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TARGET PLATELET ANTIGEN IN HOMOSEXUAL MEN WITH IMMUNE THROMBOCYTOPENIA

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Abstract A syndrome of isolated immune thrombocytopenic purpura (ITP) has recently been described in homosexual men. We have identified an antiplatelet antibody in the serum of 29 of 30 homosexual men with isolated ITP. The antibody binds to a platelet membrane antigen of 25,000 daltons, and binding is effected by the $F(ab)_2$ portion of the immunoglobulin. Similar antibody activity was not detected in serum from 30 nonhomosexual patients with either ITP or nonimmune thrombocytopenia. The 25,000-dalton antigen was not found on other hematopoietic cells, and it was distinct from the core protein of the AIDS-associated retrovirus. In contrast, serum antibody reacted with a 25,000-dalton antigen associated with cultured herpes simplex virus Types I and II. In these experiments the antigen appeared to be derived from green-monkey kidney cells in which the herpes simplex viruses were grown. Identical antigenic activity was also demonstrated in uninfected human skin fibroblasts. We conclude that ITP in homosexual men is accompanied by a serum antibody directed against a platelet antigen of 25,000 daltons. The nature of the antigen and the relation of the serum antibody to ITP require further study. (N Engl J Med 1985; 313:1375-80.)

THROMBOCYTOPENIA has emerged as a major hematologic abnormality associated with the acquired immunodeficiency syndrome (AIDS) and AIDS-related conditions. Recently, a group of homosexual men with isolated immune thrombocytopenic purpura (ITP) has been identified.[1,2] Although increased levels of circulating immune complexes have been found in the serum of these patients,[3] the pathogenesis of platelet destruction in this form of ITP remains unclear.

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Supported by grants (1F32 HL-06871-01 CLN and HL-21403) from the National Heart, Lung, and Blood Institute. Dr. Shuman is the recipient of a Research Career Development Award (1 K04 HL-00802) from the National Institutes of Health.

Recent studies have identified target platelet antigens in idiopathic immune thrombocytopenia[4,5] and in drug-induced immune thrombocytopenia[6] by means of immunoprecipitation or immunoblotting. In this study, we have attempted to define the target platelet antigen in homosexual men with ITP.

METHODS

Patient Population

Serum samples were obtained from 30 consecutive homosexual men with ITP treated at the AIDS Clinic of San Francisco General Hospital and the Hematology Clinic of the University of California, San Francisco. Serum samples were also obtained from the following groups of patients: 18 nonhomosexual adult patients with ITP, 12 patients with nonimmune thrombocytopenia, and 16 homosexual men with normal platelet counts and either the lymphadenopathy syndrome or AIDS. AIDS was defined according to the surveillance criteria of the Centers for Disease Control — i.e., a disease indicative of an underlying cellular immunodeficiency when no known cause of reduced resistance to the disease is present.[7] All serum samples were frozen at −70°C before use.

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Platelet Antibody

Platelet-associated immunoglobulin was detected by means of a fluorescence-activated flow cytometric assay. Platelets were isolated from acid–citrate–dextrose-anticoagulated whole blood by differential centrifugation. They were then washed once in phosphate-buffered saline containing glucose and resuspended in 1 per cent ammonium oxalate to lyse contaminating red cells. After three washes in calcium-free Tyrode's buffer, the platelets were fixed with 1 per cent paraformaldehyde and reacted with biotin-conjugated goat antihuman $F(ab)_2$ directed against IgG, IgM, and IgA (Tago, Burlingame, Calif.). The cells were then incubated with an avidin–fluorescein isothiocyanate label (Tago), washed, and passed through a flow cytometer (Becton Dickinson), and the mean fluorescence was determined. A normal range was defined, and each sample was compared with its own negative control by means of goat antirabbit $F(ab)_2$ conjugated to biotin. Platelet-associated immunoglobulin was expressed as mean platelet fluorescence on a logarithmic scale. A sample was defined as positive if the mean fluorescence was 2 S.D. above the mean in the control population.

Target-Cell Preparation

Platelets were isolated from a single normal O-positive donor as described above. After the final wash in Tyrode's buffer, the platelets were solubilized in 2 per cent sodium dodecyl sulfate sample buffer containing 5 mM EDTA, 0.05 M imidazole, 1 per cent (vol/vol) aprotinin, 15 per cent glycerol, and 0.005 per cent bromphenol blue dye at a final concentration of 10^9 per milliliter (1 mg of protein per milliliter).

Platelets from three homosexual patients with ITP and from patients with Glanzmann's thrombasthenia or Bernard–Soulier syndrome were prepared in a similar manner. In addition, 1-ml aliquots containing 1×10^9 control platelets were subjected to digestion with trypsin,[8] 1 mg per milliliter for 30 minutes at 37°C, or thrombin,[9] 5 U per milliliter for 90 minutes at room temperature, before solubilization in sodium dodecyl sulfate. Supernatants from the treated platelets were electrophoresed on sodium dodecyl sulfate–polyacrylamide gels to verify the adequacy of the trypsin or thrombin treatment.

Erythrocytes were obtained from the same control donor. Red-cell ghosts were prepared by washing in 0.9 per cent saline, followed by solubilization in 2 per cent sodium dodecyl sulfate at a concentration of 10^7 per milliliter (1 mg of protein per milliliter). B cells were obtained by Ficoll–Hypaque separation from control blood, followed by removal of T cells by rosetting with sheep red cells.[10] The residual B cells were solubilized at 1 mg per milliliter in 2 per cent sodium dodecyl sulfate. Granulocytes were prepared by sucrose gradient separation,[10] and membrane fractions were solubilized in 2 per cent sodium dodecyl sulfate.

Cultured green-monkey kidney (Vero) cells and human skin fibroblasts were obtained from the American Type Culture Collection (Rockville, Md.). The cells were washed extensively in phosphate-buffered saline before solubilization in sample buffer at a concentration of 1 mg per milliliter. Cytopathic testing for viral infection was negative before solubilization.

Whole-virus preparations of herpes simplex virus Types I and II and Epstein–Barr virus were obtained from Cambridge Medical Diagnostics (Billerica, Mass.). The herpes simplex viruses were isolated from infected Vero cells, and the Epstein–Barr virus was derived from the human Burkitt's lymphoma line P3H3. Cytomegalovirus isolated from an infected human lung cell line, WI38, was obtained from the American Type Culture Collection. The viral antigens were solubilized in sample buffer at 1 mg per milliliter. Human AIDS-associated retrovirus,[11] kindly provided by Dr. Jay Levy, was prepared in sample buffer at the same concentration. All samples were stored at −70°C before use.

Immunoblot Technique

Sodium dodecyl sulfate–polyacrylamide gel electrophoresis was performed according to the method of Laemmli.[12] Fifty microliters of cell samples was subjected to electrophoresis in 5 to 15 per cent linear-gradient polyacrylamide gels under nonreducing conditions. Low-molecular-weight standards (Bio-Rad, Richmond, Calif.) were subjected to electrophoresis simultaneously with the samples. Electrophoresis was stopped when the dye front was 1 cm from the bottom of the gel.

Immunoblotting was performed according to the method of Towbin et al.[13] Samples separated on gradient gels were electrophoretically transferred to nitrocellulose paper (pore size, 0.1 μm [Sartorius, Hayward, Calif.]) in a Bio-Rad Transblot apparatus. The transfer was performed at 30 V for 16 hours. It was crucial that the pore size of the nitrocellulose be smaller, since proteins of lower molecular weight were not recovered when the pore size was 0.45 μm. After transfer, the nitrocellulose was cut into strips, and the low-molecular-weight standards were stained with 0.05 per cent amido black. Thirty to 40 protein bands ranging in molecular weight from 10,000 to 300,000 daltons were routinely visible on the nitrocellulose.

The rest of the nitrocellulose strips were incubated in 5 per cent (wt/vol) gelatin in TRIS-buffered saline for one hour at 37°C to block background binding. A lower gelatin concentration or substitution of 10 per cent fetal-calf serum gave unacceptable background staining. The strips were then incubated with test serum, IgG, or $F(ab)_2$ diluted 1:100 in TRIS-buffered saline with 1 per cent (wt/vol) gelatin for two hours at room temperature. After the washing in TRIS-buffered saline, the nitrocellulose was incubated with biotin-conjugated goat $F(ab)_2$ antihuman IgG, IgM, and IgA (Tago) diluted 1:500 in TRIS-buffered saline–1 per cent gelatin for one hour. After washing, the strips were placed in an avidin–peroxidase solution (Cappel, Malvern, Pa.) diluted 1:500 in TRIS-buffered saline–1 per cent gelatin for one hour. Color development was performed, with 4-chloronaphthol used as substrate.[14]

In cases in which $F(ab)_2$ binding was investigated, the biotin-conjugated second antibody was a mixture of goat $F(ab)_2$ antihuman kappa and lambda light chains (Tago). It was found that the goat antibody raised against human heavy chains did not recognize $F(ab)_2$ digests of immunoglobulin; in contrast, the anti-kappa/lambda antibody bound to both whole immunoglobulin and $F(ab)_2$ fragments on the blots. In serum from five patients, blotting with monospecific biotin-conjugated goat antibody against human IgG, IgM, or IgA (Tago) was used to demonstrate antibody binding by specific immunoglobulin classes.

Immunoglobulin and $F(ab)_2$ Preparation

Staphylococcal protein A–Sepharose CL6B (Pharmacia, Piscataway, N.J.) was used to purify IgG from serum.[15] Protein concentration was measured by the Bio-Rad modification of the Lowry technique.[16] The IgG was stored at −20°C until use.

$F(ab)_2$ fragments were prepared by a modification of the method of Madsen and Rodkey[17]: 10 mg of IgG in phosphate-buffered saline was dialyzed against 0.1 M sodium acetate, pH 4.5, for three hours at 4°C. Freshly prepared porcine pepsin (Sigma, St. Louis) suspended in the same buffer at 4 mg per milliliter was added to give a final concentration of 2 per cent (wt/wt) pepsin per milligram of total globulin. The solution was then incubated overnight at 37°C and dialyzed against phosphate-buffered saline, pH 7.4, for eight hours. The digestion products were incubated with staphylococcal protein A bacterial adsorbent (Miles Scientific, Naperville, Ill.) for 30 minutes at 4°C. The beads were centrifuged, and the supernatant free of IgG and Fc fragments was again analyzed for protein concentration. The yield of $F(ab)_2$ by this technique was 50 to 80 per cent. Samples of IgG and $F(ab)_2$, also subjected to electrophoresis with sodium dodecyl sulfate–polyacrylamide gels, demonstrated that residual IgG was absent from the $F(ab)_2$ preparations. The $F(ab)_2$ was stored at −20°C until use.

Antibody Elution from Platelets

Ether elution of platelet-associated antibody was performed according to the method of von dem Borne et al.[18] Patient platelets were isolated as described above. After the final wash in Tyrode's buffer, 10^8 platelets were resuspended in 1 ml of phosphate-buffered saline, and 2 ml of diethyl ether was added. After being shaken for 2

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minutes, the sample was incubated for 30 minutes at 37°C. The platelets were then centrifuged at 3000×*g* for 10 minutes, and the ether and stromal layers were removed. The eluate was frozen at −70°C until use.

In the fluorescence-activated cell-sorter assay, 100 μl of eluate was diluted in 900 μl of phosphate-buffered saline and incubated with control platelets for one hour, followed by second-antibody and fluorescence labeling as described above. When used for immunoblotting, the eluate was diluted 1:100 in TRIS-buffered saline–1 per cent gelatin and incubated for two hours with the nitrocellulose.

Results

The characteristics of the patients studied are shown in Table 1. Of the 30 homosexual men with ITP, all had elevated platelet-associated immunoglobulin as demonstrated with the cell-sorter technique. The platelet counts ranged from 7000 to 105,000 at the time of study, with a mean of 43,000. Sixteen patients were taking prednisone; none had undergone splenectomy at the time of initial evaluation. None of the patients had AIDS or evidence of sepsis, and no medication other than steroids was being taken. White-cell counts and hemoglobin levels were normal in all patients.

The control group consisted of 18 nonhomosexual patients with ITP, as well as 12 patients with thrombocytopenia due to thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, hypersplenism, Hodgkin's disease, or aplastic anemia. All patients with ITP had elevated platelet-associated immunoglobulin, whereas those with nonimmune thrombocytopenia had normal platelet-associated antibody. Ten of the patients with ITP were taking steroids at the time that serum was obtained.

A third group consisted of 16 homosexual men with either lymphadenopathy syndrome (5 patients) or AIDS as manifested by *Pneumocystis carinii* pneumonia (6 patients) or Kaposi's sarcoma (5 patients). The platelet counts of these patients were normal at the time of study. Platelet-associated immunoglobulin was measured in two men with lymphadenopathy syndrome and three with AIDS; it was elevated in all five patients despite normal platelet counts. None of the patients were taking steroids; their other medications are listed in Table 1.

Figure 1 shows a typical immunoblot using control serum (Lane A) or serum from a homosexual man with ITP (Lane B). All blots contained a band at 150,000 daltons. This band was also present when test serum was omitted, and represented IgG in the control platelet preparation. A second band was present at 45,000 daltons in all blots after incubation with test serum. This represents nonspecific binding of IgG to actin in the platelet preparation. In Lane B, an additional band is seen at 25,000 daltons. This band was detected with serum from 29 of 30 homosexual men with ITP, but not with serum from any of the 30 nonhomosexual patients with ITP or nonimmune thrombocytopenia. It was also seen in 15 of 16 homosexual men with lymphadenopathy syndrome or AIDS. Antibody binding was detected on control platelets and autologous platelets from the patients with ITP, as well as platelets from the patients with Glanzmann's thrombasthenia and Bernard–Soulier syndrome (data not shown). The class of antibody was studied in five patients: three had only IgG binding to the 25,000-dalton antigen, one had IgG and IgM binding, and one had IgG and IgA.

Neither trypsin hydrolysis nor thrombin stimulation of target platelets abolished antibody binding to the 25,000-dalton antigen, suggesting that the binding site is not secreted and is an integral part of the platelet membrane. Binding did not occur with red-cell ghosts (Lane C), B lymphocytes, T lymphocytes, or polymorphonuclear leukocytes. In addition, the antigen was not found on human erythroleukemia cells[19] or spleen cells (data not shown). Megakaryocytes were not tested.

Table 1. Patient Diagnoses, Treatment, and Laboratory Findings.*

Patient Group	Associated Conditions	Therapy	Mean Platelet Count	Elevated PAIg†	Antibody to 25,000-dalton Antigen
			cells/μl	*no. with feature/no. tested*	
ITP‡					
Homosexual (30)	None	Prednisone (16)	43,000	30/30	29/30
Nonhomosexual (18)	SLE (4), infection (3), CLL (1); ITP, idiopathic (8) or drug-induced (2)	Prednisone (10)	25,000	18/18	0/18
Nonimmune thrombocytopenia (12)	DIC (5), TTP (3), hypersplenism (2), Hodgkin's disease (1), aplastic anemia (1)	Prednisone (3), heparin (5), plasmapheresis (3), oxymetholone (1), MOPP (1)	47,000	0/12	0/12
Lymphadenopathy or AIDS (16)	*Pneumocystis carinii* pneumonia (6), Kaposi's sarcoma (5)	TMP/SMX (5), pentamidine (1)	192,000	5/5	15/16

*Values in parentheses represent numbers of patients. ITP denotes immune thrombocytopenic purpura, and AIDS acquired immunodeficiency syndrome; SLE denotes systemic lupus erythematosus, CLL chronic lymphocytic leukemia, DIC disseminated intravascular coagulation, and TTP thrombotic thrombocytopenic purpura; MOPP denotes mechlorethamine–vincristine (Oncovin)–prednisone–procarbazine, and TMP/SMX trimethoprim–sulfamethoxazole.

†PAIg denotes platelet-associated immunoglobulin.

‡The criteria for inclusion in this category were clinical findings compatible with a diagnosis of immune thrombocytopenia and the presence of anti-platelet antibodies.

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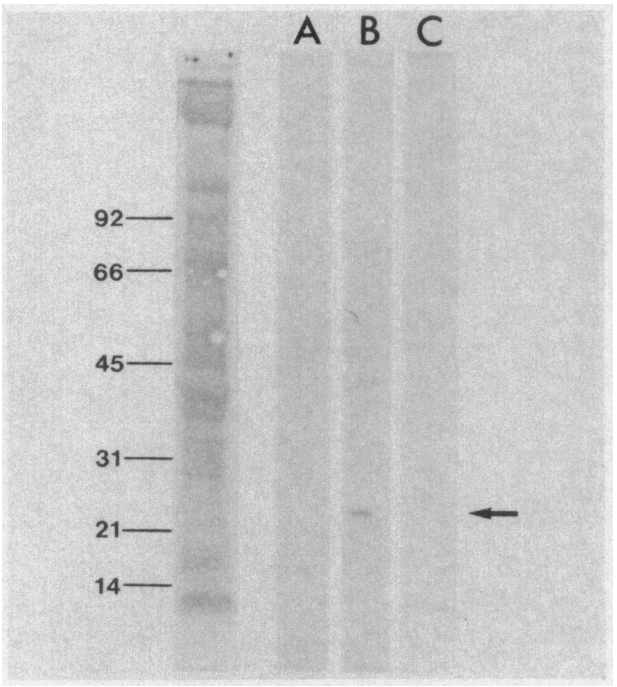

Figure 1. Identification of Antibody against 25,000-dalton Platelet Antigen in Serum from Homosexual Men with ITP.

Solubilized cells were subjected to sodium dodecyl sulfate–polyacrylamide gel electrophoresis, transferred to nitrocellulose, and incubated in stepwise fashion with test serum, biotin-conjugated goat $F(ab)_2$ antihuman immunoglobulin, and avidin–peroxidase as described in Methods.

The left lane shows amido black stain of platelet proteins transferred to nitrocellulose, with molecular-weight markers; Lane A, platelets incubated with control serum; Lane B, platelets incubated with serum from a patient; and Lane C, the same serum incubated with red-cell ghosts. Note target platelet antigen at 25,000 daltons (arrow) recognized by antibody from the patient's serum. The antigen is not seen on red-cell ghosts.

In contrast, Figure 2 shows the results of blotting with various viral preparations. Binding to an identical 25,000-dalton band occurred in samples of both herpes simplex I (Lane B) and II, but not in preparations of Epstein–Barr virus (Lane C) or cytomegalovirus. Serum reactivity with the core protein of AIDS-associated retrovirus is clearly seen in Lane D, but this band migrates at 27,000 daltons in our system and appears to be distinct from the target platelet antigen. Antibody also bound to a 25,000-dalton antigen on green-monkey kidney cells and human skin fibroblasts (Lanes E and F). Since the kidney cells were shown to be negative for herpes simplex I and II, we believe that the antigen on the herpes simplex blots was derived from the cells in which the virus was grown, and not from the virus itself. Other bands recognized by the test serum included those of Epstein–Barr nuclear antigen (80,000 daltons) and an uncharacterized 20,000-dalton protein in the Epstein–Barr virus preparation (Lane C), proteins of 41,000 and 68,000 daltons in the AIDS virus preparation (Lane D), and an as yet uncharacterized protein of 55,000 daltons in both the Vero cells and fibroblasts (Lanes E and F).

Figure 3 shows the results of blotting studies using serum (Lane A), whole IgG (Lane B), and $F(ab)_2$ fragments (Lanes C through E). In all four homosexual men with ITP who were tested, binding to the target 25,000-dalton antigen occurred with both IgG and $F(ab)_2$ fragments. $F(ab)_2$ binding could be demonstrated only with anti-light-chain antibody (and not with antibody against intact IgG), effectively ruling out the possibility of residual IgG binding in the $F(ab)_2$ preparation. Thus, antibody activity was mediated by the $F(ab)_2$ portion of the IgG. Ether eluates from each of two patients tested also bound to the 25,000-dalton antigen (Lanes F and G).

The clinical course in one homosexual patient with ITP is shown in Table 2. This patient had severe thrombocytopenia unresponsive to prednisone therapy. Tests for platelet-associated immunoglobulin and serum antibody against the 25,000-dalton platelet antigen were positive. The patient underwent splenectomy, and his platelet count rose to 327,000 per microliter. Subsequently, studies for both the platelet-associated immunoglobulin and serum antibody became negative. However, by two months after surgery, the platelet count had dropped to 160,000 and platelet antibody was again detectable by immunoblotting. Relapse occurred one month later, with a platelet

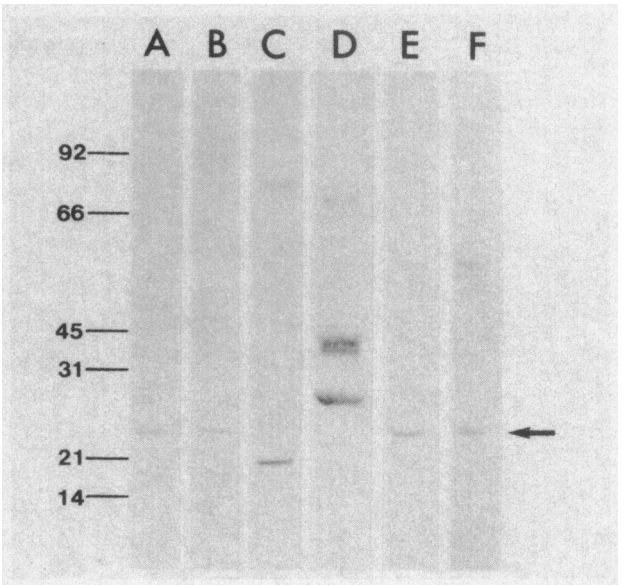

Figure 2. Immunoblot Using Serum of a Homosexual Patient with ITP.

Serum was incubated with autologous platelets — Lane A; herpes simplex virus Type I — Lane B; Epstein–Barr virus — Lane C; AIDS-associated retrovirus — Lane D; uninfected green-monkey kidney (Vero) cells — Lane E; and human skin fibroblasts (uninfected) — Lane F. Note that antibody binds to 25,000-dalton antigen (arrow) on the platelets, herpesvirus, Vero cells, and fibroblasts, but not on the Epstein–Barr virus or AIDS-associated retrovirus.

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count of 20,000 per microliter and elevated platelet-associated immunoglobulin. Testing for serum antibody remained positive.

Discussion

We have used a sensitive immunoblot technique to demonstrate serum-antibody binding to a particular platelet antigen. In 29 of 30 homosexual men with ITP, serum antibody bound to a target antigen of 25,000 daltons. This antibody activity was not detected in nonhomosexual patients with ITP or in patients with nonimmune thrombocytopenia. Furthermore, the antibody was shown to bind via the $F(ab)_2$ portion of the molecule, indicating that it is an autoantibody and not an immune complex. The 25,000-dalton antigen appears to be an integral part of the platelet membrane rather than an adsorbed antigen, since it resists trypsin hydrolysis and thrombin stimulation of platelets. Previously, Phillips[8] showed that trypsin treatment of platelet membranes resulted in increased expression of a 26,000-dalton protein, which remains uncharacterized. Whether this component and the antigen that we identified are similar has not yet been determined.

In 1982 Morris et al.[1] described a group of 11 homosexual men with thrombocytopenia, elevated platelet-associated immunoglobulin, and increased bone marrow megakaryocytes consistent with a diagnosis of ITP. A follow-up report by Walsh et al.[3] described 33 additional patients with thrombocytopenia. Although 10 of these patients had AIDS, the other 23 had a syndrome that was indistinguishable from idiopathic immune thrombocytopenia. The authors postulated

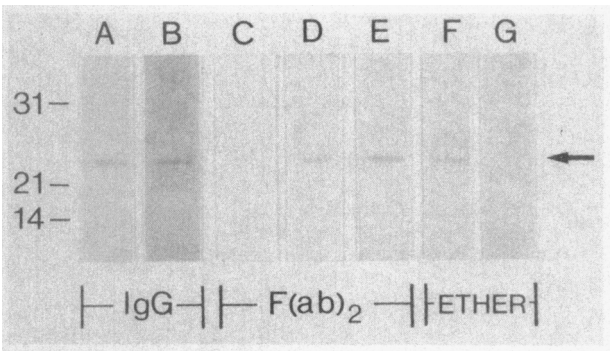

Figure 3. Immunoblot Characterization of Antibody against 25,000-dalton Antigen.

Platelets were electrophoresed and transferred to nitrocellulose as described in Methods. The nitrocellulose was then incubated with various preparations of patients' antibody: Lane A, serum from a homosexual patient with ITP; Lane B, IgG (2 mg per milliliter) purified from patient serum; Lane C, control $F(ab)_2$ fragment (2.5 mg per milliliter); Lanes D and E, $F(ab)_2$ fragments (2.5 mg per milliliter) from two patients; and Lanes F and G, ether eluates from platelets of the two patients represented in Lanes D and E. Reactivity with 25,000-dalton antigen did not occur with control $F(ab)_2$ but did occur with patient IgG, $F(ab)_2$, and ether eluates (arrow).

Table 2. Clinical Course of a Homosexual Man with ITP, Showing Correlation of Platelet Count with Platelet-Associated Immunoglobulin (PAIg) and Serum Antibody against a 25,000-dalton Antigen.

	Treatment	Platelet Count	PAIg*	Antibody* Testing
May	Prednisone	8,000	Pos	Pos
June	Prednisone	12,000	ND	Pos
July	Splenectomy			
Before operation		6,000	ND	Pos
After operation (July 12)		327,000	ND	Pos
August	None	264,000	Neg	Neg
September	None	160,000	ND	Pos
October	None	20,000	Pos	Pos

*Pos denotes positive, Neg negative, and ND not done.

that the mechanism of thrombocytopenia was related to immune-complex–mediated platelet destruction, on the basis of their observation that circulating immune complexes measured by a polyethylene glycol assay were increased in 88 per cent of homosexual patients with ITP but normal in five controls with ITP. However, Trent[20] and Lurhuma[21] and their colleagues have shown increased circulating immune complexes in 89 per cent (102 of 115) of patients with "classic" ITP, using the C1q assay. Using this assay, we found elevated circulating immune complexes in 64 per cent (7 of 11) of our homosexual patients with ITP (unpublished data). Thus, elevated circulating immune complexes appear to be a common feature of ITP in homosexual and heterosexual patients.

Walsh et al. also noted that the "immune complex" fraction of serum isolated by polyethylene glycol precipitation bound to target platelets in 79 per cent of patients.[3] However, there is doubt whether the polyethylene glycol assay is specific for circulating immune complexes, since free IgG or IgM may also be precipitated when high serum concentrations are present.[22,23] Since patients with AIDS-related syndromes have increased immunoglobulin levels,[24] the polyethylene glycol technique may precipitate autoantibody together with immune complexes in these patients. Thus, although circulating immune complexes may be elevated in homosexual men with ITP, direct evidence is lacking that thrombocytopenia results from these complexes.

Whether the antibody against the 25,000-dalton platelet antigen is responsible for thrombocytopenia in these patients has not yet been demonstrated. The presence of antibody against this antigen on the surface of platelets suggests at least a partial explanation for thrombocytopenia, since antibody-coated platelets have been shown to be phagocytosed by leukocytes.[25] Thus, accelerated destruction of these autoantibody-coated platelets by the reticuloendothelial system would be expected. In addition, the presence of serum antibody against the 25,000-dalton anti-

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gen seemed to parallel disease activity in the single patient studied longitudinally (Table 2). The role of this antibody in the pathogenesis of ITP requires further evaluation.

The possible derivation of the platelet autoantibody in our patients is intriguing. The antibody recognizes the same antigen in fibroblasts and monkey kidney cells, as well as on herpes simplex virus cultured in the kidney cells. An attractive hypothesis based on these observations is that in some patients with herpetic infections, the cellular 25,000-dalton protein may become incorporated into viral proteins or adsorbed to the virus. The protein may thus be altered, rendering it immunogenic. Alternatively, the 25,000-dalton protein may be synthesized by the herpesvirus and some mammalian cells. Antibodies raised against the virus after infection may then secondarily react with host cells, including platelets. Similar mechanisms of autoimmunity have been postulated in other forms of viral infection.[26,27] The role of the AIDS-associated retrovirus in development of the autoantibody also requires clarification.

Finally, the absence of thrombocytopenia among patients with AIDS or lymphadenopathy syndrome whose serum contains antiplatelet antibody is unexplained. As noted in Table 1, five such patients with normal platelet counts had increased amounts of platelet-associated immunoglobulin. A possible explanation is related to the finding of Bender et al.[28] that Fc-receptor–mediated clearance is defective in patients with AIDS. Thus, these patients may have increased antibody bound to their platelets but decreased clearance, as described by Kelton et al.[29] in other diseases. An alternative explanation is that compensated thrombocytolysis is present in these cases, since borderline platelet counts were recorded in three of the five patients at the time that serum was obtained, and subsequently thrombocytopenia developed in all three patients. Further studies of platelet-associated antibody and Fc-receptor–mediated clearance in nonthrombocytopenic patients with AIDS or AIDS-related conditions should help to clarify this issue.

In summary, we have identified a platelet autoantibody in the serum of 29 of 30 homosexual men with ITP. The antibody binds to an antigen of 25,000 daltons that appears to be a part of the platelet membrane. The nature of the target platelet antigen and the relation of the serum antibody to the pathogenesis of ITP in homosexual men require further study.

We are indebted to Jay Levy, M.D., and Joel Chasis, M.D., for helpful discussion, to Dr. Margaret Johnson (Medical Center of Delaware, Newark, Del.) for providing platelets from the patients with Bernard–Soulier syndrome, and to Margaret Rheinschmidt, Mary Rossi, Ramila Philip, and Bobak Banapour for technical assistance.

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