Abnormal Adherence-Related Functions of Neutrophils, Monocytes, and Epstein-Barr Virus–Transformed B Cells in a Patient With C3bi Receptor Deficiency

By E. Stephen Buescher, Thelma Gaither, Jayasree Nath, and John I. Gallin

We evaluated a 3-year-old female patient with leukocytosis, recurrent infections, severe periodontal disease, and a history of delayed separation of the umbilical stump. This patient’s polymorphonuclear leukocytes (PMNs) had normal membrane depolarization responses, normal oxygen metabolism, normal granule secretion responses, normal bactericidal activity, and normal C3b rosetting. However, by fluorescent cell analysis and C3bi rosetting, it was determined that her cells lacked the C3bi receptor. In addition, the patient’s PMNs showed markedly abnormal chemotaxis, adherence, and aggregation responses, and partial abnormalities were detected in PMN spreading and phagocytosis. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis revealed that the subject’s neutrophil cytoplasts were missing a 180,000-dalton moiety. Her monocytes also had defective chemotaxis and failed to adhere and grow normally in culture. Epstein-Barr virus–transformed B cells from the patient lacked an aggregation response to phorbol myristate acetate. Laboratory and clinical evaluations of this patient’s mother showed no abnormalities. These studies demonstrate that C3bi receptor deficiency can be associated with functional abnormalities in multiple myeloid cells and that the absence of C3bi receptor is associated with abnormal adherence-related functions of these cells.

RECENT REPORTS have noted a number of functional abnormalities in phagocytes in a group of patients with the clinical profile of delayed separation of the umbilical stump, recurrent infections, leukocytosis, and severe periodontal disease. Abnormal polymorphonuclear leukocyte (PMN) adherence, spreading, and chemotaxis have been the most frequently reported deficiencies and are associated with missing surface antigen(s) of about 110,000 to 180,000 daltons. Bactericidal activity was normal in all but one patient. Another patient was shown to be antigenically deficient in the C3bi receptor, although functionally, the receptor was present. A young female patient was chosen for extensive evaluation because of her typical clinical picture of leukocytosis, periodontal disease, recurrent infections, and a history of delayed separation of the umbilical stump. We found a gross deficiency in her PMN chemotaxis, adherence, and aggregation responses in association with a complete antigenic and functional deficiency in the C3bi receptor. Her monocytes lacked antigenic C3bi receptor activity, had defective chemotactic responsiveness, and failed to adhere and grow normally in culture. Epstein-Barr virus–transformed B cells (B cell lines) also failed to aggregate in response to a soluble stimulus in this patient. These data suggest that the C3bi receptor plays an important role in myeloid cell adherence, chemotaxis, and aggregation and that functional abnormalities exist in at least three myeloid cell lines in patients with this disease.

CASE HISTORY

The subject of this study, whose parents were first cousins, weighed 9 lb at birth, and her mother had experienced a normal full-term pregnancy. Our subject’s neonatal period was remarkable for mild respiratory distress shortly after birth and the appearance of fever and leukocytosis of unknown origin during the first week of life. The leukocytosis has continued to be a prominent aspect of her disease. At age 4 weeks, the child’s umbilical stump was surgically removed because of a failure to separate. This procedure was followed by poor operative wound healing. Because of the persistent fever, at age 3 months the child was started on trimethoprim-sulfamethoxazole, with subsequent episodes of unexplained fever occurring less frequently. At age 6 months she had a left breast abscess that was incised and drained. Minimal purulence was noted at the time of the procedure and cultures were negative. During her first year the patient experienced recurrent cutaneous infections; she was also hospitalized for an evaluation of abdominal pain and diarrhea, which did not result in a diagnosis. Over this period the patient consistently had a total WBC count of 12,000 to 18,000/μL and was prone to developing inflammation at sites of insignificant cutaneous trauma, such as lancet blood-drawing sites. At age 6 months she required an extensive incision and drainage procedure on her right quadriceps femoris to evacuate a sterile abscess caused by repeated intramuscular antibiotic injections. With the eruption of
Cappel Laboratories, Cochranville, Pa. Monoclonal antibody to the and A23 187 were from Sigma Chemical Co. St Louis. Fluorescein-anine (f-Met-Leu-Phe), dimethyl sulfoxide (DMSO), cytochrome chased from Hazelton-Dutchland Laboratories, Denver, Pa. Nitro-anced salt solution (HBSS) with or without Ca and Mg streptomycin; 2 mM L-glutamine; Gey's balanced salt solution with adherence of anti-CR, (3D-9) are described elsewhere. Monoclonal antibody OKM1 was from the C3bi receptor. Monoclonal antibody labeled F(ab')2 goat anti-mouse immunoglobulin antibody was from the C3b receptor. Evaluation. The method of Boyum. PMN functional assays were carried out by the method of Gallin et al. PMNs and mononuclear cell fractions were prepared from fresh, heparinized whole blood from the patient or normal volunteers by centrifugal differential centrifugation. PMNs and mononuclear cell fractions were prepared from fresh, heparinized whole blood from the patient or normal volunteers by centrifugal differential centrifugation. PMNs and mononuclear cell fractions were prepared from fresh, heparinized whole blood from the patient or normal volunteers by centrifugal differential centrifugation. PMNs and mononuclear cell fractions were prepared from fresh, heparinized whole blood from the patient or normal volunteers by centrifugal differential centrifugation. PMNs and mononuclear cell fractions were prepared from fresh, heparinized whole blood from the patient or normal volunteers by centrifugal differential centrifugation. PMNs and mononuclear cell fractions were prepared from fresh, heparinized whole blood from the patient or normal volunteers by centrifugal differential centrifugation. PMNs and mononuclear cell fractions were prepared from fresh, heparinized whole blood from the patient or normal volunteers by centrifugal differential centrifugation.
1640 with supplemental penicillin, streptomycin, glutamine, and 5% human AB serum (RPMI PSG5). For some experiments, monocytes were identified by nonspecific esterase staining, and monocyte numbers in patient and control cultures were equalized. Mononuclear cell fractions were then cultured in 75-cm² flasks and maintained in culture by pouring off old media and replacing fresh RPMI PSG5 weekly. Cultured monocyte size was measured as described earlier for PMN spreading.

RESULTS

PMN Monoclonal Antibody Staining

Using the commercially available monoclonal antibodies OKM-1, MAC-1, and Leu-15, we found that the patient's PMNs lacked the surface antigen recognized by these antibodies (Fig 1). The patient's monocytes were tested by fluorescent cell analysis for OKM1 antigen and were also found to lack this antigen (data not shown). PMNs and monocytes from the patient's mother and father were found to carry the OKM1 antigen. B cells from normal individuals did not carry the OKM1 antigen.

In experiments to evaluate whether there was a stimulatable pool of OKM-1 antigen in patient PMNs, as has recently been reported in normal cells, OKM1 antibody binding was assessed in patient and control cells after stimulation of cells with either f-Met-Leu-Phe (10⁻⁶ mol/L) or PMA (1 ng/mL) (Fig 2). In normal cells, OKM1 surface antigen increased after stimulation by these soluble factors; in patient cells, negligible responses to these secretory stimuli were observed. These data suggest that the patient's cells lack an intracellular pool of OKM1 antigen. This was indeed true, for when cells were permeabilized with acetone and then stained with fluorescent OKM1 antibody, whereas normal cells stained bright, the patient cells were dull (not shown).

Aggregation

The patient's neutrophils lacked aggregating responses to the soluble stimuli PMA (20 ng/mL) and f-Met-Leu-Phe (10⁻⁶ mol/L) (Fig 3). A small reversible wave of increased light transmission was seen after the addition of PMA to both patient and control PMNs, but the patient's cells did not proceed with aggregation as the control cells did after this early effect. EBV-B cells from the patient were also shown to lack aggregating responses to PMA (Fig 4). EBV-B cells from controls and from patients with other phagocytic cell disorders (chronic granulomatous disease, Chédiak-Higashi syndrome) aggregated in response to PMA (20 ng/mL) but not in response to either f-Met-Leu-Phe (10⁻⁶ mol/L) + cytochalasin B (5 μg/mL) or A23187 (10⁻⁶ mol/L) + cytochalasin B (5 μg/mL). Both PMNs and EBV-B cells from the patient's mother aggregated normally.

Phagocyte Locomotion

The patient's in vitro PMN migration toward buffer, endotoxin-activated serum, f-Met-Leu-Phe (2 x 10⁻⁶ mol/L), and casein (5 mg/mL) were all markedly depressed (Table 1). In addition, her PMNs failed to respond to f-Met-Leu-Phe as a chemoattractant, over a dose range of 2 x 10⁻¹⁰ mol/L to 2 x 10⁻⁷ mol/L. The patient's PMNs also had a severe defect in chemoki-
CONTROL

MINUTES

Fig 3. PMN aggregation responses to f-Met-Leu-Phe (10^6 mol/L) and PMA (20 ng/mL). Abscissa shows time in minutes; ordinate shows change in light transmission.

netic responses to 10^10 to 10^6 mol/L f-Met-Leu-Phe (not shown). Monocyte chemotaxis in our subject was similarly depressed to the same three stimuli (data not shown). In vivo accumulation of the patient’s PMNs and monocytes at Rebuck skin windows was not detected when assessed by ability of cells to adhere to glass coverslips using a 24-hour skin window procedure. The patient’s mother had a normal Rebuck skin window response.

PMN Membrane Depolarization and Surface Charge

The basal fluorescence of the membrane potential dye di-0-C5(3) was normal, suggesting that the resting membrane potential of the patient’s PMNs was normal. In addition, PMN membrane depolarization responses to f-Met-Leu-Phe (10^6 mol/L) and PMA (20 ng/mL) were also normal. Resting PMN surface charge was found to be normal in the patient compared with a concurrently run normal and the normals previously published by our laboratory\(^2\) (1.59 ± 0.07 v 1.45 ± 0.04 μm/s/V/cm for control v patient), and normal decreases in surface charge after degranulating stimuli were also observed (not shown).

PMN Adherence and Spreading

In two experiments, PMN adherence to glass wool and nylon wool were found to be markedly abnormal in the patient. Whereas 43% and 41% of normal cells adhered to glass wool and nylon wool, 8% and 0% of the patient’s cell adhered. However, the area of spread PMN on a glass slide was observed to be no different from that of the control subjects on four occasions (Fig 5, top). Visual examination of the patient’s spread PMN after five minutes showed them to have extended small pseudopods; however, most cells did not flatten as they spread, but had a central area of highly refractile cytoplasm (Fig 6A and B). As a consequence, the cells of our subject did not change their shape normally as they spread, and shape factor measurements (ratio of the minor axis to the major axis in each cell)\(^1\) showed that despite normal spread cell areas, the patient’s cells remained more rounded than those of the controls (Fig 6B).

PMN Rosetting, Phagocytosis, and Bactericidal Activity

PMN rosetting with certain selectively opsonized sheep RBCs as targets was abnormal in our patient (Table 2). Her rosetting with EAC3b particles was

---

Table 1. Neutrophil Chemotaxis

<table>
<thead>
<tr>
<th>Stimulus</th>
<th>Control</th>
<th>Mother</th>
<th>Patient†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buffer</td>
<td>20.3 ± 1.5</td>
<td>19.0 ± 0.0</td>
<td>12.8 ± 0.5</td>
</tr>
<tr>
<td>Activated serum</td>
<td>37.0 ± 2.9</td>
<td>30.5 ± 1.5</td>
<td>14.8 ± 0.5</td>
</tr>
<tr>
<td>Casein (5 mg/mL)</td>
<td>36.0 ± 3.8</td>
<td>35.0 ± 7.0</td>
<td>19.0 ± 2.7</td>
</tr>
<tr>
<td>f-Met-Leu-Phe</td>
<td>2 × 10^6 mol/L</td>
<td>36.5 ± 2.6</td>
<td>31.0 ± 3.0</td>
</tr>
</tbody>
</table>

*Mean ± SEM distance migrated into 3-μm-pore cellulose nitrate filters after 45 minutes, four experiments (patient and control); mother, average of two experiments.
†P < 0.05 v normal control subjects.
Fig 5. (A) PMN spreading on glass slides. Abscissa shows time in minutes; ordinate shows spread cell area in square microns. Control data are shown as mean ± SEM; four experiments. (B) PMN shape factor during spreading. Abscissa shows time in minutes; ordinate shows shape factor (ratio of minor axis to major axis). Data are the average of two experiments.

Fig 6. (A) Control PMNs after five minutes of spreading on glass slide; cells have flattened and extended pseudopods. (B) Patient cells after five minutes of spreading; cells have extended pseudopods, but retain a central area of highly refractile cytoplasm.

Table 2. Patient Cell Rosetting and Phagocytosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Normal</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>% PMN rosetting with:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EAC3bi*</td>
<td>63</td>
<td>20</td>
</tr>
<tr>
<td>EAC3bi + anti-CR,</td>
<td>41</td>
<td>0</td>
</tr>
<tr>
<td>EAC3b†</td>
<td>27</td>
<td>37</td>
</tr>
<tr>
<td>EAC3b + anti-CR,</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>% PMN phagocytosing with:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EAC1.4 + IgG</td>
<td>37</td>
<td>0</td>
</tr>
<tr>
<td>EAC3b</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>EAC3b + IgG</td>
<td>65</td>
<td>2</td>
</tr>
<tr>
<td>EAC3bi</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>EAC3bi + IgG</td>
<td>56</td>
<td>3</td>
</tr>
<tr>
<td>Whole serum + Candida</td>
<td>64.0 ± 12.3‡</td>
<td>46.5 ± 12.6§</td>
</tr>
</tbody>
</table>

*Approximately 75,000 C3bi bound per cell; rosetting was studied with suspended PMNs.
†Approximately 50,000 C3b bound per cell; rosetting was studied with adhered PMNs.
‡Data are representative results from two experiments.
§Mean ± SEM; four experiments; P > 0.05.

normal. Addition of anti-C3b receptor antibody (anti-CR, ) to the patient’s cells to block the C3b receptor caused her C3b rosetting to fall to zero. With C3bi-coated particles, similar findings were observed, ie, without anti-CR, antibody, the patient had some C3bi rosetting, but with antibody blockade of the C3b receptor, her C3bi rosetting fell to nearly zero. In contrast with normal PMNs, anti-CR, caused minimal inhibition of rosette formation with EAC3bi.

Phagocytosis of selectively opsonized targets was also abnormal in the patient’s PMNs, as shown in Table 2. Additionally, there was poor PMN phagocytosis of sheep RBCs that were opsonized with IgG and the complement components C1, C4, C3b, and C3bi in the combinations shown. However, in four experiments with whole, heat-killed C albicans opsonized with 50% fresh whole serum, our patient’s PMN phagocytosis was not significantly different from that of the control PMN by paired sample analysis. In a separate experiment, the patient’s PMNs were found to kill serum-opsonized Staphylococcus aureus normally (mean ± SEM control vs patient percentage of bacterial survival at 20 minutes, 21.9 ± 4.2 vs 9.9 ± 1.6; at 45 minutes, 6.9 ± 1.0 vs 10.6 ± 2.7; at 90 minutes, 2.8 ± 0.71 vs 7.7 ± 1.6), supporting the observation that the patient’s PMNs are capable of normal phagocytosis of particles opsonized with whole serum.

PMN Oxygen Metabolism and Granule Secretion

The PMN oxygen metabolism of our patient was examined with the PMA-stimulated NBT test and by ferricytochrome c reduction by PMNs stimulated with PMA (20 ng/mL), f-Met-Leu-Phe (10⁻⁶ mol/L) or opsonized C albicans. The patient’s cells stimulated with PMA reduced NBT normally (data not shown).
Table 3. PMN Degranulation Responses

<table>
<thead>
<tr>
<th>Controls</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>f-Met-Leu-Phe (10⁻⁸ mol/L)</td>
<td>PMA (20 ng/mL)</td>
</tr>
<tr>
<td>Lysozyme</td>
<td>35.3 ± 8.8</td>
</tr>
<tr>
<td>Myeloperoxidase</td>
<td>20.1 ± 7.7</td>
</tr>
<tr>
<td>β-glucuronidase</td>
<td>16.9 ± 5.7</td>
</tr>
<tr>
<td>Vitamin B₁₂-binding protein</td>
<td>19.3 ± 4.5</td>
</tr>
<tr>
<td>Candida</td>
<td>34.8 ± 13.5</td>
</tr>
<tr>
<td>f-Met-Leu-Phe (10⁻⁶ mol/L)</td>
<td>PMA (20 ng/mL)</td>
</tr>
<tr>
<td>Lysozyme</td>
<td>16.4 ± 5.6</td>
</tr>
<tr>
<td>Myeloperoxidase</td>
<td>18.1 ± 5.8</td>
</tr>
<tr>
<td>β-glucuronidase</td>
<td>38.1 ± 12.0</td>
</tr>
</tbody>
</table>

Responses are expressed as mean ± SEM percentage of total cell content, three experiments. ND, not done.

*10 Candida: 1 PMN. Data are expressed as average percentage of total cell content, two experiments.

When stimulated with PMA, f-Met-Leu-Phe, or opsonized C. albicans, the patient's cells also reduced cytochrome c to the same degree as those of the controls (mean nmol superoxide/10⁶ PMN/10 min, control v patient; 10⁻⁷ mol/L f-Met-Leu-Phe, 1.1 v 4.3; 10⁻⁶ mol/L f-Met-Leu-Phe, 2.14 v 1.94; 20 ng/mL of PMA, 22.0 v 15.3; opsonized C. albicans, 20.4 v 19.0). In our patient, cell secretion of the primary granule contents (myeloperoxidase, β-glucuronidase, and lysozyme) and the secondary granule contents (lysozyme and vitamin B₁₂-binding protein) were normal in response to PMA, f-Met-Leu-Phe, and opsonized C. albicans (Table 3).

**SDS-PAGE**

Neutrophilic cytoplasts of the patient and the controls were analyzed by SDS-PAGE with and without proteolytic inhibitors. Without proteolytic inhibitors, the patient and her mother were noted to be missing a PMN cytoplasm protein of 110,000 daltons. In each of three experiments repeated with proteolytic inhibitors, the 110,000-dalton band was less obvious in the controls, and examination of the high-molecular-weight bands showed a protein of slightly less than 200,000 daltons to be missing from the patient’s cytoplasts (Fig 7). In the mother, this protein band was present, although possibly in reduced amounts.

**Monocyte Cultures**

Mononuclear cell fractions from Hypaque-Ficoll gradients were cultured and observed for two weeks to assess adherent cell survival and morphology. The monocytes of the patient adhered poorly to plastic tissue culture flasks with resultant poor survival of her monocytes as adherent cells. Serial measurements of the surviving patient and control monocyte areas over two weeks is shown in Fig 8. The control cells increased their two-dimensional area approximately tenfold over 16 days of observation; the patient’s cells increased...
deficiency is associated with a lack of aggregating specifically to the C3b receptor on the patient's PMNs. C3bi receptor. As shown in Table 2, EAC3bi formed clonal antibody known as 60.3, Beatty et al reported gen(s). In one study, in which MO-1 antibody was used, Dana et al reported the antigenic deficiency, but were shown to be deficient in specific surface anti-

cles of recurrent infections, leukocytosis, and delayed separation of the umbilical stump were shared by our patient and five others. Severe periodontal disease was noted in our patient and three others; in only one patient was it specifically stated that periodontal disease was not present. A number of these patients were evaluated intensively, and phagocytic cell functional studies usually showed severe abnormalities in in vitro adherence and/or chemotaxis, as our patient did, as well as aggregation when it was examined. Bactericidal activity was normal in all but one of the patients in which it was studied. However, other commonly tested phagocytic cell functional parameters, such as enzyme secretion, oxygen metabolism, and phagocytosis, were variably reported as normal or abnormal, depending on the stimulus used. PAGE of PMN surface membrane from these patients was usually reported as abnormal because of missing components of about 110,000 to 180,000 daltons. In two reports, in which monoclonal antibodies were used to examine PMNs and monocyte surface antigens, cells from the patients were shown to be deficient in specific surface antigen(s). In one study, in which MO-1 antibody was used, Dana et al reported the antigenic deficiency, but functional presence, of the C3bi receptor in their patient. In the second study, with a different monoclonal antibody known as 60.3, Beatty et al reported the absence of an antigen on PMNs, monocytes, and lymphocytes of their patient, but whether the antigen is the C3bi receptor was not stated.

In our patient we found no evidence of antigenic and functional activity in the OKM1 antigen. The OKM1, MO-1, and MAC-1 antigens on PMNs are all felt to identify the same moiety, which is functionally the C3bi receptor. As shown in Table 2, EAC3bi formed rosettes with PMNs from our patients at one-third the level shown for control PMNs. With the patient’s PMNs, this activity was completely blocked by monoclonal antibody to the C3b receptor, whereas EAC3bi rosetting with control PMNs was inhibited only 35% by the antibody, indicating that EAC3bi bound exclusively to the C3b receptor on the patient’s PMNs. Interaction of C3bi with the C3b receptor has been reported by others. This antigenic and functional deficiency is associated with a lack of aggregating responses to the soluble stimuli f-Met-Leu-Phe and PMA. Interestingly, when PMA is used to stimulate aggregation, both the control and the patient cells showed a rapid, short-lived response leading to a brief increase in light transmission. In normal cells this early wave is often obscured by the following aggregation wave, but with the patient’s cells this early response is easily seen because of the lack of subsequent aggregation. What causes this early wave is unknown, but it may represent the same phenomenon that Yuli and Snyderman, examining normal PMNs with a specially modified aggregometer, hypothesized was caused by an initial event in stimulus-response coupling. In addition to the severe abnormality in aggregation, our patient’s cells also had severely abnormal adherence and chemotaxis, and a partial abnormality in PMN spreading and phagocytosis (phagocytosis of selectively opsonized particles). The clinical significance of her phagocytic abnormality remains to be delineated, however, in light of the patient’s normal bacterial killing activity. Her ongoing clinical problems of recurrent infections and severe periodontal disease are probably related to the severe functional defects in aggregation, adherence, and chemotaxis of her phagocytes.

It is reasonable to speculate that her persistent leukocytosis is a reflection of these abnormalities, in that it is likely, but not yet confirmed, that her cells are not capable of margination. We found our patient’s PMN spreading to be quantitatively, but not morphologically, normal. With the use of plain glass slides as the substratum, our patient’s cells appeared to attach and extend pseudopods, but her cells did not proceed to flatten out as normal cells do; the patient’s cells retained a centrally located area of heaped up, highly refractile cytoplasm. Similar morphology was frequently seen in cultured monocytes from the patient. Other investigators have also reported abnormal spreading in their patients’ cells, but they noted an absence of spreading. Whether these differences are due to technique (plain or endotoxin-coated slides) or to inherent differences in the patients remains to be seen.

We found oxygen metabolism and degranulation in our patient’s cells to be normal, both with the soluble stimuli, f-Met-Leu-Phe and PMA, and with the particulate stimulus, opsonized C albicans. One patient with antigenic C3bi receptor deficiency was reported to have normal oxygen metabolism and degranulation in response to soluble stimuli, but abnormal responses to particulate stimuli; unfortunately, bacterial killing results were not reported for that patient. As oxygen metabolism and degranulation are important facets of microbial killing, bacterial killing in such a patient
could easily be predicted to be abnormal. In our patient with functional and antigenic C3bi receptor deficiency, we found no significant abnormalities in soluble- or particulate-stimulated oxygen metabolism or degranulation.

It would be easy to assume that the functional and antigenic deficiency of the C3bi receptor (OKM1 antigen) in our patient underlies all of her abnormalities, but our results with her EBV-B cells suggest that her abnormality(s) are more complex. We could not identify the OKM1 antigen on normal EBV-B cells with fluorescent cell analysis, yet normal EBV-B cells could be shown to aggregate in response to PMA, suggesting that this response is independent of the antigen recognized by the OKM1 antibody. The patient's EBV-B cells did not aggregate in response to PMA, showing that her defect extended to other than her phagocytic leukocytes. A recent report suggests that the mouse antigens LFA-1 and MAC-1, antigens important in lymphocyte-surface interactions, share a nearly identical subunit. Perhaps such a common subunit is also shared between the PMN (C3bi receptor) and the EBV-B cell aggregation-controlling moiety, and the absence of this subunit in our patient underlies the abnormalities seen in her PMN monocytes and EBV-B cells. The monoclonal antibody 60.3, which was deficient in the leukocytes of a similar patient reported by Harlan et al, may identify such a subunit. The possibility that a subunit of the C3bi receptor is essential for adherence-related functions of myeloid cells is interesting speculation currently under investigation.

ACKNOWLEDGMENT

The authors thank Nancy Mounessa and Julia Metcalf for their expert technical assistance. Dr John O'Shea for the monoclonal antibody Leu-15 and for performing experiments with acetone permeabilized cells, and Dr Michael M. Frank for many helpful suggestions.

NOTE ADDED IN PROOF

At age 5 years (March 1985), the patient was hospitalized at NIH and transferred to Washington's Children's Hospital National Medical Center with severe stridor, fever, and laryngoscopic evidence of glottic edema and eschar on the left vocal cord. Cultures were positive for E coli. The patient responded to intravenous antibiotics and is now doing well.

REFERENCES

3. Harlan JM, Senecal FM, Taylor RF, Schwartz BR, Beatty PG, Ochs HD: The neutrophil membrane glycoprotein recognized by the monoclonal antibody 60.3 is required for phorbol ester-induced neutrophil adherence and aggregation. Clin Res 32:496a 1984 (abstr)
8. Dana N, Todd RF, Pitt J, Springer TA, Arnaout MA:


31. Frank MM, Gaither TA: Evidence that rabbit IgG haemolysis is capable of utilizing guinea pig complement more efficiently than rabbit IgM haemolysis. Immunology 19:975, 1970


Abnormal adherence-related functions of neutrophils, monocytes, and Epstein-Barr virus-transformed B cells in a patient with C3bi receptor deficiency

ES Buescher, T Gaither, J Nath and JI Gallin

Updated information and services can be found at:
http://www.bloodjournal.org/content/65/6/1382.full.html

Articles on similar topics can be found in the following Blood collections

Information about reproducing this article in parts or in its entirety may be found online at:
http://www.bloodjournal.org/site/misc/rights.xhtml#repub_requests

Information about ordering reprints may be found online at:
http://www.bloodjournal.org/site/misc/rights.xhtml#reprints

Information about subscriptions and ASH membership may be found online at:
http://www.bloodjournal.org/site/subscriptions/index.xhtml