SURGICAL CLINICOPATHOLOGICAL CONFERENCES

OF THE

MASSACHUSETTS GENERAL HOSPITAL

BENJAMIN CASTLEMAN, M.D.

Chief, James Homer Wright Pathology Laboratories, Massachusetts General Hospital
Professor of Pathology, Harvard Medical School

JOHN F. BURKE, M.D.

Assistant in Surgery, Massachusetts General Hospital
Instructor in Surgery, Harvard Medical School

Boston

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IN THIS SAME SERIES

CLINICOPATHOLOGICAL CONFERENCES
OF THE
MASSACHUSETTS GENERAL HOSPITAL
Selected Medical Cases

Benjamin Castleman, M.D.
and
H. Robert Dudley, Jr., M.D.

To

Richard Clarke Cabot

and

Tracy Burr Mallory

PREFACE

In the cases presented at clinicopathological conferences, post-mortem findings usually form the basis of the clinicopathological correlation, but an equally instructive correlation can be derived from surgical operative findings. In the early days of the CPC's of the Massachusetts General Hospital, Dr. Richard C. Cabot often selected surgical cases for discussion, and for most of those exercises he called upon Dr. Hugh R. Cabot, his brother, and Dr. Edward L. Young, both of whom were surgeons, to present the differential diagnosis. The history and development of the CPC as a teaching exercise are outlined in the introduction to Case 1 in this book.

As for the earlier book of medical cases,* we have selected surgical cases discussed during the past twenty-five years, the majority of them being within the last ten years. Because so many diagnostic procedures have since become available, cases of earlier vintage did not seem sufficiently instructive to warrant proportionate inclusion. This volume of 50 cases covers a wide spectrum of problems seen in clinical surgery today. It does not include cases in the fields of orthopedic surgery and neurosurgery, since separate volumes for these specialties are in preparation.

*Castleman, B., and Dudley, H. R., Jr. *Clinicopathological Conferences of the Massachusetts General Hospital: Selected Medical Cases.* 295 pp. Boston: Little, Brown, 1960.

Unlike the medical cases presented at CPC's, which usually reach the post-mortem stage, many of the surgical cases conclude with the operative findings. The additional follow-up history that was obtained in the preparation of this book has provided an opportunity to record the progress of the disease and to learn whether the patient was benefited by the operation. This information is recorded in the addenda to the cases.

In some cases subsequent advances in knowledge of the disease under discussion merited the addition of a comment by the discussant, the pathologist or another specialist. To document more fully the clinical, radiologic and pathological findings, several illustrations not previously published have been included.

The table of contents, list of discussants and the index enable the reader to single out a case on the basis of discussant, clinical features, and anatomical diagnosis.

It is a pleasure to record the contribution of Mrs. Betty U. Kibbee, assistant editor of the Case Records, in the preparation of the manuscript and of Dr. Jack R. Dreyfuss, associate radiologist, in the selection and description of many of the roentgenograms.

B. C.
J. F. B.

Boston

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CONTENTS

CASE 1

VINCENT P. DOLE, M.D.

Sudden Abdominal Pain and Mass in Woman with Lupus Erythematosus

Introduction

DR. PAUL D. WHITE: When the Scientific Symposia Committee began to arrange the program for this occasion,* it was perfectly obvious that we must have a clinicopathological conference, for which this hospital is justifiably famous and which is at the present time becoming popular all over the world. Without more ado I shall introduce Dr. Benjamin Castleman, the successor of many noted pathologists in this hospital.

DR. BENJAMIN CASTLEMAN: Before proceeding with the case today, I should like to say a few words about the history of the clinicopathological conference. I am sure that very few people realize that the idea originated in the mind of Dr. Walter B. Cannon when he was still a medical student in the late 1890's. He roomed with a law student who returned each evening full of excitement about the discussions at the Harvard Law School among professors and students who were using the case system that had been introduced by Professor Langdell, Dean of the Law School. Cannon, on the other hand, had been subjected all day long to a series of didactic lectures and recitations. Why, he asked, couldn't the case method be introduced into the teaching at Harvard Medical School?

At a meeting of the Boston Society for Medical Improvement on March 5, 1900, Cannon, who was then a fourth-year medical student, presented a paper entitled "The Case System in Medicine,"[1] in which he made the following remarks:

> The idea of using printed records of cases as centers of interest in studying medicine occurred to me some two years ago. Since that time I have been watching carefully for every possible opportunity to apply the method, and have tried to see all the objections which might be raised against the plan. It was only when I was fully convinced that a study of real histories could be made feasible in teaching medicine that the scheme was brought forward. The first case studied under the system was given out by Dr. G. L. Walton to a small class in neurology last December, and it revealed at once the usefulness of the plan. In January Dr. J. J. Putnam gave out printed cases in his course in neurology, and since then Dr. Richard C. Cabot, Dr. J. William White, of Philadelphia, and Dr. C. E. Riggs, of the University of Minnesota, have put the method to test. . . .

It was Dr. Cabot, however, who was responsible for promoting the CPC and getting it on the road. At this same meeting Dr. Cabot spoke as follows:[2]

> There is one point not yet emphasized as much as it should be in regard to this case system, and that is the *pleasure* of it. The touch with the men is delightful. They answer up in a way I have never heard them in any other course, because questions are thrown at them so constantly that they must be wide awake and because they are vitally interested in the story of the case. . . .

President Charles W. Eliot spoke next, presenting a paper entitled "The Inductive Method Applied to Medicine."[3] He began:

> This discussion is one very interesting to me. In the first place, it carries me back about thirty years to the time when Professor Langdell first came to Cambridge to teach law. I had something to do with that myself; it was largely owing to the statements I had heard him make as to the proper method of teaching law. He described that method in a way which inevitably commended it strongly to a man who had been brought up as a chemist. Professor Ames spoke of it just now as the inductive method. That is exactly what it is. It is the method of inductive reasoning applied to law, and that is what Mr. Cannon's method is applied to medicine. It is simply the universal method of scientific induction. . . .

Over the years the CPC has changed in format, but it remains an exercise in inductive reasoning and clinicopathological correlation. Unfortunately, in some hospitals cases impossible to diagnose are selected, and for that reason the CPC has been adversely termed "a guessing game," but that is not true if the case is selected wisely. The properly chosen case lends itself to a discussion of the differential diagnosis, with clinical clues suggesting

*The One Hundred and Fiftieth Anniversary Convocation of the Massachusetts General Hospital, at which this case was presented.

the correct diagnosis. As I stated recently in the preface to a volume containing 50 selected medical cases discussed at these conferences:[4]

> It is less important to pinpoint the correct diagnosis than to present a logical and instructive analysis of the pertinent conditions involved. On the rare occasions when the correct diagnosis is esoteric or almost unattainable, if the discusser emphasizes the practical clinical problems it doesn't matter if the answer is wrong. In fact, it is well for the student to realize that his professor is not always right, and for the instructor to learn early in his career not to fear being wrong. Allowing the young clinical staff member to discuss a CPC before his peers has undoubtedly produced a better teacher.

The case today will be discussed by Dr. Vincent P. Dole, a graduate of Harvard Medical School in 1939 and a member of the house staff at this hospital in the early 1940's. After his stay at the Massachusetts General Hospital he went to the Rockefeller Institute, and thereafter he joined the Navy and through a stroke of luck, I suppose, was assigned to the Rockefeller Institute for about five years in the Medical Naval Research Unit. After the war he came back to this hospital to work with Dr. Bauer and the Arthritis Group in 1946 and 1947 and then returned to the Rockefeller Institute as an associate member. He was promoted to a full member in 1951, and now that the Institute has become a University he is a full professor. Professor Dole, it's all yours.

Presentation of Case*

First admission. A twenty-six-year-old woman entered the hospital because of pain in the joints.

Nine years previously she experienced the gradual onset of migratory arthralgia involving the elbows, knees and ankles. She was also anorectic, and there was a transient erythematous rash over the face and trunk. X-ray films of the hands, elbows, shoulders, feet, ankles and knees were normal, as were films of the chest. The hemoglobin was 10 gm. per 100 ml. L.E.-cell tests were negative, and an electrocardiogram was normal. Slight relief was obtained with a salicylate regimen. Four years before admission, during an episode of fatigue and anorexia, Raynaud's phenomenon in the hands and feet and painful swelling of the joints of the right ankle and knee and both hands developed. An electrocardiogram was normal, and a blood Hinton test was negative. Five months later she again became anorectic, with pain, swelling and tenderness of the ankles, stiffness of the knees and a diffuse malar erythematous rash. The hemoglobin was 12.1 gm.; the nonprotein nitrogen was 16 mg., and the total protein 7.5 gm. (the albumin 5.3 gm., and the globulin 2.2 gm.) per 100 ml.; the serum electrophoretic pattern was normal. X-ray films of the chest and another electrocardiogram were normal. The pain, swelling and tenderness of the joints were relieved by salicylate therapy. Subsequently, pain occasionally occurred in the knees, ankles and heels. An L.E.-cell test was positive. Three months before entry the patient again noticed swelling, stiffness and pain in the ankles, but relief was no longer obtained with salicylate therapy. Malar erythema appeared sporadically, lasting for about a week. Two months before entry and again one month later the urinary sediment contained numerous red cells. L.E.-cell tests were positive. The ankles and shoulders were painful. Urinary frequency developed.

Mastoidectomies were performed because of persistent otitis media seven and nine years before admission.

Physical examination showed a well nourished woman in no acute distress. Slight malar erythema was present. The lungs were normal. The heart was not enlarged, but a Grade 2 apical systolic murmur was audible. The abdomen was normal. The skin over the dorsa of the hands was atrophic. The left shoulder and elbow were tender, and their motion was limited; the neck was slightly tender on movement, and the left ankle was swollen and tender.

The temperature, pulse, respirations and blood pressure were normal.

The urine gave a + test for protein; the sediment contained numerous red cells, 2 to 3 white cells and a few granular and hyaline casts per high-power field. The creatinine clearance was 124 liters per twenty-four hours. Examination of the blood revealed a hematocrit of 41 per cent, a corrected erythrocyte sedimentation rate of 50 mm. per hour and a white-cell count of 10,000, with 68 per cent neutrophils, 1 per cent eosinophils, 30 per cent lymphocytes and 1 per cent monocytes. The urea nitrogen was 12 mg. per 100 ml. X-ray films of the chest were normal. With salicylate therapy in a high dosage there was some improvement in the joint symptoms, and the patient was discharged on the ninth hospital day.

Second admission (seven months later). She remained relatively well except for persistent urinary frequency until two months before entry, when there was an episode of nonradiating pain in the middle and lower portions of the abdomen. An upper gastrointestinal series was normal. The hematocrit was 37 per cent. One hour before admission she experienced the sudden onset of severe, continuous pain in the right flank that radiated to the upper portion of the right side of the abdomen and was accompanied by nausea.

Physical examination showed a pale woman complaining of pain in the right costovertebral angle and the right upper quadrant of the abdomen, with exacerbation by breathing. The bowel sounds were decreased. In the right upper quadrant there was a large, smooth, very tender, nonpulsatile, firm mass that descended with respiration. Tenderness was present in the right costovertebral angle, with rebound tenderness that was referred to the right upper quadrant. The heart and lungs

*Case Records of the Massachusetts General Hospital (Case 1–1962). *New Eng. J. Med.* **266**:42–49, 1962.

showed no change from the previous examination. Rectal examination was negative.

The temperature was 101°F., the pulse 100, and the respirations 20. The blood pressure was 130 systolic, 70 diastolic.

The urine (catheterized specimen) gave a ++ to +++ test for protein; the sediment contained 150 to 200 red cells and an occasional white cell per high-power field; a culture was negative. Examination of the blood revealed a hemoglobin of 9.2 gm. per 100 ml., a hematocrit of 30 per cent and a white-cell count of 27,500, with 76 per cent neutrophils, 3 per cent band forms, 1 per cent eosinophils, 1 per cent monocytes, 15 per cent lymphocytes and 4 per cent atypical lymphocytes. The platelets were normal, and the erythrocytes showed + anisocytosis and poikilocytosis. The bleeding and coagulation times and clot retraction were normal. The bilirubin was 0.4 mg., the fasting sugar 140 mg., and the urea nitrogen 17 mg. per 100 ml. The prothrombin content was 100 per cent, the transaminase was 30 units, and the amylase was 24 Russell units. On x-ray films of the abdomen (Fig. 1) a large homogeneous density was

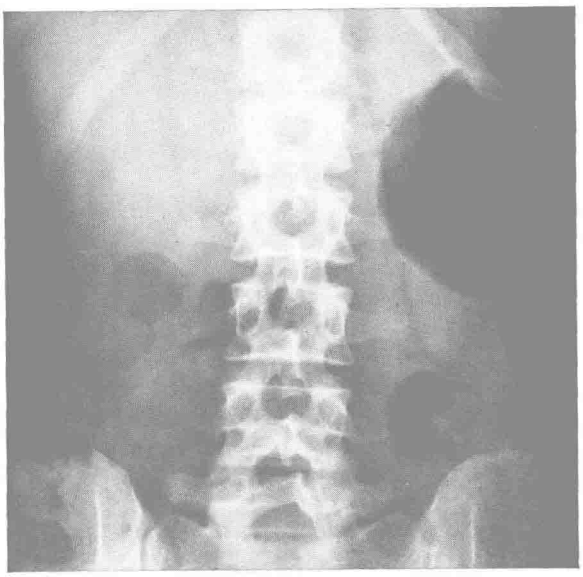

FIGURE 1. Film of the abdomen, defining a large mass in the right upper quadrant. The right psoas border cannot be seen.

visible in the right upper quadrant; the right psoas shadow was obscured, and the right renal outline was not demonstrable. Intravenous pyelograms demonstrated markedly delayed excretion and poor concentration of the contrast material in the right kidney, which was poorly outlined (Fig. 2); the left kidney appeared normal. Films of the chest showed slight cardiac enlargement.

On the second hospital day the diameter of the mass in the right upper quadrant of the abdomen was about

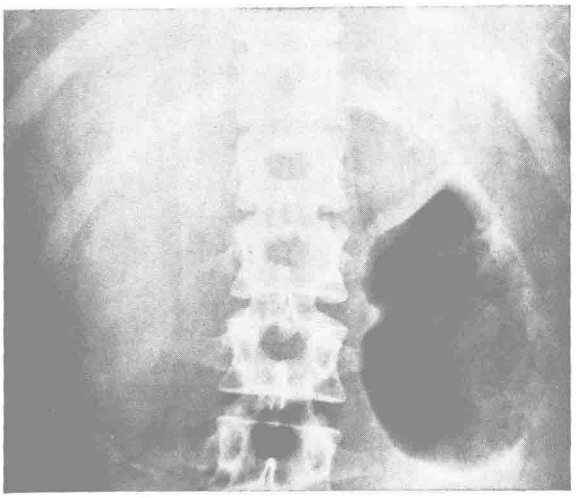

FIGURE 2. Intravenous pyelogram, showing minimal excretion of contrast material by the right kidney after 60 minutes.

2 cm. larger. The blood pressure was 190 systolic, 100 diastolic. An x-ray film of the abdomen on the next day showed a large mass in the right retroperitoneal area that appeared to involve the right kidney. Cystoscopic examination revealed elevation of the right side of the bladder, with clear urine flowing from both ureteral orifices. A right retrograde pyelogram (Fig. 3) demonstrated marked calyceal distortion, with the calyxes spread over a large cystic structure in the lateral portion

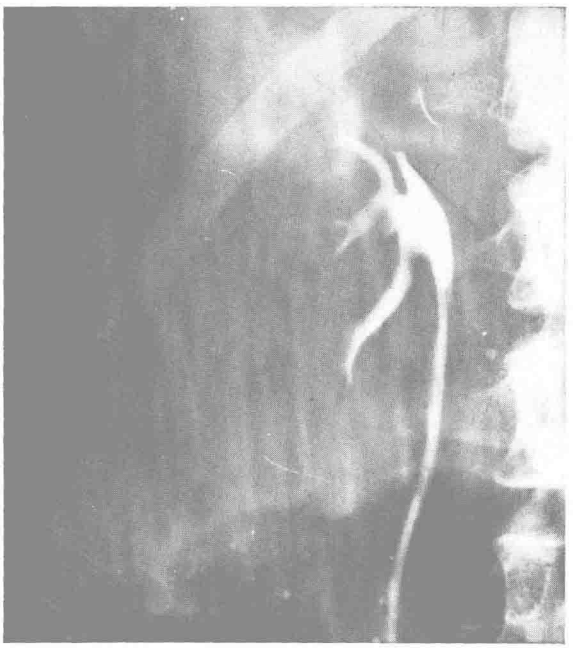

FIGURE 3. Right retrograde pyelogram, revealing a lateral pressure defect against the entire renal collecting system.

of the kidney; there was anterior displacement of the right kidney and ureter. Cytologic examination of urine obtained from the right kidney for malignant cells was negative, and a culture showed no growth. The temperature ranged between 99 and 102°F. during the hospital course. Penicillin and streptomycin were administered, and the abdominal tenderness decreased.

An operation was performed on the eighth hospital day.

Differential Diagnosis

DR. VINCENT P. DOLE*: In accepting Dr. Castleman's kind invitation to lay my neck across his chopping block today, I had a feeling of pride to be asked to mingle my blood with that of the many distinguished people who have bled on the same stump. Also, I recalled how much I learned from these conferences in my student days, and with the pride there was a feeling of duty, too. The pathologists at the Massachusetts General Hospital who have successively occupied the chair have pioneered a truly revolutionary idea in clinical teaching – namely, to abolish the concept of the infallible professor. When a physician is obliged to reach the limits of his knowledge in public, he not only exposes his own limitations, but also tests the limits of currently available medical knowledge. These public tests bring ignorance to light, and I think that they have been largely responsible for the happy and productive marriage of basic laboratory science with clinical practice in our country. Therefore, it is with a feeling of duty and no deep feeling of embarrassment about my limits that I speak today. To some extent they are the limits that we all have and that the younger people in the audience will push back.

This case concerns a young woman with typical signs and symptoms of systemic lupus erythematosus who had an acute episode of a somewhat bizarre nature leading to surgical intervention. The first problem, that of deciding the underlying chronic disease, is relatively simple since the picture was classic. The patient was of the right age and sex for systemic lupus erythematosus, and she had the characteristic rash, the joint symptoms and Raynaud's phenomenon, all of which are frequent in this disease, in addition to nephritis, as evidenced by the hematuria. Furthermore, the clinical diagnosis was confirmed by a number of positive L.E.-cell tests. Thus far, I feel on relatively safe ground and immune from the pathologist because in such a disease it is the clinician who first names the syndrome, and the pathologist subsequently describes the lesions found.

However, as we pass to the acute episode the cards are definitely in the hands of the pathologist because the additional factor entering into the picture must have been defined by anatomical examination. The outstanding new finding was a large mass in the right upper quadrant and flank that had developed within the previous few hours. The absence of the mass over a much longer period is clearly established because the patient had been examined on many occasions, and the abdomen undoubtedly had been carefully palpated at the time of the previous attack of abdominal pain that led to a gastrointestinal series. The rapidity of the development excludes a large, solid tumor or a cyst of the usual sort and is against an insidious type of perinephric abscess.

Two possible explanations of this sudden expansion are a rapidly developing inflammatory exudate or an effusion of blood. I would set aside the diagnosis of an inflammatory exudate in this case for a number of indirect reasons. First, the fever and chills that one might expect with such a massive infectious process were lacking. She apparently was not prostrated, since the attending physicians were able to study her for eight days before proceeding to an operation. The fact that she did not receive steroids simplifies my job somewhat since that therapy might have masked the signs of reaction to an inflammatory process or to perforation of a viscus. For this conservatism, which I remember from my discipline in the Arthritis Clinic, I tender herewith my thanks to my old chief, Dr. Walter Bauer. On the other hand, the findings in this patient are consistent with perirenal bleeding. The cardinal symptoms in the classic case of perirenal hemorrhage are sudden flank pain, a rapidly developing mass and evidence of blood loss, all of which were exhibited by this patient. She was pale, with tachycardia and a drop in the hemoglobin and hematocrit. Patients with this syndrome often have anorexia without the acute manifestations of intestinal obstruction, and the symptoms frequently subside simply under observation, as apparently occurred in this case. For these reasons, I am led to a provisional diagnosis of perirenal bleeding.

There are, however, a few features that are slightly disturbing and require a little more investigation. The fact that the mass was very tender is not typical of retroperitoneal hemorrhage according to the reported cases.[5-11] Also, the descent of the mass with respiration is perplexing since it should not have been movable if it was wholly retroperitoneal. Thus, if my working diagnosis is correct there must have been extension of the bleeding into the mesentery or other movable tissue. Finally, the x-ray films showed a cystic mass. At this point I should like to ask Dr. Dreyfuss to interpret the radiologic findings.

DR. JACK R. DREYFUSS: All the films that we have selected for demonstration are from the second admission. Since the film of the chest was taken with the patient in a supine position the cardiac silhouette is slightly magnified, but I think it is safe to say that mild cardiac enlargement is shown. The lungs are clear, with no evi-

*Member and Professor, Rockefeller Institute, and Physician to the Hospital of the Rockefeller Institute, New York, New York.

dence of hilar adenopathy. The preliminary film of the abdomen (Fig. 1), taken before the intravenous pyelograms, shows several interesting abnormalities. First of all, a large mass is evident in the right upper quadrant. I cannot define its margins, nor can I see the right renal shadow. The left psoas border is well defined, but the right psoas border cannot be seen. There is air in the hepatic flexure, which is riding just above the right iliac crest and therefore is depressed. The thirty-minute film from the intravenous pyelographic study shows no evidence of excretion on the right side. On the sixty-minute film (Fig. 2) contrast material is seen in apparently normal calyxes on the left side, but on the right side there is a significant lack of concentration and excretion, and only a small amount of contrast material is visible in two of the calyxes.

A right retrograde pyelogram (Fig. 3) was also done, and contrast material injected by catheter filled the drainage system very well. The calyxes are sharply cupped, with no evidence of pyelitis or hydronephrosis. There is, however, a moon-shaped pressure defect against the entire drainage system. One gains the impression of a mass deforming the calyxes and infundibula by contiguous pressure. The hepatic flexure is still depressed. The calyxes that we saw filled with dye on the intravenous pyelogram are now shown to be an upper calyx and one of the calyxes of the middle group.

DR. DOLE: The mass was described as movable by the examining clinician. Would you interpret it as an enlarged kidney, or do you find evidence of another type of mass that is likely to be movable?

DR. DREYFUSS: I cannot answer the question about enlargement of the kidney because I cannot see the renal outline. The mass in the right upper quadrant was probably movable because the hepatic flexure occupies varying positions on several films.

DR. DOLE: I notice that the mass was described as cystic. As I understand it, a cyst is a fluid-filled structure with a capsule, whereas the evidence on these films suggests only a round mass occupying space within the kidney. Can you clarify that point?

DR. DREYFUSS: I don't think one is justified in calling it a cystic structure. The only positive statement that can be made from the films is that a mass is deforming the calyceal system, and it could be either solid or cystic.

DR. DOLE: The clinical findings seem sufficiently definitive of a perirenal hematoma to make it the most reasonable working diagnosis, and I shall turn next to a number of derivative questions. If this lesion was a perirenal hematoma, what was the source of the bleeding? What is the proper treatment, and what prognosis should one expect? Finally, what, if any, relation did it have to the underlying disease of systemic lupus erythematosus?

By far the most common cause of a perirenal hematoma is trauma, which can be excluded in this case. A great number of causes of spontaneous renal bleeding have been listed, the most frequent being nephritis and an infection of the kidney.[5] In the present case the latter seems fairly well ruled out by the careful studies of the urine. The word "nephritis," of course, is nonspecific, and at the time that many of the early cases of perirenal hematoma were observed the differentiation of nephritis was not sufficiently advanced to give much information on this point. However, it is perfectly clear from the reports that there was vascular disease of the kidney of one form or another in many of the cases of spontaneous perirenal bleeding. Statistically, the most probable site of the bleeding is the cortex of the kidney, with expansion and rupture through the capsule to the periphery.

In the present case we have two significant pieces of evidence pointing to an intrarenal site of the primary lesion. The first is the round mass that was shown by the x-ray films to be distorting the calyceal system, giving the impression of a space-occupying, enlarging structure. The second finding, which is especially interesting, is the development of acute hypertension. A normal blood pressure was recorded on a number of occasions beforehand and even at the time of admission for the final acute episode, but on the next day the patient definitely was hypertensive, and that reading is confirmed by the expansion of the heart shadow described by the roentgenologist. It seems highly likely that the hypertension was a symptom of renal ischemia. If the circulation to the kidney is occluded or diminished experimentally, within a matter of hours, usually within twenty-four hours, one can observe a definite rise of the blood pressure. Therefore, we have an additional physiologic clue to the anatomic site of the lesion.

The treatment of this condition almost certainly is surgical, and one might even ask why the operation was so long deferred in this case. In 1933, a large series of perirenal hematomas was summarized,[5] including cases traced back for over two hundred years. When the outcome in 178 cases was analyzed according to treatment, it was found that all the 47 patients who had been treated without surgery died during the acute episode. When the surgeons evacuated the clot and tamponaded the bleeding area, the mortality rate fell to approximately 40 per cent. In modern times virtually all perirenal hematomas have been treated by nephrectomy, with a mortality of about 25 per cent.

However, I think that the prognosis in the present case was far more grave because the spontaneous bleeding in and around the kidney certainly reflected serious vascular disease. If, as one must suspect, the vascular disease was part of a generalized disease involving the blood vessels, then the condition was both severe and generalized, indicating a poor outcome. On reading the literature, I found about a dozen reported cases[6-11] of periarteritis nodosa accompanied by perirenal bleeding, and almost all those patients died within a year, many of them soon