TWO CASES OF INFECTIVE MONONUCLEOSIS.

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Admitted to No. 13 General Hospital on January 10, 1944.

Complaint.—Fever (T. 101.4° F., P. 120). Painful and tender discrete enlargement of cervical, axillary and inguinal glands. Febrile for three days. No rash. Spleen not palpable. Atrophied painless left testicle. Spermatic cord L.N.A.D. Painless enlargement of right testicle. This painless enlargement has been progressive since August, 1943. Size of right testicle has not increased in hospital. Nil abnormal noted in epididymis, right, or in spermatic cord, right.

Foreign Service.—Two years (Egypt, Cyrenaica, Tripoli).

Previous illnesses.—“Tonsillitis,” July, 1943. Short term febrile illness (2–3 days fever) called “sandfly fever,” July, 1943. NB. Complaints of testicles began early in Aug., 1943, following these “two illnesses” which I believe are merely the early stage of his present illness which would appear to be glandular fever (infective mononucleosis). He has also had malaria, B.T., on two occasions.

No history of mumps, venereal disease or of any previous disease of his genito-urinary system. No history of trauma to testicles.

Investigations carried out:—
10.1.44: R.B.C. 5,400,000/c.mm., Hb. 102 per cent; W.B.C. 9,600/c.mm.: Polys 35 per cent, lymphos 50 per cent, monos 15 per cent, eosinos 0 per cent.
12.1.44: Paul Bunnell reaction, “Specimen haemolysed sheep’s cells.” Urine, N.A.D.
19.1.44: R.B.C. 4,710,000/c.mm., Hb. 95 per cent; W.B.C. 8,200/c.mm.; Polys 45 per cent, lymphos 50 per cent, monos 4 per cent, eosinos 1 per cent.
25.1.44: B.S.R. 3 mm. in one hour (Westergren).
31.1.44: W.B.C. 14,600/c.mm.: Polys 51 per cent, lymphos 38 per cent, monos 11 per cent.
3.2.44: Paul Bunnell reaction, serum 1 in 128, control 1 in 16.
13.2.44: W.B.C. 8,600/c.mm.: Polys 69 per cent, lymphos 26 per cent, monos 3 per cent, eosinos 2 per cent. B.S.R. 6 mm. in first hour (Westergren).

Kahn reaction, negative.
Paul Bunnell reaction, serum 1 in 4, control 1 in 4.
Gonococcal Complement Fixation Test: Negative.
Midstream urine, culture sterile. Micro, N.A.D.

Seen and passed by venereologist.

Treatment has consisted of rest in bed and a suspensory bandage as support for the testicles. The condition of the right testicle and right epididymis is I.S.Q., otherwise the patient is well. Hospitalized for thirty-six days.

The case is believed to be one of relapsing infective mononucleosis which started in July, 1943, when he was diagnosed as having tonsillitis and later sandfly fever, and which was complicated by orchitis or probably epididymo-orchitis early in August, 1943. It has now resulted in complete atrophy of the left testicle, probably epididymis as well, and a stationary enlargement of the right testicle which may or may not atrophy just as its neighbour.

It is of interest to record that the involvement of the testicles and probably epididymis as well has been painless throughout.

I consider the case to be one of epididymo-orchitis complicating infective mononucleosis (glandular fever). It may be similar to the cases of non-specific epididymitis which have been reported in the past.

The Paul Bunell reactions were carried out in the Central Pathological Laboratory.
Case B.—No. 201704 Sapper G. S., aged 28. Service four years.

Admitted to No. 13 General Hospital on January 7, 1944.

Complaint.—Dull pains across lower abdomen for fourteen days. No nausea or vomiting. Sent into hospital as ? appendix. T. normal, P. 72.

Examination revealed the right testicle to be much enlarged and tender on palpation with slight tenderness of the associated epididymis. Right spermatic cord shows nil abnormal. Abdominal pain not relieved by supporting the testicles. The left testicle, though much smaller than its enlarged and tender neighbour, appeared to be of a reasonably normal size and testicular sensation did not appear to be abnormal. No rash. Spleen not palpable. No obvious lymph glandular enlargement.

Foreign Service.—10/12 years (Tunisia, Algeria, Egypt). No illnesses during this period.

Previous illnesses in U.K.—"Tonsillitis" and also coryza. No history of mumps, venereal disease or of any previous disease of his genito-urinary system. No history of trauma to testicles.

Results of investigations:—
14.1.44: Urine, N.A.D. B.S.R. 5 mm. in one hour (Westergren).
3.2.44: W.B.C. 8,600/c.mm: Polys 59 per cent, small lymphos 29 per cent, large lymphos 3 per cent, monos 8 per cent, eosinos 1 per cent. Paul Bunnell reaction, serum 1 in 512, control 1 in 16.
13.2.44: W.B.C. 7,000/c.mm., Polys 66 per cent, lymphos 5 per cent, eosinos 1 per cent. B.S.R. 8 mm. in first hour (Westergren). Kahn reaction, negative. Paul Bunnell reaction, serum 1 in 4, control 1 in 4. Midstream urine, culture sterile; micro N.A.D. Gonococcal Complement Fixation Test, negative. Seen and passed by venereologist.

Although this patient has been afebrile since admission, which was fourteen days after the onset of the symptoms, and showed no obvious lympho-glandular enlargement I consider that there is sufficient justification for considering him to be suffering from infective mononucleosis. It is regretted that a white blood count and a differential count was delayed until the middle of the fourth week following the onset of symptoms but even then the differential white count at this stage is suspicious whilst the result of the Paul Bunnell reaction would appear to be diagnostic. There is no doubt about the marked enlargement of the right testicle. The left testicle may or may not have been similarly involved and it may be that it is becoming smaller just as the left testicle in Case A. The lower abdominal pains may have been due to involvement of the mesenteric glands.

It is considered that the epididymo-orchitis in this case is a complication of infective mononucleosis (glandular fever).

The Paul Bunnell reactions were carried out in the Central Pathological Laboratory.

Commentary.

In five years' service in Egypt, the Anglo-Egyptian Sudan, Eritrea, Syria and Palestine it has been my good fortune to have seen a few cases of infective mononucleosis (glandular fever) in each of these countries.

The disease would appear to be as ubiquitous as infective hepatitis. In infective mononucleosis I have been struck by the relative frequency with which one has elicited a long history indicating that the disease process started months before and was characterized by a short term febrile phase with sweating, general malaise, aches and pains and weakness with or without complaints of sore throat or painful and tender lymph glands in the neck, etc.

These febrile bouts have recurred at intervals and have been given such diagnoses as "pharyngitis," "tonsillitis," "P.U.O.,” "sandfly fever," "influenza" or, as happened in the case of a pathologist who subsequently became a colleague of mine, "atypical relapsing fever," before these patients were observed in hospital and repeated blood counts were carried out well into the afebrile phase of the illness and the true diagnosis established. In this connexion it is emphasized that unless differential white blood counts are done repeatedly at intervals of a few days many cases of infective mononucleosis will be missed because the differential white blood counts may be within normal limits, for some days at least, after a
febrile phase and in the meantime the patient is discharged from hospital with one of the diagnoses already mentioned.

I have seen so many cases of infective mononucleosis diagnosed, as it were, by accident that I am convinced that the apparent incidence of this disease is by no means indicative of its true incidence. As infective mononucleosis is usually a mild, though prolonged and weakening, illness it must be overlooked on frequent occasions, more especially as the patient has probably been discharged from hospital before characteristic changes occur in the blood picture.

Of course cases which present extensive lympho-glandular enlargement and/or a rash are less apt to be missed than cases resembling simple sore throat or a short term febrile illness such as sandfly fever because a thorough examination of the white cells is usually carried out in all cases with lympho-glandular enlargement or with a rash; in such cases a Paul Bunnell reaction would also be considered a relevant investigation.

It may be of interest to record that I have heard medical officers talking about cases of sandfly fever with glandular enlargement!

Furthermore, as regards the varied symptomatology of infective mononucleosis (glandular fever), I know of two proven cases, one of which exhibited enlargement of the thyroid gland and both showed loss of weight, listlessness, lack of energy, sweating, irritability with mild emotional instability and which were diagnosed as thyrotoxicosis and "goitre" respectively. Subsequently the diagnosis of infective mononucleosis was established beyond doubt. I am not aware that the thyroid gland has ever been involved in glandular fever but it is an interesting idea.

Case A would appear to be a typical case of infective mononucleosis beginning in early July, 1943. The first period with symptoms was called "tonsillitis," the second period with symptoms was called "sandfly fever" and then, early in August, 1943, he noted changes in his testicles which were insidious in onset and which were painless, progressive and persistent and probably permanent.

He finally reported sick on January 10, 1944, and had a three-days' fever with extensive lympho-glandular enlargement but no rash. The diagnosis in this case would appear to be beyond doubt. In addition most causes of the epididymo-orchitis type would appear to have been excluded.

Case B is of marked interest because there is no evidence of fever, superficial lympho-glandular enlargement or of a rash. The lower abdominal pains, believed to be due to involvement of the mesenteric glands, resulted in the patient being admitted to hospital as "? appendix" whilst the obvious right epididymo-orchitis scarcely attracted the patient's attention although he is well aware of it now.

The symptomatology of these cases of infective mononucleosis must emphasize how vague the appearances of this disease can be.

**SUMMARY.**

(i) Two cases of infective mononucleosis (glandular fever) with epididymo-orchitis are described.

Case A shows complete atrophy of the left testicle and a painless progressive enlargement of the right testicle the rate of which the future will show.

Case B has a tender right epididymo-orchitis with obvious enlargement of the right testicle. The left testicle may be becoming smaller. The future will decide the rate of subsidence of these testicles.

(ii) Case B was sent into hospital as "? appendix" because of lower abdominal pains. Case A had been diagnosed as "tonsillitis" and then "sandfly fever" at the apparent onset of his illness and was finally admitted to No. 13 General Hospital as a case of P.U.O.

(iii) No rash or splenic enlargement in either case. No obvious lympho-glandular enlargement in Case B but glands prominent in Case A.
(iv) The blood picture and Paul Bunnell reactions in each case indicate infective mononucleosis.

(v) Both cases show: Normal B.S.R., negative Kahn reaction and G.C.F.T., sterile normal urine, no history of trauma, mumps, venereal disease or of any other disease of the genito-urinary system.

(vi) The mildness of the symptoms referable to the external genitals, their insidious onset and their obvious gravity, are most striking.

CONCLUSIONS.

(i) Two cases of epididymo-orchitis occurring as a complication of infective mononucleosis are described. This complication, insidious in onset and with relatively mild symptoms, can result in complete testicular atrophy and must be regarded as being very serious especially if both testicles suffer. The future will show whether or not both patients will have unilateral or bilateral testicular atrophy.

(ii) In all cases of epididymo-orchitis or epididymitis of vague origin, investigations for infective mononucleosis should be carried out and, what is important, repeated at intervals.

(iii) In the early stages infective mononucleosis may be missed completely and called P.U.O., influenza, pharyngitis, tonsillitis or sandfly fever, especially in the absence of a rash, absence of obvious lympho-glandular or splenic enlargement, because blood changes may not occur till later on in the disease and until the febrile phase is well over.

(iv) Case A is an example of infective mononucleosis, frequently called relapsing infective mononucleosis, which smoulders insidiously and unsuspected over a period of several months with mild febrile exacerbations before the clinical picture arouses suspicions regarding the true nature of the illness.

(v) Infective mononucleosis should be kept in mind in connection with all patients who exhibit recurring bouts of short-term fever with weakness, lassitude, sweating and a feeling of "out of sorts" or of being below par.

(vi) Complete testicular atrophy with loss of function may result from epididymo-orchitis occurring as a complication of infective mononucleosis. This is a serious complication, especially if bilateral, and the question of this disability, contracted in the tropics or subtropics, being regarded as directly attributable to Military Service should receive attention, and an official decision be made.

(vii) It is suggested that infective mononucleosis, which is believed to be due to a virus, is an infective disease in which changes in the differential white blood count are not constant features and that when such changes occur their time of appearance may be delayed considerably.

Accordingly it is suggested that the Paul Bunnell reaction may be a more frequent investigation in cases of vague ill-health or in cases with recurring bouts of short-term fever with normal B.S.R. and where the cause is not obvious.

(viii) Attention is drawn to the varied clinical manifestations of infective mononucleosis and to the various diagnoses which may be inadvertently applied to it. These seem to include disorders of the thyroid gland:

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