CASE REPORT

Aplastic Anemia with Platelet Thrombi

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A PLASTIC ANEMIA of unknown etiology is relatively infrequent. We wish to report a case since its clinical course was unusual and because the microscopic features of platelet thrombi were demonstrated in various organs. To our knowledge this represents the first recorded instance of platelet thrombi in aplastic anemia.

REPORT OF CASE

T. K., a 67 year old white female, was admitted to the Albert Einstein Medical Center, Southern Division, on September 6, 1949, with the chief complaint of fever and soreness of the mouth and gums. She was apparently well until two weeks before admission when she developed a cough, sore throat and a mild coryza. She was treated at home with aspirin, phenacetin, codeine, caffeine, sulfadiazine, and later with penicillin and aureomycin without improvement. Soreness of the mouth developed one week later, followed by enlargement and tenderness of the gums. An infection of the right hand failed to respond to local medication. Hospitalization was advised at this time. The past medical history and systemic review were essentially negative. There was no history of exposure to any chemicals or solvents.

Physical examination revealed a well developed, white woman who appeared acutely ill. The blood pressure was 120/70, pulse 100, respirations 22 per minute, temperature 102 F. The mucous membranes of the mouth were reddened, the gums were inflamed and swollen and the few remaining teeth were carious. A few dried, brownish crusts were present about the alae nase. No pallor, scleral icterus, glossitis, purpura or hepatosplenomegaly were noted. The remainder of the physical examination was normal except for a systolic apical murmur.

Laboratory tests on the day of admission revealed the following: RBC 4.24 M. Hgb. 13.9 Gm. (89 per cent), platelets 110,000 per cu.mm., WBC 1200 with 100 per cent mature lymphocytes. The peripheral smear showed only slight anisocytosis and poikilocytosis. Hypochromia was minimal. Spherocytes and polychromatophilic macrocytes were not seen. Urinalysis (uncatheterized, centrifuged) showed a straw colored urine, specific gravity 1.018, no sugar or albumin, 2-3 WBC/HPF, 2-3 RBC/HPF. The blood urea nitrogen was 12 mg. per cent, blood sugar 102 mg. per cent. A blood culture was negative. An x-ray of the chest was negative.

A sternal marrow aspiration performed on the third hospital day revealed a good preparation of a markedly hypocellular marrow; megakaryocytes were present in normal numbers and platelet production appeared adequate. Erythropoiesis was normoblastic in nature but was virtually absent. Granulopoiesis was markedly diminished with an apparent maturation arrest at the myelocyte and metamyelocyte stage; only a rare band or segmented polymorphonuclear leukocyte was present. No foreign cells were seen. (Fig. 1.)

This marrow was interpreted as illustrating a selective depression in the number of...
granulocytes and normoblasts. Megakaryopoiesis was not impaired and platelet production appeared normal. Furthermore it indicated that we were not dealing with a simple case of agranulocytosis as first suspected, but possibly presaged a more serious hematologic disorder.

The red cell count and hemoglobin level began to fall and 2,500 cc. of blood were given in an attempt to maintain normal values. The reticulocyte count averaged 0.6 per cent. The white cell count fell from 1,200 to 300 with 93 to 100 per cent lymphocytes. The platelet count gradually decreased. Four days later petechiae and ecchymoses were first noted over the entire body. At this time, platelets were virtually absent from the peripheral smear. Another sternal marrow aspiration was performed and a completely acellular marrow specimen was obtained. Complete absence of all formed elements, i.e. normoblasts, granulocytes and megakaryocytes, was found. (Fig. 2.)

![Fig. 1. Hypocellular marrow with normal numbers of megakaryocytes. Erythropoiesis and granulopoiesis virtually absent. (150 X)](image)

The typical features of an aplastic anemia were now demonstrated. Megakaryocytes, seen in the preceding marrow aspiration, were completely absent. Thus a selective and progressive depression of the formed elements in the marrow had been observed.

On the eighth hospital day the patient developed a right conjugate deviation of the eyes, flexion of the head on the chest, marked respiratory distress, and died shortly thereafter. An autopsy was performed but permission to examine the brain could not be obtained.

The important gross autopsy findings were: evidences of bleeding within the small and large intestines, the presence of eight hemorrhagic ulcers, 1.2 to 2 cm. in diameter in the rectosigmoid, and three ulcers, 1 cm. in diameter in the gingival margin of the buccal mucosa.

Description of the microscopic postmortem findings has been restricted to those considered pertinent to this case. Bone marrow showed a diffuse hypocellularity with many areas of normocellularity. The hypocellular areas consisted of fat cells with a few scattered cells of the hematopoietic series. The normocellular areas showed all marrow elements normally present, except for megakaryocytes, which were increased in numbers.

The follicles of the lymph nodes were small and compact. There was no evidence of germinal centers in the sections studied. A slight hyperplasia of the sinusoidal reticular cells was found. The sinuses contained moderate numbers of lymphocytes, plasma cells and occasional histiocytes. No phagocytic activity was seen.
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The central arteries and periportal arterioles of the spleen showed moderate arteriosclerosis and occasional platelet thrombi. The red pulp was moderately congested. It contained occasional small hematopoietic foci, consisting of a few normoblasts and one or two early granulocytes. No megakaryocytes were seen.

The lobular architecture of the liver was well preserved and the hepatic cell cords were well demarcated. The sinusoids of the central lobular areas were markedly congested; the Disse's spaces were distended. This resulted in slight compression atrophy of the parenchymal cells which showed early fatty vacuolization. A few areas, particularly in the periph-
eral sinusoids, contained normoblasts plus an occasional myelocyte. The portal triads were not remarkable.

The architecture of the lung was normal. The majority of the alveoli were normally expanded. A small hemorrhagic infarct was present in one area. Nearby, a large artery contained an extensive platelet thrombus (fig. 3).

The ovaries and uterus showed the usual changes seen in the late post-menopausal state. There was intense arteriovenous congestion of the ovarian hilar vessels and the subserosal uterine vessels. Several of these, both arteries and veins, contained large platelet thrombi.

**DISCUSSION**

The occurrence of platelet thrombi in aplastic anemia has not previously been reported. The presence of thrombi in thrombotic thrombocytopenic purpura (TTP) is well known; it was first reported by Moschowitz who described “hyalin thrombi” in the terminal arterioles and capillaries of a 16 year old female with anemia, leukocytosis and petechiae. These thrombi were most abundant in the myocardium, but were also noted in the precordial fat vessels, liver, spleen and kidneys. Platelet thrombi have been subsequently described in the pancreas, adrenals, lymph nodes, small and large intestines, skin, bone marrow, diaphragm, pituitary, trachea, thyroid and brain. The clinical course of our patient differed markedly from those individuals with TTP. Mouth ulcers and skin infection were the presenting complaints. These reflected the severity of the agranulocytosis. Anemia, resulting from the inability of the marrow to form red cells, later became prominent. The clinical signs of platelet deficiency characterized by petechiae and ecchymoses were noted only terminally. The patient died with signs of intracranial hemorrhage which suggested that vascular lesions might have been found if permission to examine the brain were granted. These neurologic signs were noted only terminally in our patient; they occupy a prominent role in patients with TTP.

The hematologic features of these two diseases vary considerably. The anemia in our patient was due to marrow aplasia rather than a hemolytic process. The thrombocytopenia resulted from the inability of the marrow to form platelets. The main cause for thrombocytopenia in TTP is apparently the diffuse platelet thrombi throughout the smaller blood vessels. Agranulocytosis is not found in TTP. It was the main cause for admission of our patient. And lastly, our patient’s marrow was predominantly hypocellular rather than normally cellular.

The thrombotic lesions were not as widespread as those found in TTP. Platelet thrombi could be demonstrated only in the vessels of the spleen, lungs, uterus and ovaries. The nature of the vascular involvement differed as well. The smaller vessels, i.e., capillaries and venules, are primarily involved in TTP. Platelet thrombi were seen in the arteries, as well as veins and capillaries of our patient. Lymph nodes, reported as normal in TTP, were characterized by scanty follicles and the absence of germinal centers. Areas of extramedullary hematopoiesis, noted in the liver and spleen of our patient, have been reported only occasionally in TTP.

A recent report has cast doubt on the platelet origin of thrombi in TTP. These thrombi were thought to be vascular in origin, being derived from the proliferation of the lining endothelial cells overlying an amorphous material in the vessels. This amorphous material was also seen in layers of the vessel wall,
and occasionally in the surrounding connective tissue. Multiple aneurysms of the arterioles and precapillaries containing both amorphous material and masses of proliferated endothelial cells were described. No such lesions could be found in our patient. These variations in histology point to a different etiology and pathogenesis. The presence and importance of platelet thrombi in our patient is difficult to assess at this time. Whether our case represents a new syndrome will depend upon similar findings in other individuals with aplastic anemia.

Platelet thrombi have not been described in many disease processes. They were reported in the eschar and rash of scrub typhus. Lesions similar to those in "generalized platelet thromboses" have been described in the Schwartzman phenomenon. Platelet thrombi, although noted in fixed sections of normal, human skin wounds have not been found in patients with idiopathic thrombocytopenic purpura. The role of iodine in the development of a case of TTP has been stressed. The discovery of large amounts of lead and mercury in the tissues of patients with fatal, acute thrombocytopenic purpura was recently reported. Platelet thrombi were found in 4 of 13 cases. The authors referred to an earlier paper which reported poisoning in 3 men who worked with mercury and developed symptoms of intermittent claudication followed by gangrene of the feet. Leukocyte-platelet thrombi were reported in the coronary arteries of patients with rheumatic carditis.

**SUMMARY**

1. A case of aplastic anemia with platelet thrombi is presented.
2. The developmental features of this anemia are stressed and comparisons made with thrombotic thrombocytopenic purpura.
3. The role of platelet thrombi in other conditions are briefly reviewed.

**REFERENCES**

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