Giant Hemangioma with Thrombocytopenia
Radioisotopic Demonstration of Platelet Sequestration

By HERBERT E. BRIZEL AND GIOVANNI RACCUGLIA

THE ASSOCIATION of thrombocytopenia with giant hemangioma has been documented in approximately 40 cases since the first report of Kasabach and Merritt in 1940. The mechanism of thrombocytopenia is thought to be related to the trapping of platelets by the abnormal endothelium of the tumor, and the accumulation of material presumably derived from the platelets has been demonstrated by histologic technics. The actual sequestration of platelets by the tumor should be easy to verify by transfusing platelets labeled with a radioactive isotope, but such studies have produced conflicting results. Petit has claimed that no platelet sequestration takes place, and Blix and Aas found no increased radioactivity over the tumor following the infusion of tagged platelets. Kontras et al. performed careful studies with baseline calculation of the tumor vascular space followed by infusion of Cr-51 tagged platelets. These authors concluded that the increased radioactivity over the hemangioma should be attributed not only to the large blood volume present in the hemangioma but to an actual trapping of the platelets. The present report describes a case of thrombocytopenia associated with giant hemangioma in which similar studies were performed. While our tracer studies are somewhat different from those of Kontras, our isotopic findings, together with the radiotherapeutic results, tend to confirm the occurrence of platelet trapping as reported by these authors.

CASE REPORT

The patient was the larger of twins, born after normal gestation, with a birth weight of 7 lb., 1½ oz. A vascular tumor was evident at birth and involved the entire anterior region of the right thigh from the inguinal crease to the medial portion of the knee. No change in size or consistency was noted in the hemangioma until about 1 month prior to the present admission when the lesion began to enlarge to approximately twice its initial size.

The patient was admitted at the age of 7½ weeks with no other significant past history. The physical examination was unremarkable except for the large hemangioma on the right thigh. The tumor had a reddish, purple color and did not blanch on pressure. Although ill-defined, its surface measured approximately 9 by 9 cm. with

From the Departments of Radiology and Medicine, University of Louisville School of Medicine, Louisville, Kentucky.

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HERBERT E. BRIZEL, M.D.: Advanced Clinical Fellow, American Cancer Society; Associate Professor of Radiology and Associate Director of the Radiation Center, University of Louisville School of Medicine, Louisville, Kentucky. GIOVANNI RACCUGLIA, M.D.: Associate Professor of Medicine and Chief of Section of Hematology, University of Louisville School of Medicine, Louisville, Kentucky.

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diffuse induration extending almost to the posterior surface of the thigh. The lesion extended from the inguinal area to the knee and involved the entire anteromedial aspect of the right thigh. The circumference of the right thigh measured 26 cm. as compared to 16 cm. on the left (fig. 1). Admission laboratory work revealed a normal urinalysis and normal white count and differential. The hemoglobin was 8.2 grams with 22 per cent hematocrit. The platelet count was 6000 per cubic millimeter. On the second hospital day, many petechiae were noted over both upper and lower extremities and to a lesser degree on the trunk.

Two hundred cubic centimeters of whole blood raised the hemoglobin to 10.7 Gm., and irradiation of the hemangioma was started on the second hospital day. A 10 by 12 cm. anterior portal was employed at 220 PKV with a half-value layer of 1.3 mm. Cu and a 50 cm. FSD. Two treatments were administered over a 3-day period with a total surface dose of 1000 r. This resulted in 800 r being delivered to the center of the lesion and approximately 500 r to the posterior surface of the thigh. Approximately 6 cc. of packed, Cr-51 tagged platelets (2 units) were administered during the 1-day interval between the two irradiation treatments.

MATERIALS AND METHODS

The platelets were tagged according to the method of Aas and Gardner. Continuous monitoring of radioactivity with dual probes, dual ratemeters, and strip chart recorders was performed from the time of injection over the hemangioma and liver. Discontinuous counts were performed over the spleen and precordium, starting at 40 minutes after injection. Each probe had a 1.5 X 1 inch NaI crystal and a straight bore collimator with a surface diameter of slightly less than 3 inches over the collimator face. Both probes and ratemeters were carefully precalibrated for equal response. The collimator surface was large enough to cover the entire surface of the hemangioma and, considering the size of the infant, to also completely cover the liver, precordium and spleen. The liver was chosen as the main control organ because it was believed that its size and vascularity were at least as great as the hemangioma on the leg. Counts were recorded over the spleen and heart as additional controls and to check the possibility of platelet sequestration in the spleen. Although it would have been desirable, serial peripheral blood samples for radioactive platelet activity could not be obtained because of the patient's poor general condition.
RESULTS

Immediately before transfusion the platelet count was 12,500/cu. mm. One hour after the injection was started it was 35,000, and at 1 hour and 15 minutes reached a maximum of 37,500. Sixteen hours following the transfusion, the platelet count had returned to the pretransfusion level of 12,500.

Three days after the second irradiation treatment, the hemangioma was slightly lighter in color and appeared smaller. The petechiae were still present, although decreased in number. However, at this time the platelet count was still only 10,000, and the hemoglobin had fallen to 8.8 Gm. No further therapeutic measures were performed, and 1 week after the completion of irradiation the platelets had risen to 38,000 and the patient was discharged. Three months later the platelet count was 260,000, and after 7 months was 390,000. The hemangioma itself continued to regress, and 7 months after treatment was almost completely obliterated (figs. 2 and 3).

Following the injection of the Cr-51 tagged platelets, an immediate rise in radioactivity was observed over both the liver and hemangioma but the radioactivity promptly leveled off over the liver at 5 minutes. A slow accumulation gradient of radioactivity was seen over the hemangioma during the next 20 minutes. During the following 50 minutes, the radioactivity slowly decreased over the hemangioma but remained constant over the liver. Counts for the heart and spleen were always lower than the liver and significantly lower than the hemangioma during the first 75 minutes. At 16 hours and 21 hours, the radioactivity over the hemangioma, spleen, and heart were lower than the liver (fig. 4).

DISCUSSION

Analysis of the hematologic data indicates that the infusion of the labeled platelet concentrate was followed by a very modest increase of the platelet counts in the peripheral blood and a subsequent rapid disappearance. Ac-
According to our previous investigation, two units of platelets contain at least $24 \times 10^{10}$ platelets. A platelet increment of at least 100,000 elements per cubic millimeter would be a very conservative estimation of the expected effects of the transfusion. This elevation has been previously observed in children with thrombocytopenias of different etiology. In a case of hemangioma and thrombocytopenia previously described, however, the platelet rise after infusion of concentrated preparations was suboptimal.

The initial rise in the radioactivity over the liver and hemangioma during the first 5 minutes probably represents immediate vascular filling of both structures. The further slow elevation over the hemangioma points to a coincident process of trapping of tagged platelets or perhaps a slow filling of sinusoids without trapping in a structure that may simply have a greater blood volume than the control organ. If the latter assumption were true, however, we would not expect the radioactivity to decrease slowly over the hemangioma, but rather to remain relatively stationary as in the liver, heart and spleen. At 21 hours the activity over the hemangioma had decreased markedly and was less than over the liver and spleen. This slow decrease in activity over the hemangioma suggests a pathologic alteration of the platelets such as thrombosis in the sinusoids and subsequent "detagging" so that free Cr-51 begins to leave the tumor at an increasing rate. Then, the ultimate activity over the hemangioma should depend on its vascular compartment alone. Since the 21-hour count over the hemangioma was of the same order of magnitude as over the other organs we concluded that the initial gradual rise and fall of radioactivity was the result of other than simple filling of a large vascular area.

Inasmuch as the spleen counts in this study were relatively low we also concluded that during the course of the experiment there were very few free circulating platelets outside of the hemangioma and therefore no significant
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Cr$^{51}$ Platelet Sequestration

Fig. 4.—Comparison of the radioactivity in the hemangioma with that of the liver, spleen and heart following Cr-51 tagged platelet infusion.

Splenitis sequestration. This finding is in disagreement with work of others, but it may be that in this particular case we have a more actively sequestrating hemangioma in competition with the spleen.

Since the petechiae gradually disappeared and the platelet count rose to normal levels after irradiating only the hemangioma, we also concluded that the radiation was the essential therapeutic factor in this patient. The tagged platelets certainly had no lasting therapeutic effect, since they were apparently all destroyed within approximately 1 day after the transfusion.

Summary
A case of giant hemangioma with thrombocytopenia has been presented. Isotopic studies with Cr-51 tagged platelets indicated that the basic mechanism of thrombocytopenia in this patient involved platelet sequestration in the tumor. The platelet response in the peripheral blood following irradiation of the hemangioma gives additional evidence that the thrombocytopenia is related to pathological changes within the hemangioma.

Summario in Interlingua
Es presentate un caso de hemangioma gigante con thrombocytopenia. Studios isotopic con plachettas a Cr-51 indicava que le mechanismo basic de thrombocytopenia in iste patiente includeva sequestration de plachettas in le tumor. Le responsa del plachettas in le sanguine peripheric post le irradiation del hemangioma rende additionalmente evidente que le thrombocytopenia es relationate con alterationes pathologic intra le hemangioma.

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REFERENCES

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