ACUTE MYELOBLASTIC LEUKEMIA*

CLINICAL AND PATHOLOGIC REPORT OF A CASE

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The patient, an unmarried white woman, 47 years of age, was brought to the hospital in an ambulance. Her chief complaint was pain in the abdomen. Two weeks previous to this examination, while walking, she had fallen on her back and after this she had become nauseated, faint and had suffered from intense cramplike pains across the upper part of the abdomen. The symptoms persisted, but she was able to continue her duties as a social worker until one week before admission to the hospital. Since that time she had been confined to bed. The abdomen became distended and tender, she had some fever and two days prior to admission she became jaundiced. She was constipated and strong cathartics had been required. The color of the urine was darker than usual.

In addition to the usual diseases of childhood, the patient had had influenza in 1918, and scarlet fever in 1926, which had been complicated by periarthritis of the knees and by nephritis. A tonsillectomy had been performed in 1928.

Examination: On admission to the hospital, the patient's temperature was 101° F., pulse rate 126, respiratory rate 20, blood pressure, 148 systolic, 74 diastolic. The patient appeared to be well developed and nourished; she was uncomfortable and seemed to be in a state of toxemia. The skin and sclerae were icteric. There were some discolorations, swelling and tenderness about the left ankle and there was tenderness over the region of the right kidney. Adenomata were palpable in the right lobe and in the isthmus of the thyroid gland. The lungs were resonant throughout and a few moist râles were present posteriorly over the base of the right lung. The heart was slightly enlarged; the sounds were clear, regular, distinct and of good quality. A soft blowing systolic murmur was audible over the apex and was not transmitted. The second aortic sound was accentuated. The peripheral vessels were normal. The abdomen was rotund and markedly distended. The liver was markedly enlarged; it had a smooth edge, was tense and tender and extended downward to a point two inches above the right iliac crest. No other tumor masses were palpable and no fluid wave was elicited.

The tentative diagnoses were hepatic abscess following hemorrhage into the liver; chronic glomerular nephritis; adenomatous goiter; contusion and strain of the left ankle.

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* Pathology Conference preceding a Staff Meeting.

A routine examination of the blood gave the following findings: Red cells, 4,890,000; white cells, 17,600. The differential count showed 57 per cent myeloblasts.

The clinical diagnosis was myeloblastic leukemia.

In addition to the laboratory findings shown in Table 1, there was a marked diminution in blood platelets; the coagulation time of the blood was fourteen minutes; the bleeding time was ten minutes. There was no retraction of the clot. Roentgenograms of the spine and genito-urinary tract showed no abnormalities. A blood culture was negative. The carbon dioxide capacity was normal. The urea clearance test showed some impairment of renal excretion.

Three days after the patient was admitted to the hospital, the spleen became palpable and was estimated to be four times its normal size. Areas of ecchymosis and petechial spots appeared over the entire body and slight bleeding occurred in the mucous membrane of the nose and throat. The spleen continued to enlarge, the leukocyte count continued to rise as shown in the table, and the number of erythrocytes decreased.

On the ninth day after admission to the hospital, the patient died suddenly. Death was attributed to embolus or hemorrhage into some vital center.

Necropsy was performed one hour after death.

Postmortem Examination

General description: The body was that of an adult, white woman, aged 47 years; it was well developed and well nourished; the weight was approximately 140 pounds and the body length was 162 centimeters. No rigidity was present. There was fairly marked lividity of the dependent parts, face, ears and upper parts of the chest, but there was no cyanosis or edema. The skin had a slight lemon tint. Petechial hemorrhages were present over the shoulders, thorax, abdomen and thighs. The hair was sparse and gray. The eyes were gray; the pupils were equal, regular, centric, dilated, and measured 6 mm. External examination of the ears and nose showed no abnormality. All the teeth had been removed and upper and lower dentures were present. The mucous membrane of the mouth showed no hemorrhages. No glands were palpable in the neck. The thyroid was irregularly enlarged; the right lobe was nodular and larger than the left. The chest was normal in shape and contour; resonance was not decreased. The breasts were small. The abdomen was distended but not rigid. A palpable mass was present in the right upper quadrant of the abdomen. A large, purplish colored, sub-

cutaneous hemorrhage was present in the right groin. Multiple hemorrhagic spots were apparent in the skin over both upper arms. Subcutaneous hemorrhages were the only abnormal findings on the extremities.

Incision: A semilunar incision was made joining both axillae and extending downward over the xyphoid process. A second midline incision joined this and extended to the symphysis pubis.

Abdomen: The subcutaneous fat was deep yellow in color; it measured 3 cm. in thickness and was dry. In the peritoneal cavity, the omentum extended over the small intestine and contained a moderate amount of deep yellow fat. The peritoneum was smooth and glistening. The liver was greatly enlarged and extended 12 cm. below the costal margin in the right mammary line, 14 cm. below the costal margin in the midline and 8 cm. below the left costal margin in the left mammary line. The dome of the diaphragm extended to the third vertebral space on the right side and the fourth rib on the left side. The contents of the upper abdominal cavity were displaced downward by the enlarged liver so that the lower pole of each kidney lay at the level of the brim of the pelvis. The stomach also was displaced downward. Otherwise the organs of the peritoneal cavity were in their normal positions. There were many enlarged, soft, yellowish-white lymph nodes surrounding the abdominal aorta.

Thorax: The right lung was firmly adherent to the thoracic wall by firm, old, fibrous adhesions and the right pleural cavity was completely obliterated. The left lung contained a few old, firm, fibrous adhesions at the apex and in the posterior portion. The heart was not enlarged and was free in its pericardiac sac.

The thyroid gland was almost entirely removed.

Portions of the lumbar vertebrae and the right tibia were removed for bone marrow examination.

Lungs: The right lung weighed 330 grams and measured 19x8x8 cm. It was composed of two lobes which were separated by a fairly deep interlobar sinus which contained numerous, old, fibrous adhesions. The pleura over the lung was thickened, most of the thickening being anterolateral; it was shaggy and grayish-white. A layer of brownish clotted blood was present on the lateral aspect of the upper lobe of the lungs. The lung was somewhat deflated; it was steel gray and had a moderate amount of anthracotic pigmentation and there were crepitations throughout. The hilar blood vessels were patent and clear and the pulmonary artery showed thickening of its wall and irregular areas of atheromatous change were present in its intimal coat. The bronchi were patent, they contained a small amount of mucoid exudate and there were a few fine, brown-

ish-red areas which suggested the presence of petechial hemorrhages in the mucous membrane. The hilar lymph nodes were somewhat enlarged and showed marked anthracotic pigmentation; they were soft and elastic for the most part, but a few showed calcified centers. Section of the upper lobe showed a dry, pinkish-gray cut lung surface with no areas of degeneration due to pneumonia or neoplasm. The marginal areas revealed slight emphysema and at the apex there were areas of brownish discoloration in that portion of the lung which was in apposition to the clotted blood on the pleural surface. Section of the upper portion of the lower lobe of the lung beneath an area of thickened pleura showed pinkish-red, firm lung tissue which contained no air and was surrounded by a zone of brownish discolored lung tissue. Section of the remaining portion of the lobe showed a pinkish-red cut surface with scattered, small, irregular areas of petechial hemorrhage. In the lower portion of the lobe, in comparison with the diaphragmatic surface, the lung was more firm, was deeper red in color and contained no air.

The left lung weighed 300 grams and measured 20x8x9 cm. It was composed of two lobes which were separated by a shallow interlobar sinus. The pleura was thin, transparent and glistening except for the presence of a few old, fibrous tags at the posterior portion of the apex. It was steel gray and irregular; blotchy areas of anthracotic pigmentation were present which were associated with numerous small purplish-red spots, particularly on the lateral aspect of the upper lobe and along the lower margin of the lower lobe. There was a moderate amount of marginal emphysema. The lung contained air throughout except beneath the purplish-red discolorations and in the posterior portion of the inferior lobe where it had a rubbery-consistency and did not contain air. The hilar blood vessels were patent, clear, and somewhat dilated. The intimal coat of the pulmonary artery showed irregular, yellowish thickening. The bronchus was patent and there were a few, small, petechial hemorrhages in the mucous membrane and a small amount of glary mucoid exudate on its surface. The hilar lymph nodes were enlarged; they were grayish-black but were elastic and showed no calcification. Section of the upper lobe showed a pinkish-red cut surface with hemorrhagic discoloration of the marginal areas and a few small pinkish-red petechial hemorrhages throughout the lung substance itself. Section of the upper portion of the lower lobe revealed whitish-gray lung tissue with a few small, brown pigmented areas. Section of the lower portion of the lobe showed a grayish-red, firm substance containing no air. Throughout the lower portion of the lobe there were larger, blotchy, pinkish-red areas. The marginal

tissue in this portion of the lobe was collapsed.

Heart: The heart weighed 350 grams. It was not enlarged and measured 12 cm. from apex to base. The apex was sharp and it was made up of the musculature of the left ventricle. The epicardium was thickened, pearly gray, less transparent than normal and had brownish pigmented areas scattered over it. The coronary vessels were visible as fine, tortuous, whitish-gray ridges coursing over the surface of the heart. There was only a moderate amount of subepicardial fat. The cavities of the heart were not dilated. The endocardium was slightly thickened and less transparent than normal. The foramen ovale was closed. Few abnormalities were seen in the pulmonary and tricuspid valves. The margins of the mitral valve which were moderately distorted were somewhat thickened. The aortic valve cusps were thick and disclosed some atheromatous degeneration, particularly about their attachment in the sinuses of Valsalva and the adjacent portion of the aortic ring. The valve rings measured: tricuspid, 11 cm., pulmonary, 6 cm., mitral, 8 cm., and aortic, 7 cm. The chordae tendineae were thin and web-like in the right ventricle and were somewhat thickened and hyalinized in the left ventricle. The papillary muscles showed some hypertrophy in the left ventricle. The columnae carneae were poorly developed in the left ventricle. The myocardium was softer than normal and measured 0.3 cm. in thickness in the right ventricle and from 1.5 to 2 cm. in thickness in the left ventricle. It was soft, friable and pale yellowish-brown with darker, blotchy, deeper reddish-brown areas scattered throughout. The intimal surface of the pulmonary artery was smooth and glistening. The aorta was somewhat thickened; it showed yellowish plaques in its intimal coat and a few areas of brownish discoloration. The coronary orifices were patent and they showed a small amount of atheromatous change but the lumen was not narrowed. The right coronary artery was considerably smaller than the left.

Liver: The liver weighed 3600 grams. The right lobe measured 29x17x9 cm. and the left lobe measured 22x10x7 cm. It was greatly enlarged, its capsule was irregularly thickened and there was a constriction across the central portion of the right lobe. Over this constriction, the capsule was very thick, opaque and yellowish-white. The liver was grayish-brown with irregular, lighter colored areas on its surface that were raised slightly above its general contour and varied from 1 mm. to 1 cm. in diameter. These slightly elevated areas were firmer than the surrounding liver substance. The anterior margin was rounded, the liver was very much firmer than normal and on section showed a greenish-brown colored

cut surface with indistinct lobular markings, with darker colored peripheral zones and paler areas around the central veins of the lobules. There were non-encapsulated, yellowish-white, glistening, homogeneous areas scattered throughout the liver, varying from 2 mm. to 1 cm. in diameter. In some areas the structure of the liver was almost completely replaced by pale yellowish-white tissue which corresponded with the lobular arrangement of the liver substance but which had a waxy, glistening appearance. The inferior vena cava, portal vein and hepatic vein were patent.

The gallbladder contained about 25 c.c. of glistening, glary bile. Its wall was not thickened and its mucous membrane was intact. There were no stones present. The cystic duct and hepatic duct were patent.

The glands about the gastrohepatic ligament were greatly enlarged, soft and friable. The hepatic duct was patent.

Pancreas: The pancreas weighed 100 grams. It measured 17x4x1 cm. Its capsule was edematous and somewhat thicker than normal. There were many enlarged lymph nodes about the head of the pancreas. On section, it was yellowish-brown, fairly uniform in appearance and showed no areas of inflammation or ay tumor mass.

Spleen: The spleen weighed 800 grams and measured 19x12x7 cm. It was regular in outline, normal in contour but was greatly enlarged. Its capsule was purplish-gray, slightly wrinkled and had a few small, depressed, scarified areas. On section, it was deep, purplish-red, homogeneous, and was scattered with fine, whitish colored spots. There was marked hyperplasia of the splenic pulp.

Kidneys: The left kidney weighed 270 grams and measured 13x5x4 cm. It was irregular in outline and the posterior aspect was greatly distorted. The capsule was pearly gray, somewhat thicker than normal but stripped fairly readily, leaving a smooth, pale yellowish-brown kidney substance. The distorted posterior half of the kidney showed an irregular scar that involved the middle and inferior pole. The scarred, depressed area was yellowish-brown and multiple, fine, petechial hemorrhages were scattered over it. Section of the kidney substance revealed slight bulging and the cortex had a fine, granular appearance. It was pale, yellowish-brown with a sprinkling of lighter yellow areas which were present particularly about the medullary tissue where it was in apposition to the cortex. The medullary tissue contained purplish-brown streaks which were suggestive of petechial hemorrhages. The pelvis was not dilated but was somewhat distorted by the scarring of the kidney. Its mucous membrane was finely irregular and had fine, brownish col-

ored hemorrhagic spots. There were no areas of ulceration or scarring.

The right kidney weighed 307 grams and measured 15x8x4 cm. It was regular in outline, its shape was normal and it was somewhat enlarged. Its capsule was thickened, pearly gray, less transparent but stripped fairly readily leaving a pale yellowish-brown, smooth surface which had a scattering of fine, lighter colored pin-point spots. The kidney substance bulged slightly above the cut margin, and showed similar, paler zones about the medullary substance. The cortex had a finely granular appearance and was fairly well differentiated from the medulla. Petechial hemorrhages were seen in the medullary portion and in the mucous membrane of the pelvis of the kidney. The pelvis was not dilated and the mucous membrane, apart from the hemorrhages, showed nothing abnormal.

Bladder: The bladder was empty and the wall was somewhat thickened. There was no evidence of cystitis. The mucous membrane was irregularly rugated and showed no areas of ulceration or scarring.

Genital organs: The uterus measured 5.5x3x2 cm. It was small and atrophic and contained a rounded, pedunculated fibroid tumor 4 cm. in diameter which was attached to the fundus by a narrow pedicle. Protruding from the right anterolateral aspect of the uterus, near the fundus, was another rounded tumor mass measuring 3 cm. in diameter. The uterine wall was 1 cm. in thickness. The endometrium was smooth and regular and the cervix contained a large quantity of white, thick, mucoid secretion. There were a few cysts in the cervix. The cavity of the uterus measured 2x1.5 cm.

Each of the ovaries was 2.5 cm. in length and each measured 1.5 cm. transversely. They were yellowish-white and irregularly scarred. The ovarian tubes appeared normal.

Adrenals: The right adrenal gland weighed 9 grams and measured 6x2.5x1 cm. The left adrenal weighed 8 grams and measured 6x2x1 cm. They were yellowish-brown with lighter yellow spots, were uniformly firm in consistency and on section showed fairly deeply pigmented, narrowed, cortical substance with considerably more medullary tissue than normal.

Thyroid: Examination of the thyroid revealed a thickened, pearly gray capsule, extremely firm in consistency, which was nodular and on section showed a greatly increased stroma separating partially encapsulated early adenomata. In some of these early adenomata marked recent hemorrhage was present.

Gastro-intestinal tract: The stomach was small and contracted

and contained a small amount of mucoid brownish material. The serous surface was smooth. The mucous membrane was edematous and covered by a mucoid exudate. The pyloric ring was not hypertrophied and there were no areas of ulceration or scarring. The mucous membrane of the duodenum showed irregular, fine, small swellings, but no areas of ulceration or scarring were seen. The entire gastro-intestinal tract showed a marked hyperplasia of the solitary lymph nodes to the extent of the production of almost pedunculated tumor masses in some parts of the lower ileum. Here and there in the small intestine, injected areas suggesting recent petechial hemorrhage were present. In the cecum this hyperplasia involved almost the entire mucous membrane. The appendix measured 7 cm. in length and 0.5 cm. in diameter. The lumen was greatly narrowed particularly in the distal portion where the wall was thick, boggy, edematous and sclerosed.

Microscopic Examination

Lungs: Sections of the left lung showed areas of relative atelectasis; there was no acute bronchitis, pneumonia nor leukemic infiltration.

Sections of the right lung were similar to those of the left, except that there were numerous small areas of subpleural hemorrhage; there was no leukemic infiltration.

Heart: There was considerable fat infiltration in the right myocardium and fairly large areas of hyaline degeneration in the left papillary muscle; otherwise, there was no significant abnormality.

Liver: There was no thickening of the capsule nor increased fibrous tissue, but many lobules contained considerable fat infiltration. Throughout, there was a diffuse infiltration in the periportal spaces and, to a lesser extent, in the lobules, by large relatively undifferentiated cells of variable size and character. In some areas, the accumulation of these cells was such as to form nodules which were from a few millimeters to a centimeter or more in diameter. The sinusoids were injected and contained many of these cells. The infiltration was of a leukemic type.

Section of the gallbladder showed no leukemic infiltration.

Pancreas: There was no leukemic infiltration.

Spleen: There was neither thickening of the capsule nor increased fibrous tissue. The lymphoid follicles were greatly diminished. There was marked hyperplasia of the splenic pulp and numerous mitotic figures were present. The sinuses and pulp tissue of the spleen were made up largely of cells of variable size and character,

apparently of myeloid origin, as indicated by the presence of large numbers of eosinophilic leukocytes and myelocytes, and myelocytes of neutrophilic and basophilic type. The predominant cell, however, was of the myeloblastic type in various stages of differentiation. There were numerous megalokaryocytes.

Kidneys: There was considerable diffuse leukemic infiltration in the cortex and medulla of both kidneys. In some areas, there was well marked arteriolar sclerosis, but the majority of blood vessels and glomeruli showed no significant sclerosis. There was cloudy swelling of the renal epithelium.

Genital organs: Sections of the uterus showed slight chronic cervicitis, multiple fibromyomata and atrophy of the endometrium. There was no leukemic infiltration.

Sections of the ovaries showed a few small peritoneal inclusion cysts and, in one ovary, there were small collections of myeloid cells diffusely distributed in the stroma.

Adrenals: A few areas of myeloid infiltration in the medulla and cortex of each adrenal were present.

Thyroid: Section of the thyroid gland revealed a colloid goiter, with irregular lobulation and increased stroma; there was no lymphoid or myeloid infiltration. A large amount of colloid material was present and early adenomatous change was observed in some of the lobules. There was an encapsulated adenoma with extensive recent hemorrhage but there was no leukemic infiltration.

Gastro-intestinal tract: Section of the stomach showed no abnormality of significance.

Section of the small intestine showed small and localized areas of myeloid hyperplasia in the mucosa.

Lymph nodes: Peri-aortic and mesenteric lymph nodes showed marked diffuse hyperplasia of cells similar to those in the spleen, with numerous mitotic figures and, in sections stained with eosin, methylene-blue, Wright's and Giemsa's stain, numerous eosinophilic leukocytes and myelocytes were seen. The predominant cell, however, was of the myeloblastic type.

Bone marrow: Sections from the tibia showed normal fatty bone marrow, with no myeloid hyperplasia.

Sections from the spinal bone marrow showed diffuse myeloid hyperplasia, with numerous mitotic figures and large numbers of myeloblastic cells.

The pathologic diagnoses were as follows:

1. Acute myeloblastic leukemia with myeloid hyperplasia of the

spleen, lymph nodes, liver and intestine and myeloid infiltration of the kidneys, adrenals and ovary.

2. Petechial hemorrhages of the lungs, kidneys and intestines, and ecchymosis of the skin on the groin.

3. Multiple fibromyomata of the uterus.

4. Colloid goiter, with multiple adenomata.

5. Right pleural adhesions and an old infarct of the right kidney.

Clinical Discussion

C. L. Hartsock: This case is interesting because all the symptoms seem to have appeared since the time of the accident when the patient fell on her back. It was the consensus of opinion among the physicians here that some internal injury associated with a ruptured viscus and hemorrhage had occurred as the result of the trauma, and it remained to be discovered which organ had been injured and what treatment should be instituted. Immediate operation seemed to be indicated and consultation with the surgeons confirmed this opinion, but this was delayed while further blood studies were made. A differential blood count was made to determine whether the blood clot had become infected and this gave the clue to the correct diagnosis.

An interesting speculation in this case is what would have happened if the patient had been seen one week earlier. The extremely rapid progress of the leukemic condition suggests that no finding of diagnostic significance would have been discovered in the blood one week previous to our examination and the patient undoubtedly would have been subjected to a useless operation.

Table I

Blood Findings in a Case of Acute Myeloblastic Leukemia

Day after admission to Hospital	*1*	*3*	*4*	*5*	*6*	*7*	*8*
Red Blood Cells	4,890,000			3,920,000		3,610,000	
Hemoglobin	87.0%			71.0%		68.0%	
White Blood Cells	17,600	16,000	15,100	14,700	26,000	36,000	48,000
Neutrophiles	32.0%	14.0%					
Eosinophiles	4.0%	3.0%					
Lymphocytes	7.0%	7.0%					
Myeloblasts	57.0%	75.0%					
Myelocytes	0	1.0%					
Color Index	0.88			0.91		0.94	
Icteric Index	40.0						
Blood Urea	33.0		78.0			105.0	
Creatinine			1.9		2.8	2.7	
Cholesterol						300.0	
Chlorides						478.0	