INFECTIOUS MONONUCLEOSIS

AN ANALYSIS OF 395 CASES

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BETWEEN 1956 and 1960 many patients were admitted to Military Hospitals suffering from infectious mononucleosis. The case notes of 10% of these cases were examined. A certain number were useless but 395 case sheets were analysed.

Himsworth (1941) thought that there is a correspondence between the Paul Bunnell reaction and the number of monocytes present in the peripheral blood. Israels (1941) disagreed. Hobson, Lawson and Wigfield (1958), in a study of 498 patients, described two groups. In Group I the Paul Bunnell reactions were positive and a typical lymphocytes were seen in peripheral blood. There were 248 patients in Group I. In Group II the Paul Bunnell reactions were negative and atypical lymphocytes were seen in peripheral blood. There were 100 patients in Group II. In Group I there were more patients who had relative and absolute increase of mononuclear cells than there were in Group II. These authors took as positive a Paul Bunnell reaction in which there was a titre of 1: 80 or more after absorption with guinea-pig cells, with a reduction in titre of at least two tubes after absorption with ox cells. They thought that a doubtful Paul Bunnell reaction means that the disease is either waxing or waning.

Tidy (1934) believed the essential features of the illness to be fever, glandular enlargement, faucial affection and changes in the blood, that is, lymphocytosis. Bernstein (1940) in a description of 65 patients, with a review of the disease and a full bibliography, considered that infectious mononucleosis is a generalised disease in which an essential sign is a increase, at some time in the course of the illness, in the mononuclear elements of the blood.

The Analysis

Sex and Age

All were male and the ages ranged from 15-44 years with an average of 20.7 years.

Time ill before Admission to a Medical Unit

The average was 5.5 days ranging from a few hours to 10 weeks.

Duration of Illness

This was taken from the onset of symptoms to the time when the patient was considered fit to return to duty, usually after a period of sick leave. The average time was 34.6 days and the longest 122 days, with one case each of 72, 78, 80, 81, 82, 84, 86, 95 and 110 days.

Temperature

The records shewed that 5 (1.2%) patients had no fever. In 14 (3.5%) the maximum was 99°, in 12 (3%) 99.5°, in 54 (13.6%) 100°, in 24 (6%) 100.5°, in 52 (13%) 101°, in 32 (8%) 101.5°, in 49 (12%) 102°, in 24 (6%) 102.5°, in 37 (9.3%) 103°, in 16 (4%) 103.5°, in 16 (4%) 104°, in 3 (0.7%) 104.5°.

Duration of Fever

In 79 (20%) there was no record but in the remainder the average was 7.5 days with one case of 77 days duration of intermittent fever and one of 45 days duration.

Leucocyte Count

Out of 390 records, in 318 (80%) the total count lay between 5,000 and 15,000 cells per cu.mm. The highest total count was 32,900 per cu.mm. The highest count of mononuclear cells was 25,696 per cu.mm. which represented 88% of a total count of 29,200 cells per cu.mm. In 331 (84.7%) there were seen what were variously described as glandular fever cells, atypical lymphocytes consistent with a diagnosis of glandular fever or atypical mononuclears. There were 34 notes (8.7%) in which there was no record of the presence of glandular fever cells but in which a preponderance of the mononuclear series was recorded.

There were 229 patients (58%) for whom there were either records of atypical cells or preponderance of mononuclear cells and in whom either the Paul Bunnell reactions were positive or the spleens were enlarged or both. Of these 4 (1%) shewed granular cell counts of between 5,000 and 6,000 per cu.mm., 68 (17%) between 3,000 and 4,000, 94 (24%) between 2,000 and 3,000, 55 (14%) between 1,000 and 2,000 and 8 (2%) less than 1,000 per cu.mm., the lowest count being 234 per cu.mm.

In 205 patients (52%) for whom there was a record either of the presence of glandular fever cells or of a preponderance of mononuclear cells or both, the Paul Bunnell was negative, incomplete or not recorded. In 162 patients (41%) both were positive.

Time of Appearance of Diagnostic Count

In 173 patients (43.6%) this lay between the 2nd and 15th days. In one it was recorded at the 35th day and in one at the 42nd day.

Paul Bunnell Reaction

The criteria taken as indicating a positive result were those of Hobson et al. (1958) recorded above. There were a number of results in which a high titre of antibodies was found in the serum and after absorption with guinea-pig cells but in which the test had not been completed, e.i. there was no record of absorption with ox cells, or in which a high heterophil antibody titre had not been followed by any absorption tests at all. In the majority the tests had only been done once whether negative or positive.

In 168 patients (42.5%) the Paul Bunnell reaction was unequivocally positive. Of these results 145 (36.7%) were noted in the first 2 weeks and the first day on which the test was recorded as being positive ranged from the 2nd to the 107th day of illness. The highest recorded titres in the Paul Bunnell reaction were 1: 20,480 which remained at 1: 20,480 after obsorption with guinea-pig cells but fell to 1: 2,560 after absorption with ox cells. This reaction was recorded on the 30th day of illness.

Spleen

The spleen was palpable up to 3 fingers' breadth below the left costal margin in 211 patients (53.4%). In 97 (25%) the Paul Bunnell reactions were positive and the spleens were felt. In 71 (18%) the Paul Bunnell reactions were positive but the spleens were not felt. In 47 (11.9%) the Paul Bunnell reactions were negative but the spleens were felt. In 67 (16.9%) the Paul Bunnell reactions were either indeterminate, incomplete or not

recorded and the spleens were felt. In 200 (50.6%) either glandular fever cells were seen or there were many mononuclear cells and the spleens were felt.

214 patients (54.2%) had total leucocyte counts exceeding 10,000 per cu.mm. In 125 (31.6%) there were enlarged spleens. In this group 98 (25%) had mononuclear counts between 6,000 and 14,000 per cu.mm. In the 89 (22.5%) without palpable spleens 63 (16%) had mononuclear counts between 6,000 and 14,000 per cu.mm. and 41 (10.4%) had mononuclear counts between 8,000 and 12,000 per cu.mm.

The spleen was not felt in the patient whose Paul Bunnell reaction was 1: 20,480. It was felt in the patient whose Leucocyte count was 32,900 per cu.mm.

Liver

The liver was palpable or tender in 38 patients (9.1%) of whom 14 (3.5%) had jaundice. 21 patients (5.2%) whose livers were enlarged had positive Paul Bunnell reactions. 11 patients (2.8%) with enlarged livers had enlarged spleens.

Jaundice

Jaundice was observed in 28 patients (7%) in 14 (3.5%) of whom the livers were enlarged or tender. In 12 (3%) the spleens were enlarged and in 18 (4.6%) the Paul Bunnell reactions were positive. In 25 patients (6.3%) with jaundice, glandular fever cells were reported and in 16 (4%) glandular fever cells were present and the Paul Bunnell reactions were positive.

Rash

A rash of various types occurred in 43 patients (10.9%) in 21 (5.2%) of whom the Paul Bunnell reactions were positive. In 38 (9.6%) there were glandular fever cells or marked mononuclear preponderance and in 6 (1.5%) jaundice. In 24 patients (6%) with rashes the spleens were enlarged but in only 6 (1.5%) of the patients with rashes were there also reports of palatal petechiae.

Palatal Petechiae

These were noted in 65 patients (16.4%). In 45 (11.4%) they were associated with positive Paul Bunnell reactions and in 57 (14.4%) with the presence of glandular fever cells. In 36 (9.1%) there were both positive Paul Bunnell reactions and glandular fever cells. In 35 patients (8.8%) with palatal petechiae the spleens were enlarged.

Whether or not palatal petechiae were reported seemed to depend very much on personal awareness of their occurrence in this illness for their presence tended to be reported more from some hospitals than from others.

Correspondence between Paul Bunnell Reaction and Leucocyte Count

There were 214 patients (54.2%) in whom there were total leucocyte counts exceeding 10,000 per cu.mm. and of these 93 (23.5%) had positive Paul Bunnell reactions, and 121 (30.6%) Paul Bunnell results which were either negative, incomplete or not recorded. In the patients whose Paul Bunnell reactions were not positive, 60 (15.2%) of the mononuclear counts lay between 8,000 and 12,000 per cu.mm. and in the 93 patients with positive reactions, 42 (10.4%) counts lay between 8,000 and 12,000 per cu.mm. 94 (23.8%) of the 121 and 74 (18.7%) of the 93 had mononuclear counts between 6,000 and 14,000 per cu.mm.

The Throat

There was either sore throat or dysphagia or both in 266 patients (67.3%). Of these in 10 (2.5%) the throats were reported as being normal in appearance. Of these without sore throats the throats were inflamed in 65 (16.1%). 320 patients (81%) in all shewed inflamed throats and in 107 (28.1%) these changes went no further. In 34 (33.9%) both tonsils were enlarged in and 20 (5.1%) one only. In 234 (59%) follicular exudate was seen, in 5 (1.3%) membranous exudate, in 16 (4%) there were sloughs. Ten patients (2.6%) had peritonsillar oedema. The severity of the sore throat was seldom commented on.

Symptoms

The symptoms in general were non-specific and of the symptoms complained of, headache was the most frequently occurring and was noted, from mild to severe, in 204 patients (51.6%). Only 38 patients (9.6%) were said to have vomited.

Upper Respiratory Tract

Affection was recorded in 81 patients (20.5%), shewn either by nasopharyngeal catarrh or cough with or without sputum. 3 patients (0.8%) had epistaxis and 3 (0.8%) had haemoptysis.

In one patient a confusional state was recorded which lasted about 24 hours.

Duration of Illness

As stated above, the average duration of illness was 34.6 days for all the patients but those with positive Paul Bunnell reactions had an average duration of illness of 39.2 days. All the patients with long illnesses noted above had unequivocally positive Paul Bunnell reactions and of the patients with positive Paul Bunnell reactions 98 (25%) were ill longer than the average for the whole series. There was no correspondence between the length of the illness and the height of the Paul Bunnell titre nor was there any correspondence between the Paul Bunnell reaction and the degree of fever experienced.

Glandular Enlargement

In 383 patients (96.4%) there were records of lymph node enlargement. In 202 (52.1%) there was a general enlargement, in 78 (19%) cervical enlargement only, in 56 (14.2%) cervical and auxillary enlargement. In 131 (33.4%) the tonsillar nodes were enlarged and in 12 (3.0%) no other nodes were enlarged. There was tenderness of lymph nodes in 74 (18%). Enlargement of one or other lymph node at the upper third of sternomastoid was noted in 19 (4.8%).

Other Features

A right facial palsy was recorded in one patient as developing while in hospital.

One patient, admitted because of bronchitis, had no other symptoms at all, but had a total leucocyte count of 17,850 per cu.mm. in which there were 84% of mononuclear cells and a Paul Bunnell titre of 1: 896 before absorption, 1: 896 after absorption with guinea-pig cells and 1: 7 after absorption with ox cells.

Discussion

An attempt has been made, by the study of case notes of patients suffering from infectious mononucleosis, to observe any constant features of the disease. This study suffers, plainly, from the fact that it is retrospective. For instance, in 165 patients (42%)

the Paul Bunnell reactions were certainly positive. Of the remainder there were many in whom the heterophil antibody tests were positive but in whom no absorption tests were done. It is likely that a certain number of these would have been positive if the further tests had been done. Similarly, Paul Bunnell reactions which were negative at the first attempt were seldom repeated and it is well known that there may be considerable delay before the test becomes positive. In this series the longest delay was 107 days before a positive result was noted. In this particular case the patient was first ill with malaise and swollen lymph nodes in July, was discharged but remained unwell and had recurring lymph node enlargement. He had to be re-admitted in September and again in October of the same year. It was only at the final admission that the Paul Bunnel test was positive. Hobson et al. (1958) record one case in which the test only became positive in 89 days. Certainly it appears that a positive Paul Bunnell test is by no means a " sine qua non " in making the diagnosis of infectious mononucleosis for it may well not become positive in the average course of the illness.

Lymph node enlargement was a relatively constant feature, occurring in some group in 383 (96.4%). Next in order of frequency was the changes in peripheral blood (either a preponderance of mononuclear cells or the presence of atypical lymphocytes or both), which were found in 365 patients (93.4%). A noticeably inflamed throat was seen in 320 patients (81%). Fever was present at some time in 333 (84.3%). Thus neither Tidy's nor Bernstein's criteria were fulfilled in all the cases in which the diagnosis was made in this series.

There appeared to be no correspondence between the Paul Bunnell reaction and the number of mononuclear cells in the peripheral blood. This finding is not in agreement with the findings of Himsworth (1941) and of Hobson et al. (1958) quoted above. Nor was there any difference between the total mononuclear counts of the patients with palpable spleens and those of patients whose spleens were not felt.

Summary

A study has been made, in retrospect, of 395 case notes of patients in whom a diagnosis of Glandular Fever or Infectious Mononucleosis was made in military hospitals between 1956 and 1960. Some comparisons are made between findings in the present series and those of previous writers. Such comparisons are invalidated, to some extent, by the fact that the present study is retrospective and that essential information was often lacking. This applies, in particular, to the Paul Bunnell reactions. No conclusions can be drawn from the series but some features which were noted during a study of the case notes are described.

It does seem that when the Paul Bunnell reaction is positive the patient is likely to be ill for somewhat longer than the average. It is shewn, too, that in many patients in whom the diagnosis was either certainly or probably Infectious Mononucleosis, there was an absolute reduction in the number of cells of the granular series in the peripheral blood.

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