement was soft and gave the impression that it was due to œdema although one case did at one stage resemble tuberculous epididymitis, subsequently to resolve completely. There was tenderness and soft swelling of the spermatic cord in 4 cases (19 per cent). Scrotal œdema was present in 5 cases from the start (23 per cent) and developed in nearly all cases at some stage. 2 of the early cases had scrotal and crural dermatitis with angular cheilitis syndrome of which there was an outbreak here in June 1948 and which is attributed to a dietetic deficiency, possibly ariboflavinosis (Mackay, 1948). These changes are entirely different from the typical lesion which is most characteristic: there is a brawny, almost shiny, œdema which broadens the folds of the scrotal skin but does not entirely obliterate the sulci. Ulceration may rarely occur superficially. In no case was acute inguinal lymph-node inflammation seen. There was a urethral discharge in 4 cases in 2 of which it was due to a concomitant attack of acute gonorrhœa.

General symptoms were slight. Fever was absent except in the 2 very severe cases and nothing like a typical temperature chart was seen. Pulse and respiration were normal and there was no abnormality of bowel movement or micturition except some minor complaints of dysuria probably due to local tenderness. No abnormal signs were found on general routine examination. Rectal examinations showed no abnormality of the prostate or vesicles. There was no enlargement of the spleen or lymph nodes or of the salivary glands.

After admission to hospital the swelling and symptoms increased for a few days and then settled slowly. It is not possible to give the exact duration as many cases were discharged as soon as progress was satisfactory, the average period of hospitalization being seventeen days. All were stationary within six weeks and most within one month so that clinically it is a self-limiting disease of probable duration of three to four weeks. Confinement to bed was necessary for a few days only. Resolution appeared to be complete in all except 3 cases although it was felt that there was some slight increase in density of the testicle and slightly diminished sensation. In 2 cases a large hard testicle remained on discharge which caused a dragging sensation although clinically all inflammation had subsided. In one other there was a residual hydrocele which was, however, getting progressively smaller. One case had a relapse on the same side and had to be readmitted in a very sick condition, one was bilateral from the start and in one extension to the other side occurred while under treatment.

CLINICAL PATHOLOGY

Urethral discharge: in 2 non-gonococcal cases there were scanty pus and epithelial cells but no micro-organisms were seen.

Prostatic massage: sufficient material for a smear was obtained in 8 cases only (26 per cent) and these showed a few pus cells as the only abnormality.

Hydrocele fluid: average protein content 4.3 grammes per cent. All specimens showed a few lymphocytes; no micro-organisms were seen and all cultures remained sterile.

Urine: In no case was urinary infection conclusively demonstrated (Handley, 1946). Pus cells were present in small numbers in one case and one had albuminuria. All cultures remained sterile.

Stools: Routine testing showed *Strongyloides stercoralis* as the only abnormality in one case only.

Hæmatological Findings.—Blood cultures from 2 patients were sterile. Hæmoglobin 13.5–14.5 grammes per cent. E.S.R. 15–48 mm. in one hour (Wintrobe), average 28 mm. Average P.C.V. was 45 per cent so that is a “marked” increase in rate of sedimentation. The average total white cell count was 7,200 per c.mm.; this is probably a little above the average for this race but is not significantly different from that of a parallel series of 19 gonococcal epididymitis cases. No abnormality seen in thin-stained films; thick smears

	<i>Orchitis</i>		<i>Gonococcal epididymitis</i>		<i>Racial normals</i>
Total W.B.C.		7,200		7,400	4,000–7,000
Polynuclears	47%	3,400	60%	4,400	40–70% 2,000–5,000
Large lymphocytes	15%	1,100	10%	700	} 20–60% 1,000–4,000
Small lymphocytes	30%	2,200	25%	1,900	
Monocytes	5%	300	2%	200	
Eosinophils	3%	200	3%	200	

showed no malarial parasites or filariæ. No microfilariæ were seen in wet preparations from 2 patients in whom scrotal œdema was particularly marked.

Serological Findings.—The Kahn reaction was positive in 47 per cent of cases. Owing to the high incidence of healed yaws this is slightly below the average for normal recruits; several of the negative results were repeated and in no case was “Kahn conversion” observed. Widal reactions, Brucella agglutinations and Weil-Felix reactions were each negative in 3 cases.

Histopathology.—Biopsies were made from 2 cases, one of which had a small hydrocele. Both were severe cases and the specimen was removed from both quite late in the disease, one in the second week and in the other in the fourth week. On discharge the former had a residual painless swelling but the latter was apparently normal. The procedure is apparently harmless (Wiesner, 1947) and incision of the tunica has actually been used in the treatment of orchitis due to mumps (Wesselhoeft and Vose, 1942).

The picture in the early case was that of an acute, non-suppurative inflammation affecting mainly the interstitial tissue. The visceral endothelium of the tunica vaginalis was irregularly hyperplastic with adherent small fibrin masses. The albuginea appeared normal. In the testicle itself spermatogenesis was at a standstill except possibly for one small area. Most of the tubular lumina were filled with hyperplastic germinal epithelium: there was considerable variability in cell size but no true differentiation. The interstitium was oedematous and grossly infiltrated with small round cells and showed fibroblastic activity. There was some histiocytic infiltration, a few of these cells containing ingested degenerate lymphocytes. The interstitial cells themselves were well preserved. Some Sertoli cells could be distinguished and the basement membrane and supporting tissues of the tubules were apparently healthy. Careful search revealed no inclusion bodies as found in the acinar cells of the parotid gland in experimental mumps (Johnson and Goodpasture, 1936).

The sections from the later case show mainly fibrous tissue and few tubules could be made out. There was considerable interstitial fibrinous exudate which was undergoing organization in one area. No normal functioning tubules were seen. The sections were small, however, and may have been taken entirely from just beneath the capsule.

The general picture is one of non-suppurative interstitial inflammation with secondary effects on the tubular epithelium and a tendency to fibrosis.

Specimens from both cases were cultured on a wide variety of media under varying conditions but remained sterile. No attempts at virus culture were made.

TREATMENT

General Measures.—All cases were treated with bed rest in the early stages and in the severe cases the scrotum was suspended on an "Elastoplast" sling across the thighs. In one case with an initial scrotal diameter of 31 cm. this measure alone produced a diminution in size of 2–3 cm. per day. All patients were fitted with suspensory bandages and encouraged to drink large volumes of fluid.

Drug Treatment.—Analgesic and soporific drugs were required by most patients for a few days. The other drugs used were penicillin (25,000 or 50,000 units three-hourly for five days), sulphathiazole (30 grammes in five days with potassium citrate grains 20 t.d.s.) and N.A.B. (0.15 gramme, 0.3 gramme and two doses of 0.45 gramme at three-day intervals). The series is too small for analysis of the results to be significant and no completely untreated controls are available. The impression was gained, however, that none of the drugs used has any therapeutic value in this condition. Thus, in 3 cases two drugs were administered consecutively (in one case penicillin after sulphonamide, in one sulphonamide after penicillin and in the third arsenic after sulphonamide) and in each case improvement is recorded only as following the course of the second drug; while these combinations administered concurrently have given little immediate response. Further, the duration of stay in hospital for those receiving one drug only was 11.8 days (9 cases) in the case of penicillin and 9

days (3 cases) for sulphathiazole whereas for those receiving two drugs it was 25.3 days for penicillin and sulphathiazole (3 cases) and 29 days for arsenic and sulphathiazole (3 cases). Thus it appears that the milder cases only stayed long enough to receive one drug. Finally if the 13 cases that did receive penicillin are compared with the 8 that did not it is seen that there is no significant difference (15.1 as against 16.6 days).

FOLLOW-UP

It was possible to trace only 6 cases, which were seen at periods varying from four to six months. Of the remaining 15, 10 had been discharged from the Army and were marked "A.1" in their release books and the other 5 were posted to inaccessible stations. Of the 6 seen personally, 3 had returned completely to normal, 3 had residual inguinal lymph-node enlargement that may have been completely unrelated to orchitis and in only 1 case was the testicle itself definitely abnormal. There was slight enlargement, hardness and diminution of pain sense. All 6 claimed full potency. An attempt was made to get semen specimens but in only one case was a usable specimen obtained—this was 0.5 ml. in volume and contained a few small round cells only. No spermatozoa were seen. The evaluation of this result is complex. For numerous reasons all specimens in this country are collected in the laboratory or its side-rooms and it was not felt that an exception could be made of this test (Harvey and Jackson, 1945). On the other hand suitable specimens of adequate bulk are thus obtained in about three-quarters of routine semen analysis although in these cases the patient has usually asked to be investigated. All things being considered it does seem probable that there is a reduction in testicular secretion and spermatogenesis at least for four months from the onset of the disease. No semen analyses were performed in the early stages as it was felt to be therapeutically undesirable.

DISCUSSION

I believe the above considerations to show that there is in this area a disease *sui generis* of the male reproductive apparatus forming a syndrome of sufficiently definite characteristics to justify the assumption of a single aetiology. As far as I am aware it has not been previously described.

It is apparently infective in origin although no information about site of entry or transmission was discovered. It is felt that were the infecting agent anything other than a virus it would have been found. This assumption is strengthened by the type of histological picture found and the similarity it shows to that of mumps orchitis.

That it is different from the gonococcal complications of the gonads is shown by the following considerations. There was a history of gonorrhoea in only 4 cases (19 per cent) with an average period since cure of ten months. This is certainly not above the average rate of infection in routine non-venereal case histories in this hospital and a series of 19 proven cases of gonococcal epididymitis over the same period all had a history of recent infection. The testicle

was affected first in all cases except one (5 per cent) and the epididymis was involved in less than half the cases (47 per cent). Finally the enlargement of the testicle was much greater than could be accounted for by mere inflammation of the tunica (Boyd, 1948).

The condition is probably not a venereal one. If the history of cohabitation is compared with that obtained in gonococcal epididymis, a condition occurring in a similar group of persons and no fixed time after intercourse, it is seen that they are very similar and that no true pattern can be discerned. This gives only indirect evidence and such histories are notoriously unreliable; further an excessively long incubation period comparable e.g. to that of inoculation hepatitis, would not be disclosed in such an analysis. It may be significant that two young patients strenuously denied ever having had intercourse, their ages being 17 and 18 years respectively. Two others would admit no more recent connexion than three and five months previously.

	<i>Orchitis</i> (21 cases)	<i>Gonococcal epididymitis</i> (19 cases)
<i>Last cohabitation:</i>		
Shortest interval	1 week	2 days
Longest interval	5 months	6 months
Average	4 months	4½ months
<i>Cohabited with:</i>		
Prostitute	76 per cent	78 per cent
Wife	9 per cent	16 per cent
	Total 85 per cent	94 per cent
No history	15 per cent	6 per cent

There is, therefore, no evidence to suggest that it is a venereal condition and if it should be, a possibility that cannot be excluded, the incubation period must be at least one month. There was no clinical evidence of infection by any of the usual venereal routes, no case having a genital sore and only two having scanty non-specific urethral discharges.

Histologically the lesion in the earlier case is very similar to that of mumps orchitis as seen in a case dying from embolism eleven days after the testicle became involved (Gall, 1947). From operation specimens taken within the first five days, however, this author showed that although the early lesion was lymphocytic in the interstitium and capsule a polynuclear exudate collected in the tubules. Of the lesion at eleven days he comments that "It is interesting that in none of the tubules of this case were polynuclear leucocytes so prominent a feature as in the earlier and more acute lesions . . ." In the present 2 cases polynuclears were practically absent from the sections as might be expected if they do represent a later stage of the same process. Gall's case showed some tubular organization manifested by increased thickness of the lamina propria and collagenization of both the lamina and the Sertoli remnants attached to

the wall a later stage of which is seen in these cases. In the small piece removed during the fourth week commencing organization is seen and although there is no evidence that this is necessarily a diffuse change it does suggest in combination with the limited follow-up findings that atrophy may ensue. This contrasts with Gall's view that "Despite the degree of damage it would seem from the nature and extent of the changes that complete atrophy of the testis would be an unusual sequela."

The commonly reported causes of orchitis are mumps, undulant fever, typhoid fever and trauma (Mason and Reifenstein, 1944). Rarely reported causes are infectious mononucleosis (Mackay-Dick, 1944), acute rheumatism (Trasoff and Goodman, 1944), pyogenic infection (Reyes, 1944), *Klebsiella pneumoniae* infection (Serri, 1946), meningococcal and lymphocytic choriomeningitis, Bornholm disease, atypical pneumonia and Dengue (de Langen, 1936).

The features of these cases do not suggest that any of these diseases was the cause of the orchitis seen.

Mumps in this area is not uncommon, but is as far as is known always typical; none of these patients had any salivary gland enlargement. Undulant fever is very rare and typhoid fever is uncommon—no case of either occurred at the same time nor was there any serological evidence of these infections. 2 cases only had a history of trauma and in neither case was it of such a nature as to account for the lesion seen. Falciparum malaria is very prevalent in the Gold Coast but apart from 2 cases that developed pyrexia while under treatment and had a typical attack with a positive film while in hospital routine blood films were negative in all cases. Owing to the freedom given to patients in this department and the fact that native troops do not take suppressives this is not an uncommon occurrence. No evidence of filariasis was found despite intensive search of numerous wet preparations taken six-hourly in two patients and routine thick film examination in all the others.

The cases were very similar to Mackay-Dick's first case seen in England in which there was no lymph-nodular enlargement or increase into the diagnostic range (Whitby and Britton, 1947) of mononuclear cells (large lymphocytes, 3 per cent, monocytes, 8 per cent). A diagnosis of infectious mononucleosis was made on a heterophile agglutinin titre of 1 : 512 against a control of 1 : 16 but absorption tests were not done. It is, of course, possible that this agglutination was due to another agent than that which causes glandular fever although this is unlikely. Unfortunately, this report was not seen until the epidemic died down and this reaction was not investigated; however, no abnormal cells had been seen and in no case was a mononucleosis present. His second case was quite unlike these on clinical grounds.

Apart from the marked increase in the E.S.R. there is no evidence that rheumatic fever can be implicated and the majority of patients received salicylates at some stage for the pain without any noticeable effect on the local lesion although the dosage was, of course, small. The results of the pathological

investigations dispose of the possibility of pyogenic or *Klebsiella pneumoniae* (Serri, 1946) infections.

No suspicion that any of the conditions of meningococcal meningitis, lymphocytic choriomeningitis, Bornholm disease or atypical pneumonia was the cause of the epidemic can be entertained but it is interesting to note that the last three of these conditions are due to virus infections and that lymphocytic meningitis has been found to be associated with a raised heterophile agglutinin titre (Tidy, 1947). The position with regard to dengue must, however, be carefully examined. The disease does occur in this area and *Aedes aegypti* are very numerous. Variability of the disease is stressed by the authorities and a series of 1,000 cases without a rash has been described (Jack, 1937). The uniform complaint of these soldiers of "pain in the waist" usually denoting spinal pain is suggestive. It is then possible, although unlikely, that they represent an atypical disease of this group.

The majority of descriptions of non-specific epididymo-orchitis (Report, 1943) relate to a different type of case although involvement of the testicle is a late feature. There is more similarity between these cases and those of an epidemic in Malta in summer 1943 (Tunbridge *et al.*, 1946) although there are again certain marked differences. Fever was uncommon in the Accra cases and the "testicular" rise in temperature was not seen. In both epidemics the left side was more often affected (Accra 62 per cent, Malta 69 per cent) but in Malta there appears to have been more severe involvement of the epididymis and in only 4 cases was the testicle alone involved (14 per cent). In both series one case was seen in which the physical signs of tuberculous epididymitis were present at one stage. There is no significant difference in the duration or sequelae and the clinical pathology is markedly similar with the exception of the raised E.S.R. in the Accra cases. It is interesting that one of the Malta cases had cervical adenitis. It is possible that the quantitative differences in the frequencies of the different characters are due to variations in local conditions and in the races that are affected more than to any intrinsic difference in the infecting agent.

SUMMARY

Twenty-one cases of orchitis are described and it is suggested that they represent a small epidemic of an infection endemic in the Accra area. There is some evidence that a similar condition occurs elsewhere.

The lesion is a painful non-suppurative inflammation unaffected by the treatments tried and running a self-limiting course of three to four weeks.

It is suggested that it is due to infection by a virus.

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