The Significance of Proplasmocytes and Atypical Plasma Cells in the Benign Lymphocytic Meningitis Syndrome

By Peter Wolf

In the differentiation of tuberculous meningitis from other forms of lymphocytic meningitis, difficulty may arise when tubercle bacilli are not initially found in films of cerebrospinal fluid (C.S.F.) deposit, and this is accentuated when a low C.S.F. sugar is found. The clinical history is often of no help. Thus, since the early diagnosis is important for appropriate therapy, any additional diagnostic help that the laboratory can give in these difficult cases will be valuable.

The blood films from two proved cases of lymphocytic choriomeningitis, initially diagnosed as tuberculous meningitis because of low C.S.F. sugars and suspicious chest signs, showed the conspicuous presence of large atypical plasma cells. The possibility that these cells might be a characteristic finding in lymphocytic choriomeningitis was considered amid patients admitted to hospital with a lymphocytic meningitis had their blood films carefully examined on the day of admission. The blood and C.S.F. findings of ten patients suffering from a benign, nontuberculous, lymphocytic meningitis were then compared with twelve cases of proved tuberculous meningitis admitted during the same period. The blood films from nine of the ten patients with benign meningitis showed large atypical plasma cells. Repeated search for the presence of these cells in the blood films from the patient with tuberculous meningitis was always negative.

It is well known that plasma cells and atypical plasma cells appear in the blood in various infections and irritations of the bone marrow. A survey of the rate of occurrence of these cells in various diseases was made, to find if they occurred predominantly in virus diseases. This appeared to be the case, but they were also found occasionally in nonvirus diseases, e.g., bacterial pneumonia, erysipelas, bronchitis, whooping cough, and urinary infections; table 3 lists the diseases showing the largest incidence.

Although the ten cases of benign meningitis have been grouped together as a disease entity because of the similar clinical and laboratory findings, they were in fact a heterogeneous group. Only four of the ten patients showed a positive, or rising serum titre for the lymphocytic choriomeningitis virus. The similarity of the blood pictures, however, can be seen in table 1.

The atypical cell is illustrated. It is a mononuclear cell whose nucleus is at least twice the diameter of the average red blood cell in the film. The nucleus is usually spherical, rarely elliptical, and nucleoli are uncommon. The nuclear

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The work for this paper was done at Crumpsall Hospital, Manchester. The complement fixation tests for lymphocytic choriomeningitis were done by Dr. Tobin in the University of Manchester.
chromatin is in large clumps, showing clear spaces in between sharply demarcated chromatin masses which may be coarse or fine. The cell has an abundant, slaty blue, foamy cytoplasm, often showing vacuolation. There is often a halo of lighter colored cytoplasm in the zone surrounding the nucleus. The cell usually exceeds 15μ in diameter.

This cell is illustrated among typical plasma cells and irritation cells by Pappenheim; it appears identical with the proplasmocytes and atypical plasma cells illustrated by Sandoz; and the nuclear features correspond to Type II Downey cells.

**Comparison of the Blood Picture in Detail**

In comparing the blood pictures of twelve proved cases of tuberculous meningitis with those of ten patients showing the benign meningitis syndrome in which bacteria were not isolated from the C.S.F., the following differences were noted:

1. The atypical cells described above were found in the blood films in nine out of ten patients in the benign lymphocytic meningitis group, but were not found in repeated blood films from any of the twelve cases of tuberculous meningitis.

2. The total white cell count for the patients with tuberculous meningitis showed a wide variation, ranging from as low as 3400 per cu.mm. to as high as 34,400 per cu.mm. In contrast, the total white cell count in the patients with benign, lymphocytic meningitis averaged approximately 7000 per cu.mm., the range being only between 5000 and 11,300 per cu.mm.

3. The percentage count of polymorphs showed a tendency to be lower in the benign, lymphocytic meningitis group.

In addition, two of the patients in the benign, lymphocytic meningitis group had a blood picture resembling that of glandular fever. One of these patients was a proven case of lymphocytic choriomeningitis and the other gave two nega-
tive complement fixation tests for this virus. In both cases, numerous Downey cells were present, but Paul-Bunnell tests were repeatedly negative. The ratios of Downey cells to the atypical plasma cells described were 15:6 and 17:4.

CLINICAL FEATURES FOUND IN PATIENTS WITH BENIGN MENINGITIS

Although the ten cases of benign meningitis were not all of the same type, only four giving a positive complement fixation test for lymphocytic chorio-
TABLE 2.—Blood Picture and Other Relevant Findings in Cases of Tuberculous Meningitis

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* Glucose in mg. per 100 cc. cerebrospinal fluid.

TABLE 3.—The Incidence of Atypical Cells in Various Illnesses

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<th>Type of illness</th>
<th>Number of patients investigated</th>
<th>Number of patients showing atypical plasma cells</th>
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<td>9</td>
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<tr>
<td>Measles</td>
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<td>Glandular fever†</td>
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<tr>
<td>Tuberculous meningitis</td>
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</table>

* Two of these cases showed the presence of Downey cells, the ratios of Downey cells to atypical plasma cells being 15:6 and 17:4.
† All of these cases showed Downey cells and seven also showed the atypical plasma cells described, the ratio of Downey cells to atypical plasma cells ranging from 31:1 to 13:1.

meningitis, the history of onset of illness was always similar. It was gradual, with malaise, headache, backache, and a feeling of cold. Six patients complained of a cough seven to fourteen days prior to admission and all showed marked mental retardation during the acute phase of the illness. The following complications occurred: impaired liver function without jaundice; nerve deafness, although streptomycin was not used; psychosis; miscarriage; general lymphadenopathy.

**DISCUSSION**

Considering the ten patients in the benign, lymphocytic meningitis group, none of the clinical findings could exclude a diagnosis of tuberculous meningitis; moreover, a low C.S.F. sugar level was found in four of these patients. One patient in this group (case 8), had an initial C.S.F. sugar level of 48 mg. per 100 cc. and showed on the two consecutive days the low values of 28 and 20 mg. per
100 cc. Similar findings were recorded by Green, et al. in a series of twenty-one proved cases of lymphocytic choriomeningitis. Seven of these twenty-one patients had a low C.S.F. sugar level, one of them after an initially normal value of 79 mg. per 100 cc.

It is in patients like these where a provisional diagnosis of tuberculous meningitis is made, that there is often a temptation to start a course of intrathecal streptomycin without waiting for a report of tubercle bacilli in the C.S.F. For example Jamieson, in reviewing streptomycin and para-amino salicylic acid treatment of thirty-five cases of tuberculous meningitis, recorded five patients who received treatment without tubercle bacilli being found in the C.S.F. on direct examination. Three of these patients also gave negative cultures, and tubercle bacilli were never isolated throughout the period of observation.

The possibility, therefore, exists that patients with a nontuberculous, lymphocytic type of meningitis accompanied by a low C.S.F. sugar level are treated and recorded as cases of tuberculous meningitis. It is in excluding this error that the comparison of the blood picture is significant.

Although the number of cases studied is small, it appears justifiable to draw attention to the frequent occurrence of atypical plasma cells in peripheral blood in benign nonbacterial lymphocytic meningitis, and the absence of these cells in tuberculous meningitis. The atypical cells can readily be picked up under the low power of the microscope, especially when immersion oil is smeared over the slide, and so a blood film may very quickly be searched completely. The fact that these cells are not specific for lymphocytic choriomeningitis or for virus diseases, does not detract from their significance in helping to exclude a diagnosis of tuberculous meningitis.

**Summary**

A nontuberculous, lymphocytic meningitis with a low C.S.F. sugar level may be confused with a tuberculous meningitis. Additional diagnostic help may be obtained from examination of the blood. The blood pictures of twelve patients with tuberculous meningitis were compared with those from ten patients with a nontuberculous, nonbacterial lymphocytic meningitis, four of whom had low C.S.F. sugar levels. These ten patients appeared clinically to be suffering from the same disease and only the serum complement fixation test for lymphocytic choriomeningitis showed them to be a heterogeneous group.

The main differences in the blood were (1) a uniformly low total white cell count in the benign meningitis group as opposed to a widely varying total white cell count in tuberculous meningitis; (2) a lower percentage count of polymorphs in the benign lymphocytic meningitis group; (3) the presence of atypical plasma cells in nine of the ten patients in the benign, lymphocytic meningitis group. Two of the patients with benign meningitis, who had repeatedly given negative Paul-Bunnell tests showed a blood picture indistinguishable from that of glandular fever.

Although these atypical plasma cells are not specific for lymphocytic choriomeningitis or for virus diseases in general, they were found in no case of tuberculous meningitis. The presence of these cells is therefore of considerable aid in excluding a diagnosis of tuberculous meningitis.
PROPLASMOCYTES AND ATYPICAL CELLS IN LYMPHOCYTIC MENINGITIS

SUMMARIO IN INTERLINGUA

Meningitis lymphocytic nontuberculotic a hasse nivello de sucro in le fluido cerebrospinal es facilemente confundite con meningitis tuberculotic. In tal casos le diagnose pote profitar del examine del sanguine.

Le condition del sanguine de 12 patientes con meningitis tuberculotic esseva comparate con illo de 10 patientes con meningitis lymphocytic nontuberculotic nonbacterial del quales 4 hadeva un hasse nivello de sucro in le fluido cerebrospinal. Clinicamente iste 10 patientes pareva suffrer del mesme morbo. Solo le essayo a fixation del complemento seral, usate pro differentiar choriomeningitis lymphocytic, poteva demonstrar que illes representava un gruppo heterogenee.

Le major differentias del sanguine esseva (1) un conto total uniformemente basse de leucocytos in le grupo con benigne meningitis, contrastate con un conto total multo variabile de leucocytos in le casos de meningitis tuberculotic; (2) un plus basse conto percentual de polymorphos in le grupo de benigne meningitis lymphocytic; (3) le presentia de atypic cellulas plasmatic in 9 inter le 10 patientes con benigne meningitis lymphocytic. Duo del patientes con benigne meningitis, qui repetitemente habeva reagite negativemente a essayos Paul-Bunnell, monstrava un configuration del sanguine non distinguibile de illo de febre glandular.

Ben que le presentia de iste atypic cellulas plasmatic non es un caracteristica specific de choriomeningitis lymphocytic o de morbos a viruses in general, illos non esseva trovate in ullle caso de meningitis tuberculotic. Le presentia de iste cellulas es consequentemente de considerabile adjuta in excluder un diagnose de meningitis tuberculotic.

REFERENCES

4 Atlas of Haematology, Basle, Sandoz Ltd., 1952, plate 26, figs. 145 C and D and 148 A.
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