MEDICAL GRAND ROUNDS
PARKLAND MEMORIAL HOSPITAL

MARCH 5, 1959

[Combined cases: purpura and thrombocytopenia]

Case I:

A 67 year old [redacted] first noted purpura over the lower extremities accidentally while at the beach in 1955 (one year before the first admission here). The purpura lasted 3 weeks. She was taking no medication at that time. The only known departure from her usual routine was the high intake of seafood. Three months later she was considered to have had a small cerebral hemorrhage.

First [redacted] admission for purpura ([redacted]-56 to [redacted]-56): The patient was admitted with diffuse purpura. Recently she had been given gantrisin and chloramphenicol for diffuse cystitis. A severe occipital headache was present on admission.

The past history revealed the following: Four normal pregnancies; hemorrhoidectomy 1914; incomplete abortion and D & C 1918; vaginal repair and hysterectomy 1931; cervical amputation 1933; radical mastectomy for "cancer" 1937; urethral operation and operation for cystocele and rectocele 1951.

The physical findings were normal except for petechiae over the skin and a liver palpable 3 cm. below the costal margin. The vital signs were normal.

The laboratory data indicated: Hb 12.3 gm/100 ml; hematocrit 35.5%, RBC 3.66 mil (MCV 97, MCH 34, MCHC 34); platelet count 30,000/cu mm (direct), 15,000 cu/mm (indirect); reticulocytes 1%; WBC 2400 (normal differential count).

Bleeding time 15 mins. Lee-White clotting time 19 mins; no clot retraction in 24 hours; prothrombin (Quick) 100%; prothrombin consumption (1 hr.) 14%; thromboplastin generation test 5% in 10 minutes.

L E test negative; direct Coombs test negative; platelet isoagglutinin (pt. serum) 3+; Bone Marrow: normal cellularity, hemosiderin present, M E ratio 4:1; adequate megakarcyocytes with poor platelet differentiation.

Urine negative. Lumbar puncture: opening pressure 21 cm H_2O, protein 60 mg%, sugar 70 mg%, no cells, fluid clear.

STS negative, heterophile test negative, febrile agglutinins negative; BUN 16 mg%, cholesterol 250 mg%, serum albumin 5.4 gm%, globulin 1.7 gm%, FBS 130 mg%, serum bilirubin 0.4 mg%, cephalin flocculation test 3+ in 48 hours, alkaline phosphatase 0.8 B. U. BSP 19% retention decreasing to 3% as liver size receded.

The administration of ACTH and adrenocortical steroid was attended by disappearance of petechiae and return of the peripheral blood to normal.

Follow-up observations [redacted]-56: Hb 14.4, hemat. 43.7, RBC 5.15 (MCV 85, MCH 28, MCHC 33); platelet 220,000 (direct), 664,000 (indirect); WBC 15,000 (left shift). Life span of RBC (Cr^{51}) 70 days during the acute episode and 105 days later.

[redacted]-57: A bout of purpura occurred 24 hours after cleaning and painting the car port. Hb 12.5; hemat. 39%; RBC 4.14 (MCV 94. MCH 30, MCHC 32), platelets 126,000 (direct) 264,000 (indirect); WBC 3600 (42 segs, 53 lymphs).

Bleeding time 9 mins. Lee-White clotting time 15 mins. clot retraction poor (49% fluid volume in 1 hour, 12% in 24 hours); Rumple-Leede test 2+; prothrombin (Quick) 100%; prothrombin consumption 62%.

The petechiae cleared in two weeks while she was given prednisone 15 mgm daily. Periodic checks on the blood revealed normal results until [redacted], 1958.

[redacted], 1958: There occurred an upper respiratory infection with fever, malaise and myalgia. She was given achromycin. Severe purpura occurred at this time. Steroid management was instituted. The purpura disappeared. A few days later the platelet count was 178,000 (direct), Hb 13.5 and WBC 3800.

Second [redacted] admission ([redacted]-58 to [redacted]-58): The patient related contact with a pungent paint solvent 24 hours before hemorrhages and petechiae occurred over the lower extremities. The platelet count was 36,000/cu mm. She was given prednisone (60 mg daily gradually diminished to 10 mg daily). The purpura abated and at the time of discharge the platelet count was 94,000/cu mm. Bone marrow preparation revealed evidence for erythroid hyperplasia (M E ratio 2:1), many megakaryocytes with poor platelet differentiation. Hepatic and renal function studies gave normal results. One week after discharge the platelet count was 38,000.

A check on the patient's home environment revealed potential contact with several types of cleaning fluids and various insecticides among which were malathion, toxaphene, dieldrin, chlordane, lindane and heptochlor. The air conditioning system seemed to be related to the storage compartment of several of these substances.

Third [redacted] admission ([redacted]-58 to [redacted]-58): While still on prednisone (10 mg per day) purpura developed over the lower extremities. The prednisone dosage was increased to 30 mg per day. The purpura remained. The blood revealed Hb 14.5 (MCV 90, MCH 29, MCHC 32), platelet count 46,000 (direct) and WBC 9500 (normal differential count). Another bone marrow preparation was similar to former ones. L E preparations were negative. As before the patient remained afebrile.

Fourth [redacted] admission [redacted]-58 to [redacted]-58): The patient was given 40 units ACTH per day for 5 days with the following changes: Hb 12.8 to 14.4 gm%, WBC 14,000 to 27,000(with a left shift) and platelets 36,000 to 54,000 (direct). During this time purpura scattered over the extremities disappeared.

A test for autoagglutinin for platelets using concentrated platelets was negative. Splenectomy was contemplated.

Fifth [redacted] admission ([redacted]-59 to [redacted]-59): Despite steroid medication the purpura remained (platelets 16,000) and a slight anemia occurred (Hb 11.5). Consultation elsewhere was obtained.

At another clinic platelet autoagglutinins were observed and splenectomy was recommended.

Sixth [redacted] admission ([redacted]-59 to [redacted]-59): A splenectomy was performed followed by a gradual rise in the platelet count to 320,000 over a period of 7 days. Withdrawal of steroids seemed to be related to a fall in the platelet count to 200,000 at the present time.

Case 2:

A 16 year old male was well until 3 weeks prior to admission. At this time he developed sore throat and fever lasting for 5 days. The illness was minor enough not to bar participation in interscholastic basketball. A blow to the nose resulted in moderate hemorrhage which was followed shortly by petechial hemorrhages over the skin. A tentative diagnosis of idiopathic thrombocytopenic purpura was made and prednisone was given.

The physical findings were confined to purpura and generalized lymphadenopathy.

Laboratory findings: Hb 14.2 gms, RBC 4.51, hemat. 40.1 (MCV 89, MCHC 35.5); platelets direct 26,000, indirect 196,000, retic. 1.1%, WBC 12,350, poly 52%, lymphs 48%, majority of lymphocytes were Downey types 1 and 2 (virocytes). Bleeding time 3' 35", prothrombin time 100%, prothrombin consumption 36%, no clot retraction; heterophile antibody titer 1:896, after guinea pig kidney absorption 1:896, after beef RBC absoprtion 1:7. The bone marrow revealed megakaryocytic hyperplasia and poor platelet differentiation.

Prednisone was continued and recovery was prompt and complete. Two weeks later gradual reduction of steroid produced no relapse.

Case 3:

A 78 year old retired [redacted] developed weakness and fatigue in [redacted] 1957. This was attributed to an exacerbation of asthma which had been present intermittently throughout life. In [redacted], 1958 he passed tarry stools which abated after 2 pints of blood. The tarry stools recurred in [redacted], 1958. At this time there developed also bleeding from the mouth and purpura over the skin. Except for the purpura the examination was non-revealing.

A tentative diagnosis of toxic or allergic purpura was made on [redacted]-58. The patient had had a great deal of contact with an atmosphere of intensive crop dusting.

A hypochromic anemia was present (Hb 8.7 gm%, MCHC 27.7%). The platelet count was 22,000/cu mm (direct, 52,000 (indirect); WBC 12,000 (normal differential count). Clot retraction was poor; prothrombin 100%, prothrombin consumption (1 hour) 85%. Multiple bone marrow aspirations revealed erythroid hyperplasia, many megakaryocytes with left shift and poor platelet differentiation.

Following parenteral iron medication (1300 mg) the Hb rose to 10.3 gm. and on steroid management (30 to 15 mg Meticorten per day) the purpura disappeared, the stools were negative for blood and the platelet count rose to 120,000/cu mm.

The patient returned to his original environment while on steroid management. The purpura and tarry stools recurred ([redacted], 1958). He was admitted to [redacted] ([redacted]-58). Following additional parenteral iron and continuation of Meticorten the sense of well being was reinstituted. The bone marrow preparations at this time contained few megakaryocytes. The purpura and thrombocytopenia abated slowly (see table).

A bout of asthma on [redacted] 25, 1958 was followed by purpura and a very low platelet count. The only variant appeared to be contact with chocolate. He had not eaten chocolate for a long time. The bone marrow had many megakaryocytes and no evident platelets. At present his status is improving.

Case 4:

A 55 year old [redacted] had an episode described as "flu" 40 days earlier. He was in bed for 2 days during which time he was febrile and coughed considerably. The cough was non-productive. One week later generalized purpura developed (involvement included lower extremities, trunk, portions of upper arms). There was one prominent nose bleed. He was given Meticorten and the purpura abated. (A few small bruises recurred).

During the illness the patient had penicillin, Chlortrimeton and "flu capsules" known as Achrocidin.

The physical examination was normal except for an occasional ecchymatic area in the skin of the thighs.

Laboratory data: Hb 14.0 (MCV 93, MCH 31, MCHC 33); WBC 14,000 (normal differential count); platelets 16,000 (direct 49,000 (indirect).

Bleeding time ovar 15 mins.; Lee-White clotting time 10 mins.; no clot retraction in 1 hour; Rumple-Leede test negative (95 mm Hg for 5 mins); prothrombin (Quick) 11 seconds (100%); prothrombin consumption 37%.

Bone marrow: Adequate cellularity, normal cells, many megakaryocytes with poor platelet formation. M:E 2:1.

Platelet agglutinin studies

Patient platelet poor plasma + Patient platelet rich plasma - negative
Pt. platelet poor plasma + pt. platelet rich plasma + Achrocidin - 3+ agglutinin
" " " " + " " " " + Chlortrimeton - negative
Controls negative
Achrocidin contains: Achromycin, phenacetin, caffeine, salicylamide, chlorothen citrate.

Case 3

Date	Hgb.	RBC	Hemat.	Retic.	MCV	MCHC	Platelets Dir.	Platelets Ind.	WBC	Poly.	Lymphs	Occult Blood	Occult Alb.	Occult F	Prednisone mg/day	Fe Mgm.	Pur.
[redacted]	8.7	3.71	31.4	2.4	85	27.7	22,000	52,000	12.2	25	69				30 x 3 20 x 2 15	50 500	2+
[redacted]	10.3		34.4	5.6	75	30.5	120,000	552,000	32.2	41	48	0	0	0	20	800	±
[redacted]	6.6		24.5			27.0	25,000					Tarry	trace		20	900	4+
[redacted]	8.4	3.72	31.4	14.4		26.7	80,000		42.0	37	63				20		1+
[redacted]	11.2	4.02							22.4	20	80				20		
[redacted]	11.1						6,000		20.3	40	49	0	0	0	30 x 3 20	Ulcer Mouth	3+
[redacted]	13.2						3,000								20		2+
[redacted]	11.1		35.7			33.0	48,000		38.0	50	29				20	Ulcer healing	1+
[redacted]							106,000	Normal		26	70				20		1+
[redacted]	12.5			.3			12,000					2+	trace		20		2+
[redacted]	12.8						6,000		48.0	40	60						

REFERENCES

Thrombocytopenia vs Purpura

1. Bedson, S. P.: Blood-platelet anti-serum, its specificity and role in the experimental production of purpura, J. Path. and Bact. 25:94, 1922

2. Bedson, S. P.: Effect of splenectomy on production of experimental purpura, Lancet 2:1117, 1924

3. Madison, F. W.: The role of allergy in the pathogenesis of purpura and thrombocytopenia, Blood 3:1083, 1948

4. Roskam, J.: Platelets and vascular walls in pathogenesis of chronic thrombopenic purpura, Sang. 27:856, 1956

5. Ackroyd, J. F.: Allergic purpura, including purpura due to foods, drugs and infections, Am. J. Med. 14:605, 1953

Life span of platelets

6. Leeksma, C. H. W. and Cohen, J. A.: Determination of the life span of human blood platelets using labeled diisopropylfluorophosphonate, J. Clin. Invest. 35:964, 1956

7. Aas, K. A. and Gardner, F. H.: Survival of blood platelets labeled with chromium 51, J. Clin. Invest. 37:1257,1958

Thrombocytopheresis

8. Craddock, C. G. Jr., Adams, W. S,, Perry, S. and Lawrence, J. S.: The dynamics of platelet production as studied by a depletion technique in normal and irradiated dogs, J. Lab. and Clin. Med. 45:906, 1955

Bone Marrow in Thrombocytopenia

9. Dameshek, W. and Miller, E. B.: The megakaryocytes in idiopathic thrombocytopenic purpura, a form of hypersplenism, Blood 1:27, 1946

Platelet ABO blood type and other incompatibilities

10. Coombs, R. R. A., Marks, J. and Bedford, D.: Specific mixed agglutination: mixed erythrocyte-platelet anti-globulin reaction for the detection of platelet antibodies, Brit. J. Hematol. 2:84, 1956

11. Stefanini, M., Dameshek, W. and Adelson, E.: Platelets: VII. Shortened "platelet survival time" and development of platelet agglutinins following multiple platelet transfusions, Proc. Soc. Exp. Biol. and Med. 80:230, 1952

12. Dausset, J., Colonibani, J. and Evelin, J.: Presence de l'antigene Rh (O) dans les leucocytes et les plaquettes humanies, Vox Sanguinis 3:266, 1958

13. Moulivier, J. and Servantie, X.: Detection par le test de consonmation d'antiglobuline de l'antigene D sur les plaquettes des individus Rh-pocitif (D+) Vox. Sang. 3:277, 1958

REFERENCES

Platelet antibodies in disease

14. Harrington, W. J., Sprague, C. C., Minnich, V.; Moore, C. V., Ahlvin, R. C. and Dubach, R.: Immunologic mechanisms in idiopathic and neonatal thrombocytopenic purpura, Ann. Int. Med. 38:433, 1953

15. Tullis, J. L.: Identification and significance of platelet antibodies, New Eng. J. Med. 255:541, 1956

16. Jaeger-Draafsel, E., Wiegman, D. and van Loghem, J. J.: Detection of incomplete platelet antibodies by means of the anti-human globulin test, Vox Sang. 1:78, 1956

17. Nelken, D. and Gunvitch, J.: Positive Coombs test on blood platelets, Vox Sang. 1:106, 1956

18. Weinreich, J.: Thrombocytopenias and platelet-antibodies, Vox Sang. 2: 294, 1957

General consideration, emphasis on management

19. Harrington, W. J.: Therapy of the purpuras, J. Chronic Dis. 6:365, 1957

20. Dameshek, W.; Rubio, F. Jr., Maloney, J. P., Reeves, W. H. and Burgin, L. A.: Treatment of idiopathic thrombocytopenic purpura with prednisone, J.A.M.A. 166:1805, 1958

Functional pathology of platelets

21. Van Creveld, S.: Functional pathology of platelets, Acta. Hematol. 12:229, 1954

22. Bannin, J. A.: Studies of platelet function as guide to severity of thrombocytopenic purpura and possible mechanism of purpura and hemorrhage, Australasian Ann. Med. 6:196, 1957

23. Haverbach, B. J., Dutcher, T. F., Shore, P. A., Tomich, E. G., Terry, L. L. and Brodie, B. B.: Serotonin changes in platelets and brain induced by small daily doses of reserpine: Lack of effect of depletion of platelet serotonin on hemostatic mechanism, New Eng. J. Med. 256: 343, 1957

24. Hardisty, R. M. and Stacey, R. S.: Platelet 5-hydroxytryptamine (HT) in disorders of blood, Brit. J. Hematol. 3:292, 1957

25. Sharp, A. A.: Viscous metamorphosis of blood platelets: A study of the relationship to cooagulation factors and fibrin formation, Brit. J. Hematol. 4:28, 1958

26. Neely, R. A., Carson, N. A. J. and Fisher, O. D.: Thrombocytopathia hemorrhagica: A case report, Brit. J. Hematol. 1:234, 1955

27. Hardisty, R. M. and Wolff, H. H.: Hemorrhagic thrombocythemia: A clinical and laboratory study, Brit. J. Hematol. 1:390, 1955

REFERENCES

28. Krevans, J. R. and Jackson, D. P.: Hemorrhagic disorder following massive whole blood transfusions, J.A.M.A. 159:171, 1955

29. Hougie, C. and Glover, H. M.: The hemophilioid states, A.M.A. Arch. Int. Med. 103:239, 1958

Deficiency state and thrombocytopenia

30. Merskey, C. and Hansen, J. D. L.: Blood coagulation defects in Kwashiorkor and infantile gastroenteritis, Brit. J. Hematol. 3:39, 1957

Platelet thromboplastic factor

31. O'Brien, J. R.: The similarity of the action of phosphatidyl-ethanolamine and platelets in blood coagulation, J. Clin. Path. 9:47, 1956

32. Troup, S. B. and Reed, C. F.: Platelet thromboplastic factor: Its chemical nature, in vitro activity, and the identification of similar thromboplastic substances in red blood cells (Abst), J. Clin. Invest. 37:937, 1958

33. Marcus, A. and Spaet, T. H.: Platelet phosphatides: Their separation, identification and clotting activity, J. Clin. Invest. 37:1836, 1958

34. LeBaron, F. N. and Folch, J.: Structure of brain tissue lipides, Physiol. Rev. 37:539, 1957

35. Wolff, P.: Lipid extracts of platelets and brain as substitute for platelet coagulation test, Brit. J. Hematol. 2:375, 1956