Immunopancytopenia Associated with Incomplete Cold Hemagglutinins in a Case of Primary Atypical Pneumonia

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In a case of primary atypical pneumonia with pancytopenia, incomplete antibodies of the cold hemagglutinin type with a very wide thermal range could be demonstrated. These were presumably the cause of the pancytopenia in the form of severe hemolytic anemia, agranulocytosis, and thrombocytopenia.

Serologic investigations by Davies, Dameshek, and Schwartz, Gasser, Heilmeyer, Maier, Schubothe and Altmann, and Tischendorf have brought much new insight to the field of acquired hemolytic anemia. Special progress in the understanding of the mechanism of acquired hemolytic anemia has been made in recent years by the discovery in 1944 of antibodies of the cold agglutinin type with a high thermal amplitude and by the discovery of incomplete antibodies of blocking antibodies (glutinins).

Boorman, Dodd, and Loutit and Neber and Dameshek were the first to demonstrate the presence of incomplete antibodies in hemolytic anemias, and in 1951, Van Loghem, Stallmann, and Hart demonstrated for the first time the presence of incomplete antibodies of the cold agglutinin type active at body temperature as the causative agent in a case of acquired hemolytic anemia. The development of cold hemagglutinins has been described in many different diseases such as: atypical pneumonia, hepatitis, infectious mononucleosis, leukemia, Hodgkin's disease, carcinoma, myeloma, ectodermosis, pernicious anemia, etc.

Case History

The patient (P. P.) was a 36 year old white male who entered hospital in November 1951. The past history was not significant. For three days prior to admission he had been acutely ill, with dyspnea, orthopnea, and cough productive of viscid blood-tinged sputum.

Physical examination revealed an acutely ill man with severe dyspnea, orthopnea, temperature 38.5°C., respiration 35 per minute, pulse 90 to 100. The lips were cyanotic and the chest findings were those of a bilateral pneumonia. X-ray examination of the chest showed a bilateral parahilar pneumonia. (The heart was normal.) The liver and the spleen were not enlarged. Sputum examination revealed no pneumococci and no tubercle bacilli.

E.S.R. 39 mm./47 mm., Hb. 96 per cent, WBC 4300. The leukocyte differential count was as follows: juveniles 36 per cent, polymorphonuclears 52 per cent, eosinophils 2 per cent, basophils 0.5 per cent, monocytes 1 per cent, lymphocytes 12.5 per cent. The complement fixation test for Q-fever was consistently negative. However, at the time of hospital admission, the cold agglutinins were already positive to 1:512. Wassermann reaction negative. Bilirubin 0.3 mg. per cent. The other chemical determinations done were within normal limits.

The patient was started on penicillin 1.8 million units a day without effect, so that the therapy was changed to aureomycin 3 Gm. daily for eight days, which was accompanied...
by a slight decrease in fever. He once more became febrile and the therapy was changed to terramycin. Fifteen days after his admission to hospital his condition suddenly deteriorated. His temperature once more rose to 38.8 C. and the sedimentation rate was now 77 mm./80 mm. At that time signs of a severe hemolytic reaction became evident with mild icterus, a serum bilirubin of 1.9 mg. per cent, serum iron of 260 μg per cent and the tests for urobilinogen and urobilin in the urine were positive. The cold agglutinins had now risen to 1:1024.

At this time the erythrocyte count was 1.4 millions with marked anisocytosis, polychromasia, and basophilic stippling. The Hb was 27 per cent, color index 0.96, reticulocytes 48.1 per cent. WBC 12,800 with the following differential: juveniles 28 per cent, mature neutrophils 64.5 per cent, eosinophils 2.5 per cent, basophils 0.5 per cent, monocytes 2 per cent, lymphocytes 2.5 per cent; thrombocytes 372,000 (phase contrast method). Prothrombin (Quick) 60 per cent, factor V 50 per cent, factor VII 37 per cent, prothrombin consumption test normal. Bleeding time 2 minutes, coagulation time 5 minutes. Sternal marrow: marked erythrobatic hyperplasia with 330 erythroblasts per 100 white cells. Two days later this had risen to 532 per 100 white cells (see fig. 1). There were many polychromatic erythroblastic elements.

**Special Serologic Investigations**

During the period of severe hemolysis besides the nonspecific cold agglutinins an incomplete cold antibody was also present. In contrast to the usual cold agglutinin whose thermal amplitude does not reach 37 C. the incomplete cold antibodies were found to be active at body temperature. The direct Coombs test performed at 37 C. was strongly positive with dilutions of the antiglobulin serum up to 1:32 (no prozone).

<table>
<thead>
<tr>
<th>Cold agglutinin titer</th>
<th>4 C</th>
<th>22 C</th>
<th>37 C</th>
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<tr>
<td>Incomplete cold antibody titer (indirect Coombs test)</td>
<td>1:512</td>
<td>1:32</td>
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The incomplete cold antibody was thermolabile and could be demonstrated only with the antiglobulin test and not with the albumin-plasma test.

During the acute phase a hemolysin active against normal erythrocytes was demonstrated; this was even more active against trypsinized red cells at 37 C. and at a pH of 6.8 and 7.6.

During the acute phase, the cold hemagglutinin was so marked that it could be demonstrated in vitro without the use of special investigative technics. This phenomenon also rendered blood grouping difficult. In the test tube, heparinized blood agglutinated readily in an ice bath and returned to normal on warming and shaking. In vivo it was not possible to demonstrate this agglutination phenomenon in the skin vessels by the immersion of the hands in ice-water, as has been described by Baumgartner et al.

The change in titer of the complete and incomplete antibodies is shown in figure 1. The complete cold agglutinins showed a great variation even during ACTH therapy. Despite ACTH therapy the titer of the incomplete antibody did not decrease but there was a diminution in the thermal amplitude of the incomplete antibody. The direct Coombs test was, at this time, negative at 37 C. although still positive at 22 C.
The blood group of the patient was O, MM, Rh+ CcDE. Investigation of the erythrocyte mechanical and osmotic fragility was done by Dr. C. Maier. An increase of both the mechanical and the osmotic fragility was noted. Osmotic fragility: initially 0.56 to 0.34 per cent; after 24 hours incubation 0.68 to 0.28 per cent. Mechanical fragility: after 4 hours of rotation 4.9 per cent; after 5½ hours of rotation 5.7 per cent.

**Transfusion Tests**

Transfusion of 300 cc. of blood two months after the acute illness but during the leukopenic phase to a recipient of the same blood group showed a pronounced fall of the leukocytes (after 40 minutes and remaining for 3½ hours) from 5600 to 2300 (910 granulocytes). Control transfusions of a normal individual to the same recipient produced no change. The same is true for the transfusion experiment performed one year later from the convalescent patient (P. P.) to the same recipient (see fig. 2), demonstrating that now this leukopenic factor had disappeared.

**Leukocyte Agglutination**

Tests performed with the patient’s serum and isolated leukocytes of both the same and other blood groups were carried out both during the acute phase and at a later date. The only definite agglutination occurred at 0°C. The method employed was that previously described by Moeschlin and Schmidt.

**Bone Marrow Aspiration**

This is set forth graphically in figure 1. The erythroblasts are enumerated per 100 white cells according to the technic of Rohr. Early in the course of the disease there was a marked hyperplasia of the erythroblastic elements with a normal leukocyte distribution. Later the leukocytes exhibited a distinct shift to the left which after a few weeks returned to normal.

**Therapy and Further Course**

A blood transfusion was of no benefit as the transfused erythrocytes were rapidly hemolyzed. For this reason ACTH therapy was begun (dosage see fig. 1). Despite the previously ominous outlook rapid improvement was now noted and the hemoglobin and erythrocytes rose as shown in figure 1. The temperature during ACTH therapy remained only slightly elevated. In contrast to the hemoglobin and the erythrocytes, the leukocytes and thrombocytes decreased on this therapy. The thrombocytes fell to 50,000 per cu. mm. and then subsequently rose. The leukocyte count steadily decreased and in three weeks had reached a level of 230 per cu. mm. of which only 143 were granulocytes (fig. 1).

The cytopenias of the three cell systems occurred during different time intervals. The erythrocytopenia was followed in turn by thrombocytopenia and leukopenia. As can be seen from figure 1, the leukopenia, occurring just after the severe hemolytic reaction and despite the ACTH treatment, showed a slight but distinct improvement each time cortisone therapy was instituted. However, permanent improvement resulted only after the disappearance of the incomplete antibodies one year later. At this time the leukocytes rose to 7000 per cu. mm.
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During the recovery phase, the cold acid hemolysins of the Dacie type could be demonstrated only at a pH of 6.8 using trypsinized red cells. The optimum temperature for this acid hemolysin was 22 to 30 C.

Investigation of Drug Sensitivity

Following the acute phase of the disease, the patient was tested for sensitivity to Terramycin, Aureomycin, and penicillin. This was done by several determinations of the leukocyte count following the administration of these drugs. As no leukopenia resulted, an allergic, drug-induced granulocytopenia can be excluded in this case. Sulfonamides were never used in this patient.

DISCUSSION

We may summarize briefly the essential points which are also set forth graphically in figure 1: A previously healthy male, 36 years of age, developed a severe primary atypical pneumonia with the occurrence of cold agglutinins in a titer
of 1:1024. On the sixteenth day of the illness, a severe hemolytic anemia suddenly appeared, followed by a severe leukopenia (140 granulocytes) and thrombocytopenia. The severe hemolytic reaction responded well to ACTH therapy, the leukopenia only slightly during the second and third trial of this hormone. The pronounced granulocytopenia returned to normal only after one year. Serologically incomplete antibodies of the cold agglutinin type, active at a temperature of 35 to 37 C., were found in the serum at the height of the hematologic illness as well as antibodies of the complete type. Despite clinical improvement on ACTH the direct and indirect Coombs test remained positive for three months at lower temperatures, only the agglutinations at higher temperatures (35 to 37 C.) becoming negative.

This case of pancytopenia has several aspects of interest which will be discussed.

Serologic Findings

In this patient with a primary atypical pneumonia and a severe acquired hemolytic anemia the cold agglutinins rose to a maximum of 1:1024 and could be demonstrated up to 1:512 even one year after the termination of the hemolytic episode. It is obvious that hemolysis was not induced by these cold agglutinins which were active in a dilution of 1:1024 at a temperature of 4 C. and only at 1:32 at 22 C. By means of the indirect Coombs test, incomplete antibodies (so-called autoantibodies) with a very high thermospectrum, i.e. an activity of up to 1:16 at 22 C. and 1:8 at 37 C., could be demonstrated.

Van Loghem and coworkers33 demonstrated the significant role of high-titered incomplete cold antibodies active at body temperature in a case of acquired hemolytic anemia. Such a finding is a rare event, meanwhile low titered incomplete antibodies are found in most if not all sera from apparently healthy individuals.24

In the acute phase of the disease a cold hemolysin active at a pH of 7.6 to 6.8 and at an optimum temperature of 30 C. for normal erythrocytes, though even more active against trypsin pretreated red cells, could be demonstrated. In the preconvalescent period this hemolysin of the Dacie type remained active only at an acid pH of 6.8 and then only for trypsin pretreated cells. As this hemolysin was only slightly active at 37 C. it is unlikely that it was responsible for the acute hemolytic episode. Opsonins which have been reported to be present in other similar cases2 could not be demonstrated in special investigations carried out through the kindness of Dr. Baumgartner of Interlaken. This is of special interest regarding the etiology of granulocytopenia and will be discussed below.

It is of interest that during and after treatment with ACTH the titer of the cold agglutinins did not change definitely but the indirect Coombs test became negative at 37 C., although still positive at 22 and 4 C. Electrophoretic studies revealed no definite changes in the β- and γ-waves, before and after treatment.

It is still uncertain as to how ACTH produces its effect in acquired hemolytic anemia. It may be that in this case only the titer of the incomplete antibodies active at high temperatures became diminished, but it seems possible to us that the fixation of these special incomplete antibodies on the erythrocytes may be inhibited in some way by ACTH. Other investigators could not find any depression of hemolytic antibodies either during or after effective treatment with
ACTH. Some authors believe that the fixation of the antibody on the erythrocytes corresponds to the adsorption of an anti-virus-antibody on the virus covered surface of the erythrocyte. If this concept finds further experimental support, one might also consider that the action of ACTH could inhibit either the virus fixation on the erythrocytes or perhaps the fixation of the virus antibodies on the virus charged cell surface. Several investigators have demonstrated that ACTH and cortisone have no direct inhibitory effect on antibody formation itself but that they may lead to a secondary depression in antibody formation by the inhibition of the adsorption of the antigen containing substances or by inhibition of their breakdown into specific antigens.

Some authors speak of autoantibodies. As Witebsky recently pointed out at the International Congress of Hematology in Buenos Aires, one has to be very careful with this expression and up to the present day true specific autoantibodies directed against human blood cells (in the sense of Ehrlich) have not been demonstrated in humans. However, it is possible that in some cases the formation of specific autoantibodies occurs secondarily when an enormous destruction of cells to which an abnormal protein of virus is fixed takes place. This fixation of a foreign substance on the blood cells may result in the transformation of the cells into an antigen as has been demonstrated for kidney cells with streptococcal toxins. At present this remains pure speculation for the blood cells and the various forms of immunocytopenia.

Blood group O and acquired hemolytic anemia: Recently Lucia and Hunt have reported a very high predominance of blood group O in their cases of acquired hemolytic anemia. In this connection it may be noted that this case was of group O, MM, Rh+, CcDE. If this finding of Lucia can be confirmed by other investigators, it may be of interest to study whether the production of antibodies in the O group is more marked than in other blood groups, or whether the more frequent occurrence of acquired hemolytic anemias in this group is linked to some other factor.

Sulphonamides which may lead to severe hemolytic anemias had never been used in this patient.

Immunosgranulocytosis and Immunotherbocytopenia

The leukopenia in this case began about ten days after the onset of the severe hemolysis and was nearly complete four weeks later (140 granulocytes of a total of 230 leukocytes!) (see fig. 1). The thrombocytopenia which was much less severe (minimum 50,000 platelets) started simultaneously with the leukopenia but persisted only for about two weeks, while the leukopenia persisted at very low levels (see fig. 1) for about one month and remained at about 2000 during the following year. Evans and coworkers were the first authors to draw attention to the occurrence of immunotherbocytopenia in acquired hemolytic anemia. However agranulocytosis has not been previously described in this disease.

It is very puzzling that this leukopenia and thrombocytopenia occurred despite nineteen days of intensive ACTH treatment which had been instituted earlier (see fig. 1) because of the severe hemolytic reaction. Nevertheless, cortisone administration for twelve days, two and three months later, reversed the
leukopenia to nearly normal values on both occasions, but the levels dropped again as soon as the cortisone was discontinued. This phenomenon is difficult to explain, but it seems probable that the causative agent of the cytopenia was too strong initially to be inhibited despite intensive ACTH treatment, but that after a longer period, the slow decrease in the amount of this cytopenic factor made it possible for cortisone to show a distinct inhibiting effect on it.

As to the nature of this cytopenia inducing factor, it seems logical to relate it to the same agents which produced the hemolysis, i.e. to an agglutinin. As we have reported elsewhere, we could demonstrate that agranulocytosis of so-called drug-anaphylactic origin (amidopyrine) is due to the occurrence of an agglutinating factor which leads to an intensive agglutination of the leukocytes. The transfusion of 300 cc. blood (three hours after the administration of 0.3 Gm. amidopyrine) from an amidopyrine sensitive patient led to a severe leukopenia in the recipient. In vitro, the serum of this patient produced agglutination of his own and foreign leukocytes belonging to the same blood group.

The presence of agglutinins for the leukocytes in this case could, unfortunately, not be proven by direct methods in the patient's serum. They were, however, demonstrated indirectly two months after the acute illness but still during the leukopenic phase by the transfusion of 300 cc. of blood to another patient of the same blood group (fig. 2). This recipient showed a pronounced fall of the leukocytes from 5600 to a minimum of 2300 leukocytes with 910 granulocytes after 40 minutes which slowly returned to normal over a six hour period, while the control transfusion of 300 cc. of normal blood produced no depression of the leukocyte count. One year later, no depressive effect was produced on the

Fig. 2.—Left: Transfusion of 300 cc. blood, two months after the acute illness but still during the leukopenia phase, showed a pronounced fall of the leukocytes (remaining for 3½ hours) from 5600 to 2300 (910 granulocytes). Control transfusion of normal blood to the same recipient produced no change (interrupted line). Right: Transfusion experiment performed one year later from the reconvalescent patient to the same recipient produced no distinct change.
leukocytes of the same recipient either during or after transfusion of 300 cc. blood from the recovered patient. Various attempts to demonstrate complete antibodies for leukocytes in the patient's serum failed to give a distinct positive result as in the case of amidopyrine sensitivity and in our previous work in testing the leukocyte blood groups through cross matching, using the same technic as described in that paper. However intravenous injection of 2 cc. serum of this patient into three rabbits led also to a transient leukopenia during three to six hours, which could not be demonstrated in the controls.

As the serologic investigation with erythrocytes proved the presence of incomplete antibodies, one may assume that the same may be true for the leukocytes and the platelets. However, no direct serologic proof for the presence of these incomplete antibodies, i.e. of incomplete leukocyte agglutinins, could be found aside from the above transfusion experiment (fig. 2). These experiments probably failed because of the exceptional liability to damage and tendency to spontaneous agglutination of the isolated leukocytes, as the cells had to be washed several times with saline solution before the addition of Coombs antiglobulin serum. In all of these experiments, agglutination of the leukocytes occurred during the washing of the cells, so that the final result could not be evaluated. We are at present at work on this problem and perhaps an accurate method for the demonstration of incomplete antibodies for leukocytes in other cases may be forthcoming.

The destruction of the agglutinated leukocytes probably takes place principally in the lungs. In experimentally reproduced agranulocytosis we could demonstrate the agglutinated leukocytes trapped in the lung capillaries.

Bone Marrow Changes

On the basis of our experimental findings in aminopyrine (Pyramidon) agranulocytosis, it is believed that the changes in the marrow are brought about by a precipitate depletion and exhaustion of the bone marrow due to the enormously increased peripheral destruction of the granulocytes rather than to an actual inhibition of the marrow. The changes in the bone marrow take a step-wise course, first leading to a disappearance of the mature forms (metamyelocytes and ripe myelocytes), then, with more intense and prolonged peripheral destruction of the leukocytes, the myelocytes disappear, and finally, in severe cases, the promyelocytes and myeloblasts disappear, leaving only the reticulum cells.

This conception of the bone marrow changes as a secondary phenomenon to the primary enormously increased peripheral destruction could be further demonstrated by experimental work in the production of agranulocytosis by means of repeated injections of an antileukocytic serum.

We also believe that in this case the appearance of agglutinins led to an increased destruction of leukocytes by agglutination in the peripheral blood. In the beginning, the bone marrow was able to compensate for the increased demand by an increased production (see first marrow examination), but later as the bone marrow could no longer compensate fully for the increased peripheral destruction a shift to the left, i.e. a predominance of the immature forms in the marrow, occurred (see fig. 1, marrow nos. 2 and 3).
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Some other possibilities of the mechanism of the leukopenia may be briefly discussed here. A drug sensitivity or toxicity can be ruled out by the negative result obtained on testing the patient with the drugs which had been employed. The persistence of the leukopenia for one year also is against a toxic or allergic origin. So-called hypersplenism can be excluded by the absence of splenomegaly. The leukocytopenic factor demonstrable by transfusion and the persistence of immunologic changes (positive direct and indirect Coombs test) during the twelve months of leukocytopenia are also against this interpretation.

Jordan and coworkers recently referred to a case of paroxysmal cold hemoglobinuria in which a marked leukopenia (75 to 80 per cent) occurred at the height of maximum hemolysis. It may also be that in Jordan's case the mechanism of leukopenia could be explained on the basis of agglutination of the leukocytes by complete or incomplete antibodies. Phagocytosis of erythrocytes could not be demonstrated in our case despite a careful search of the blood smears during and after the hemolytic episodes, as well as the special examination of the opsonic effect of the serum by Dr. Baumgartner.

In conclusion considering these various possibilities of leukopenia-promoting factors we may say that the various facts in this case suggest an immunologic basis for the leukopenia and probably also for the transient thrombocytopenia. Complete agglutinins have been demonstrated to be responsible for many forms of idiopathic thrombocytopenias and incomplete antibodies have been found recently.

Therapy of Immunopancytopenia

ACTH therapy probably saved the life of this patient during his severe hemolytic reaction and produced dramatic improvement, as described in other patients with acquired hemolytic anemia. Sometimes this treatment must be followed by splenectomy to obtain sustained improvement. Blood transfusions may be contraindicated in these cases as they sometimes lead to a severe exacerbation by the production of instantaneous hemolysis of the transfused erythrocytes.

SUMMARY

In a case of primary atypical pneumonia (blood group O), incomplete antibodies of the cold agglutinin type with a very wide thermal spectrum (35 to 37 C.) led to a severe immunopancytopenia in the form of severe hemolytic anemia, agranulocytosis, and thrombocytopenia.

It is obvious that hemolysis was not induced by cold agglutinins which were active 1:1024 at 4 C. and only 1:32 at 22 C. The indirect cold antibodies which were probably responsible for the hemolysis which occurred were thermolabile (1:16 at 22 C., 1:8 at 37 C.) and could be demonstrated only in the antiglobulin plasma test. During the acute phase, too, a hemolysin of the Dacie type active for normal erythrocytes, but even more active for trypsinized cells, at 37 C. and at a pH of 6.8 and 7.6 could be demonstrated. The severe hemolysis could be stopped by ACTH treatment but the titer of the complete and incomplete cold antibodies showed no distinct change and the direct and indirect Coombs
test remained positive for a long time. However, there was a distinct diminution of the thermal amplitude of the incomplete antibodies.

A severe agranulocytosis (140 granulocytes) developed which could be improved each time by cortisone. However, permanent improvement resulted only after the disappearance of the incomplete antibodies one year later.

A leukopenic factor could be demonstrated by transfusion of 300 cc. blood to a recipient of the same blood group producing a pronounced fall in the granulocytes of from 4200 to 910. Control transfusions from a normal individual to the same recipient showed no change and the same is true for the transfusion experiment performed one year later from the now cured patient to the same recipient. Leukocyte agglutination tests were negative, but it is presumed that agglutinins of the incomplete type may have been present. Opsonins could not be demonstrated. The thrombocytopenia never descended below 50,000.

The bone marrow showed a distinct shift to the left, i.e. a predominance of immature forms. On the basis of our previous experimental work (amidopyrine agranulocytosis) it is believed that the changes in the marrow are brought about by a depletion and exhaustion of the bone marrow due to the enormously increased peripheral destruction of the granulocytes by agglutination rather than to an actual inhibition of the marrow.

The relation of this immunoleukopenia in our previous findings to the occurrence of leukocyte agglutination in agranulocytosis of allergic origin is discussed. Agranulocytosis and leukopenia may be produced on an immunologic basis in many other cases and thus some form of agranulocytosis may be related to the mechanism of erythrocyte destruction in acquired hemolytic anemia and to the agglutination of thrombocytes in essential thrombocytopenia on an immunologic basis.

**Summario in Interlingua**

In un caso de primari pneumonia atypic (del gruppo sanguinee O) incomplete anticorpos del typo agglutininia frigide con un largissime spectro thermal (35 a 37 C.) duceva a sever immunopancytopenia in le forma de sever anemia hemolytic, agranulocytosis, e thrombocytopenia.

Il es evidente che hemolyse non eseva inducita per agglutininias frigide, proque istos eseva active a un titro de 1:1024 a 4 C. e solmente a un titro de 1:32 a 22 C. Le indirecte anticorpos frigide que probablemente eseva responsable pro le hemolyse eseva thermolabile (1:16 a 22 C., 1:8 a 37 C.), e poteva esser demonstrate solmente in le tests a plasma antiglobinie. Etiam durante le phase acute il eseva possibile demonstrar un hemolysinsa del typo Dacie. Isto eseva active contra erythrocytas normal. Sed contra cellulas trypsinate, a 37 C. e a un pH de 6.8 e 7.6, illo eseva mesmo plus. Le sever hemolyse poteva esser arrestate per tractament a ACTH, sed le titro del anticorpos frigide complete e incomplete monstrava nullo cambio notabile, e le tests Coombs, directe e indirecte, remaneva positive durante un longe tempore. Nonobstante, il hava un marcate diminution in le amplitude thermal del anticorpos incomplete.

Se disveloppava un sever agranulocytosis (140 granulocytas). Cata vice illo poteva esser mitigate per cortisona, sed melioramento permanente resultava solo post le disparition un anno plus tarde del anticorpos incomplete.
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Le existencia de un factor leucopenico es缴纳 demonstrated per la transfusion de 300 cc. de sanguine del patiente a un recipiente del mesme gruppo sanguinee.

Isto resultava in a marcate diminucion del granulocytas (ab 4200 a 910). Transfusiones de controlo ab un individuo normal al mesme recipiente resultava in nullo cambiamento. Le mesmo occurriva etiam in un transfusion un anno plus tarde ab le patiente, nunc restablite, al mesme recipiente. Tests del agglutination de leucocytas dava resultatos negative, sed il es a presumer que agglutinis del typo incomplete pote haber essite presente. Opsoninas non es缴纳 demonstrabile. Le thrombocytopenia nunquam descendeva infra 50.000.

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