Staff Meeting Bulletin
Hospitals of the » » »
University of Minnesota

Pernicious Anemia and Carcinoma of the Stomach

Volume XIV | Friday, December 4, 1942 | Number 9

STAFF MEETING BULLETIN
HOSPITALS OF THE . . .
UNIVERSITY OF MINNESOTA

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INDEX

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during the school year, October to June, inclusive.

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William A. O'Brien, M.D.

I. LAST WEEK

Date: November 27, 1942

Place: Recreation Room
Powell Hall

Time: 12:15 to 1:15 p.m.

Program: "Highlights of 1942 Minnesota Football Season"
Ralph Piper, Narrator

Attendance: 111

Gertrude Gunn,
Record Librarian

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II. MEETINGS

1. BACTERIOLOGY SEMINAR

December 10, 4:30 p.m. in room 214 Millard Hall.

"Pauling Work on Preparation of Antibodies in Vitro"

Margaret Houlton

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2. ANATOMY SEMINAR

Saturday, December 5, 11:30 a.m. in room 226, Institute of Anatomy.

"The chemical and physical composition of the developing human skeleton"

R. E. Scammon

- - -

3. ST. PAUL SURGICAL SOCIETY

Thursday, December 10, 1942
7:30 p.m. at the
University Club of St. Paul
in the Lounge Room

(1) Personal Experiences with the Treatment of Burns

N. Logan Leven
Discussion: Ernest A. Strakosch

(2) Blast Burns — R. F. McGandy

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III. D.S.C.

Minneapolis Morning Tribune,
Thursday, December 3, 1942

A Minneapolis officer-physician, who ignored his own severe wounds to direct treatment for paratroopers after their plane had been shot down, has been awarded the distinguished service cross, dispatches from Lt. Gen. Dwight Eisenhower's north African headquarters revealed Wednesday night.

The officer, Capt. William W. Moir, who practiced medicine at Stillwater, Minnesota, for several months before he entered the army, has recovered from his wounds and rejoined his parachute battalion.

"While acting in the capacity of medical officer in a flight of 3 transport planes moving personnel in his battalion on the morning of November 8, he was suddenly shot down by attacking enemy planes near Oran," Captain Moir's citation said.

"During the attack in the air and in the ensuing strafing on the ground, Capt. Moir distinguished himself by the extraordinary heroism against the armed enemy by inspiring administration of medical attention to wounded personnel before attention to himself, despite severe wounds to his head and back."

Capt. Moir is a son of the late Dr. William W. Moir, who died early this year after practicing medicine here for many years. His mother now lives at Cambridge, Mass., where another son, Alfre K. Moir, is a freshman at Harvard University. Capt. Moir's wife, Dr. Jane Moir, is a member of the staff of Wisconsin General Hospital at Madison, Wis. Another brother, Lt. T. L. Moir, is with a medical detachment in Texas.

Capt. Moir, a 1931 graduate of Shattuck School, Faribault, was graduated from University of Minnesota in 1938. He later was a resident in medicine at University Hospitals here, and entered the army medical corps in January, 1941.

IV. PERNICIOUS ANEMIA AND CARCINOMA OF THE STOMACH

Leo G. Rigler
Daniel L. Fink

One of the prominent gastro-enterologists in this country relates the following story about his father, an elderly physician. At about the age of sixty he discovered that he had a profound anemia which, on some study, had many of the characteristics of a pernicious type. The gastric analysis showed a complete achlorhydria. The discovery of the beneficial effects of liver in pernicious anemia had just been made and this physician was promptly started on a course of therapy. The treatment had good results, although it was not pursued as thoroughly as it might be. He had no gastric symptoms whatever, but after a short period it was thought advisable to exclude the possibility of a lesion of the stomach as the source of this anemia. Roentgen examination of the stomach was done and a large, apparently benign, polypoid tumor of the posterior wall of the middle third of the stomach was found. Because of the possibility that this might be the cause of his anemia, rather than a deficiency of the anti-anemic factor, and also because of the possibility that it was malignant, he was operated upon and the tumor was locally excised. He was about sixty at the time, but he recovered from the surgical procedure without incident. Histologically the tumor proved to be a benign polyp with some questionable carcinomatous changes.

But the anemia remained and an intensified course of treatment with liver extract produced a prompt and characteristic response typical of true pernicious anemia. Eight years later, almost at the age of seventy, his anemia reasonably well controlled, he developed gastric symptoms. Re-examination with the roentgen ray revealed a large carcinoma approximately at the site of the benign polyp. He again submitted to surgery and a rather extensive resection of the stomach was performed. A polypoid, undoubtedly malignant, epithelial tumor was removed and he recovered without particular incident. Following this he again resumed the practice of medicine and, 6 years later, well over the age of seventy, he was still active. Also, he still had pernicious anemia, which was under control with liver-therapy.

Such a case speaks volumes for the progress of medicine during the past two decades. Attacked by two diseases, either of which was formerly considered fatal, this individual has survived both conditions, because of improved methods of therapy.

There is, however, in addition, much to learn in such a case with regard to the coincidence of certain diseases. Is this simply a co-existence of three lesions in the same elderly individual, or is there a relationship between mucosal tumors of the stomach and a pernicious anemia-like syndrome. It has been reported that this co-existence was first noted by Quinke in 1876 and since that time there has been considerable study devoted to this possible relationship. An illustration from our own experience is given in the following case , which was seen both at the University Hospitals and the Minneapolis General Hospital during the past eight years.

Case Report

, a male, aged 68, gave a history of anemia for many years. In 1934 he was admitted to the University Hospitals where the diagnosis of pernicious anemia was established. The blood findings were characteristic. He was given therapy wit liver and improved, but later developed sensitivity to injections of liver extract and had to be treated orally.

He was first seen at the Minneapolis General Hospital on April 14, 1941 at which time he appeared to be having a relapse. Blood was typical of pernicious anemia and at a later period a sternal aspiration biopsy revealed the characteristic megaloblastic bone marrow. He developed lobar pneumonia at this time, from which, however, he recovered. He had no gastro-intestinal complaints except

for somewhat poor appetite, which had been present for a long period of time, but he was sent up for x-ray examination as a matter of routine. On Apr. 21, 1941 a roentgen examination revealed some small polypoid enlargements of the mucous membrane in the antrum of the stomach and a large polyp apparently on the posterior wall in the middle third of the stomach. This tumor defect was rounded, sharply defined, and very readily movable. The gastric walls showed flexibility and good peristalsis in this whole area. Gastroscopy was later done on May 13, 1941 and revealed a single polyp in the middle third of the stomach. Surgery was advised at this time, but refused, and the patient left the hospital. He returned on May 13, 1942 complaining of loss of weight and appetite. This had commenced in January and he noticed black stools in the interim. The anemia had become much more severe. Reexamination at this time with roentgen rays showed an extensive carcinoma involving most of the stomach. He went rapidly down hill and died June 1, 1942.

Comment

The progression from pernicious anemia through gastric polyps to a full-blown gastric carcinoma is well illustrated in this instance. Contrary to the case of the physician cited at the outset, this resulted in a most unfortunate outcome, possibly due to the refusal of the patient to submit to operation a year earlier. It is, of course, impossible to exclude some malignant degeneration of the polyps present the year before, but the whole appearance, both roentgenologically and gastroscopically, was that of a benign non-infiltrating lesion. What the result would have been if he had submitted to operation as advised originally, no one can absolutely predict. Yet the roentgen examination of the stomach, despite the absence of marked symptoms, permitted the early diagnosis of a gastric tumor in what appears to be certainly an operable stage.

The association of benign polyps and carcinoma of the stomach has been noted for a long period of time. We have, in a previous publication, reported upon this finding and also emphasized the fact that benign polyps or benign epithelial tumors of the stomach are much more common than is generally considered. Konjetzny has been one of the foremost advocates of this relationship and Stewart likewise, has brought out the frequency with which benign polyps degenerate and become malignant. Many others have pointed to this same relationship and McRoberts was of the opinion, from a careful histologic study of many benign polyps, that all of them showed some evidences of malignancy, at least in some of the superficial cells. In the series of cases which Ericksen and I reported, e.g., we were able to demonstrate at least four cases in which malignant degeneration of a benign tumor of the stomach was shown by pathologic examination. In addition, we found at least four cases from our own roentgenological series of a similar type. Many such authentic cases are now reported in the literature and it seems reasonable to suspect that in the stomach, as well as in the colon, one of the precursors of carcinoma of the stomach is the benign polyp.

The relationship between pernicious anemia and carcinoma of the stomach is on a much less firm basis. The literature is filled with numerous individual case reports and extensive studies which appear to bring considerable evidence to bear upon both sides. Several possibilities exist in regard to this relationship. Is carcinoma of the stomach and pernicious anemia an accidental association of two diseases occurring in somewhat the same age group? Or does carcinoma of the stomach produce a pernicious anemia-like picture or, possibly, even a true pernicious anemia as the result of some toxic effect of the malignancy? Or do patients with pernicious anemia tend to develop carcinoma of the stomach as a result of the pernicious anemia? And, finally, is there a common precursor for the two diseases which tends to produce either or both?

Konjetzny in 1913, together with Saltzmann, first proposed the thesis that carcinoma was accompanied by an inflamma-

tion of the mucosa, a gastritis. More recently Konjetzny has studied 18 cases of carcinoma in which the lesion was small and he reports some degree of atrophic or "hyperplastic--atrophic gastritis" in all of them. Hurst found that 75 per cent of 100 cases of carcinoma of the stomach exhibited gastritis and 5 per cent showed benign tumors. He also has reported, as have others, the development of carcinoma in patients in whom achlorhydria had been observed for many years. Orator studied 25 cases of cancer and found a diffuse atrophic gastritis in 15, and hyperplastic gastritis with areas of atrophy in four. The literature contains many other reports of a similar nature, notably that of Usland who, on the basis of clinical observations concluded that most cases of gastric cancer were preceded by gastritis. He believes that 15 per cent of his cases of gastritis developed cancer. Kapp found this progression in 13.4 percent of the cases of gastritis. Schindler likewise believes, on the basis of gastroscopic observations, that chronic atrophic gastritis is the most frequent precursor of carcinoma of the stomach.

Fenwick in 1880 described the atrophic gastric mucosa which is now recognized as a constant accompaniment of pernicious anemia. Since then many studies, notably those of Faber, Hurst, and Magnus and Ungby have emphasized this relationship. Faber, particularly has emphasized the role of chronic gastritis in the production of pernicious anemia. Brown studied 42 cases seen at autopsy and found chronic gastritis regularly. The gastroscopists likewise report atrophic gastritis present in almost all cases of pernicious anemia. Magnus and Ungby, on the other hand, report only atrophy without evidence of inflammation.

Does the gastritis of pernicious anemia produce the achlorhydria, the deficiency of the anti-anemic factor? Recently some opinion has arisen to indicate an exactly opposite mechanism. Jones, Benedict and Hampton report the observation of a regeneration of gastric mucosa after liver therapy. Schindler also now believes that the gastritis may possibly be secondary to the deficiency as is the case in sprue and other deficiency diseases.

One other line of evidence should be mentioned briefly. Several investigators have reported a marked familial trend in the occurrence of achlorhydria, gastric cancer and pernicious anemia. Thus a family has been reported in which the father had achlorhydria and gastric cancer and five sons all had achlorhydria. Of these, two developed pernicious anemia and one both pernicious anemia and carcinoma of the stomach. In another report there were two instances of pernicious anemia with carcinoma of the stomach and one of pernicious anemia alone in the children and grandchildren of one individual who had pernicious anemia. This would imply some hereditary predisposition toward the two diseases or more likely toward a common percursor of the two diseases.

A facile but probably oversimplified theory of the relationship of gastric tumors to pernicious anemia might be expressed as follows:

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Chronic gastritis → atrophy of gastric mucosa → pernicious anemia
atrophy of gastric mucosa → benign mucosal tumors → carcinoma
atrophy of gastric mucosa → carcinoma
atrophy of gastric mucosa → achlorhydria

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Without doubt such a relationship has not yet been established.

The fact is that considerable opinion has been expressed to the contrary, namely; that there is nothing more than an accidental relationship between pernicious anemia and gastric tumors. Giffin and

Bowler, e.g., in 1923 found only one case of gastric cancer in 628 cases of pernicious anemia from the Mayo Clinic although 4 other malignant tumors were discovered. In 1933, also from the Mayo Clinic, Connor and Birkeland found 11 cases of the coexistence of the two diseases with four more cases of polyps and pernicious anemia together. In a consecutive series of 658 cases, however, only four cases of cancer were found, an incidence of .6 per cent. Wilkinson, also in 1933, reported 370 cases of pernicious anemia in only one of which gastric cancer was found, while there were five other carcinomas of various organs. At the same time he collected from the literature reports of 35 cases of pernicious anemia with associated cancers, 25 of which were in the stomach.

Numerous other opinions have been advanced to the same general effect that this was an accidental coexistence, but with little proof. The most common argument is that there is a very high incidence of cancer as a cause of death in individuals past the age of 40, hence the coexistence is bound to occur.

The answer to this question is not simple for a number of reasons. First, it has not always been possible to make a certain diagnosis of pernicious anemia. It is only in recent years that definite criteria, such as pointed out by Watson, enable a reasonably certain diagnosis to be adduced. Secondly, the older literature on the subject, insofar as statistical evidence is concerned, is worth very little. This is true because of two reasons. First, at the time when these papers were written, pernicious anemia was a short-lived disease and the patients had no period of survival sufficient to permit them to develop carcinoma of the stomach. Secondly, the diagnosis of carcinoma of the stomach was extremely faulty and in all probability many cases were not observed at all. As will be shown later, in the majority of these patients with pernicious anemia who develop carcinoma of the stomach, the symptoms are either not present at all or not sufficiently characteristic to direct attention to this diagnosis.

It would seem at first glance that the best method of attacking the subject from a statistical standpoint, would be by examination of autopsies. Here, too, however, the findings are very uncertain and insofar as I can determine from present studies, are scarcely worthwhile. First of all, it appears difficult for the pathologist to make a diagnosis of pernicious anemia. In the last few years routine biopsies of the bone marrow have been made at autopsy on cases suspected of pernicious anemia and the demonstration of a typical megaloblastic marrow may make the diagnosis certain. Up to a few years ago, however, the diagnosis of pernicious anemia was a clinical one and the pathologist in general, with his well known skepticism about clinical findings, was inclined to discount the diagnosis. If, in the course of the autopsy, a large polypoid tumor of the stomach were discovered, whether benign or malignant, the pathologist was very much inclined to discard the diagnosis of pernicious anemia, even though there was good clinical evidence in its favor and assign the entire cause of death and of the anemia to the stomach tumor. The pathologist would find clear-cut evidence, which was visual and concrete, of a tumor of the stomach, but no such clear cut, visual concrete evidence of pernicious anemia. The result is that most of the evidence that can be adduced from autopsy finding is faulty.

Several studies have been made on autopsy material. Rambach found 641 cases of carcinoma of the stomach and 50 cases of pernicious anemia in 11,849 autopsies. The statistically expected incidence of the association of the two diseases was 2.4 cases. Actually there were 11 such cases or $4\frac{1}{2}$ times the expected frequency. Jenner reports on 76 cases of pernicious anemia at autopsy. He found 5 cases of gastric carcinoma, four benign tumors of the stomach and only one other malignancy, a case of carcinoma of the uterus. Brown found 151 cases of pernicious anemia in 18,200 autopsies. In this group there was only one carcinoma, an incidence much lower than the average

found post mortem. But there were 12 benign polyps, an incidence of 8 per cent, which is so extremely far in excess of the number found in the other autopsies that it is very significant. She reports but .003 per cent of polyps in routine autopsies which must represent an error. Ericksen and I found that in .8 per cent of 6,172 autopsies, gastric polyps were present. Brandes, in a small autopsy series of 27 cases of pernicious anemia, found 4 gastric cancers.

I began a search of our own autopsy records in the Department of Pathology with the thought in mind of determining what the incidence of carcinoma of the stomach was in cases of pernicious anemia. I soon discovered that the incidence in pernicious anemia apparently was less than that of the remaining autopsy cases. A careful reading of some of the case reports, however, indicates the reason for this seeming paradox. The pathologist obviously was uncertain of the clinical diagnosis of pernicious anemia and was, therefore, reluctant to classify cases with obvious tumors of the stomach under the heading of anemia. It seems likely, therefore, that some of the cases of carcinoma of the stomach with pernicious anemia would not be found if the classified cases of pernicious anemia alone were reviewed. A study of all the cases of carcinoma of the stomach in our autopsy records with a review of the clinical data to determine by Watson's criteria whether or not they also had pernicious anemia, together with a study of the classified cases of pernicious anemia would give us a much truer picture of this coincidence. This study remains to be done. I suspect that some such deficiency may hold true in other autopsy series except where, as Rambach did, both the cases of gastric tumor and of pernicious anemia were studied.

The two diseases, unfortunately, simulate each other in many respects so that it is easy to conclude that the abnormality which is obvious, both clinically and pathologically, the tumor, is responsible for all the symptoms. Finally, neither disease has a high incidence in the population as a whole so that large enough bodies of statistical studies have not yet been accumulated. One of the most significant papers on this subject was that of Velde, who studied 42 cases of pernicious anemia with great care. He found polyps of the stomach in 14 per cent in contrast to .71 per cent in a series of 1271 patients of various types. In three case reports of pernicious anemia and carcinoma of the stomach Velde points out that all three patients had been followed for 3 to 6 years with pernicious anemia before the carcinoma appeared. Schindler's observations with the gastroscope are likewise of considerable interest. He examined 2167 patients of all types and found 36 cases with polyps in the stomach, or 1.65 per cent. In 310 of this same group in which atrophic gastritis alone was present, the incidence of polyps was 4.8 per cent, while in 43 patients with atrophic gastritis and pernicious anemia, the incidence was 14 per cent. If we break down the original 2167 cases, we found 1814 without gastritis showing an incidence of .83 per cent polyps and 353 with gastritis, with or without pernicious anemia, showing an incidence of 6 per cent or a ratio of at least 7 to 1.

Murphy and Howard have reported on 440 patients in whom 5 cases of tumor of the stomach were found. Groen reported two cases of gastric carcinoma in 117 cases of pernicious anemia. Numerous other reports of a similar nature have been published.

It is perhaps of great significance that in the third report from the Mayo Clinic by Washburn and Rozendall published fifteen years after Giffen and Bowler's report and five years after Connor and Birkeland's report, a markedly different result was obtained than on the previous reports. They analyzed 906 cases of pernicious anemia seen from 1931 to 1934 and found that 1.76 per cent showed malignant tumors of the stomach and 2.50 per cent showed either

malignant or benign tumors of the stomach. The apparent increase in incidence in the cases at the Clinic may be based upon the greater span of life such patients exhibit since the introduction of liver and also upon greater accuracy in the finding of stomach tumors. Their figures are based upon the entire series. The fact is, however, that only 60 per cent of these patients were examined roentgenologically to determine whether there was a lesion, hence their figures probably should be corrected to indicate that they have really studied only 544 cases. With that finding, the percentage of gastric tumors as a whole would be 4.4 per cent.

This figure of over 4 per cent does not appear to be an extremely high one if one considers that in a series of 6142 autopsies of all ages which Ericksen and I studied in the Department of Pathology, 2.01 per cent showed carcinoma of the stomach and .8 per cent, in addition, benign tumors making a total incidence of about 2.9 per cent. Much has been made of this fact that carcinoma of the stomach is not rare in individuals of the age groups of pernicious anemia and a figure of roughly 4 per cent has been given for the incidence of death from carcinoma of the stomach in individuals past the age of 50.

Jenner in a very thorough paper has analyzed this whole subject and comments on the statistical relationships. Jenner studied 181 cases of well established pernicious anemia, these being living individuals. Seven of these developed carcinoma of the stomach at some time after the diagnosis of pernicious anemia had been made. One had carcinoma of the stomach found at the same time as the pernicious anemia. One additional one had a carcinoma of the esophagus and the cardiac end of the stomach which he is inclined to omit from this consideration because it probably arose in the esophagus. One additional case had a carcinoma of the uterus. The incidence of carcinoma then in this group was 4.4 per cent. Jenner compared his figures with that of the general population of Amsterdam, as shown in the mortality statistics, then proceeds to correct the mortality figures for the number of living individuals for each age group during the year when this mortality was reported. In this way he arrives at some figures to indicate the actual incidence, the morbidity in other words, of carcinoma of the stomach in the living population in certain age groups. A comparison of this incidence in these age groups with that found in the same age group in his pernicious anemia patients would indicate that the carcinoma of the stomach exhibits twelve times the expected rate found amongst other individuals. Some criticism of these figures may well be adduced. The diagnosis of carcinoma of the stomach is notoriously unreliable and is frequently missed so that in the mortality figures from the general population, the incidence is probably lower than actual. He makes the correction of 11 per cent on this group because that appears to be the difference between the autopsy records and the death certificate rate. That may be an insufficient correction. Despite these discrepancies, it is clearly apparent from his figures that there is a vast difference in the incidence of carcinoma of the stomach in individuals with pernicious anemia and in the non-pernicious anemia portion of the population. One further observation may be recorded, that of Cotti, who found that 86 per cent of all the neoplasms observed associated with pernicious anemia were in the stomach.

The co-existence of the two diseases is commonly noted by internists of long experience who are treating cases of pernicious anemia. A typical case is reported here to illustrate this situation.

Case Report

, a female aged 66 years was admitted 4-24-40. She had first been seen in 1934 when she was found to be anemic. Studies indicated a macrocytic, hyperchromic anemia with other features typical of pernicious anemia. There was an achlorhydria after histamine. In 1935 she had cataracts removed. She was treated with liver with a good response. Remarkably enough, she was submitted

neither to roentgen examination nor to gastroscopy. She did not return until at this time when she complained of a mass growing in her epigastrium for the past five to six months. She had lost 10 pounds in weight. She consulted her physician because of constipation. Later she noted tarry stools. Roentgen study revealed a large carcinoma of the stomach. Surgery was undertaken, but a palliative resection only could be done. It is interesting to note that a large carcinoma was found, but alongside it there was a benign polyp. There were also metastases to the lymph nodes. She died four months later.

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In 1939, impressed by the numerous cases in which the co-existence of carcinoma and pernicious anemia of the stomach had been observed and stimulated by the same observations made by Doctor C. J. Watson and Doctor Macnider Wetherby, we undertook to reexamine all our cases of pernicious anemia by the x-ray method at semi-yearly intervals, regardless of whether or not the patient had any gastric complaints. In part, this was due to a desire to determine at how early a point carcinoma or benign tumor of the stomach could be discovered in patients without apparent symptoms. A number of years ago we had considered the utility of making routine examinations of the stomach on all individuals past the age of forty with a view to discovering carcinoma at an early stage. The statistical evidence of the incidence of cancer of the stomach in the living population, as recently reported by Collins, Gover and Dorn, would indicate that certainly not more than three individuals per thousand of the living population over the age of forty would have carcinoma of the stomach at any one time. Such an incidence indicated that such a procedure would be highly expensive and not very productive. However, the examination of a selected group of cases, such as patients with pernicious anemia, in which the incidence appeared likely to be much higher, seemed much more fruitful. We also felt that such a procedure would permit us to determine more definitely whether this relationship actually existed. The first fruit of this procedure is illustrated in the following case report.

Case Report

M.F., a female aged 57 was first seen May 15, 1936 complaining of numbness of the extremities and weakness. The hemoglobin was 67 per cent, the red blood cell count 3,200,000. Gastric expression showed no free hydrochloric acid. Although the blood smears were atypical for pernicious anemia, liver therapy was instituted and gave a good response. She was followed in the Out-Patient Department receiving 10 c.c. of liver extract at monthly intervals. Numbness persisted despite adequate therapy. She had no complaints at this time except for some sinusitis and was coming in for routine check-ups.

Roentgen examination of the stomach was done in 1936, as a routine procedure, and was found to be negative. Roentgen examination was again done on September 9, 1940 as a part of the usual routine and three large polypoid tumors were found, two on the posterior wall and one on the greater curvature, each one measuring between three and four centimeters in diameter. They were rather sharply defined, but not entirely movable. There was a definite invasive character on the greater curvature indicating a malignant type of polypoid lesion.

Gastroscopy was done September 18th and showed some questionable infiltration, but the polyps themselves were not visualized.

On September 23rd surgery was undertaken and the polyps were found in the middle portion of the stomach. A subtotal gastrectomy was done.

Examination of the excised specimen revealed that external evidences of malignancy were entirely lacking; near the greater curvature on the posterior wall were found two polypoid masses. One of these immediately adjacent to the greater curvature measured 2 x 2 x 1 cm. and was suspended on a relatively narrow pedicle at a point 7 cm. above the pylorus. The second measured 6 x 3 cm., was from

1 to 1.5 cm. in height and was proximal to the smaller mass. The base of attachment was almost as large as its surface, it was soft, papillary and the surface was partially hemorrhagic. Between the polypoid masses there was an indurated opaque plaque-like thickening of the mucosa extending over an area about 1.5 cm. in diameter. No gross involvement of the submucosa was found. Microscopically, the polypoid masses showed papillary processes in varying sizes and shapes. The tumors were not far removed from the structure of a benign polyp, but there was some histologic evidence of malignant change. Conclusions were: Superficial polypoid adenocarcinoma of stomach.

The patient recovered and at the present time is still well. She has gained five pounds since her operation and is apparently getting along well, although her pernicious anemia appears to be in much the same condition. She is being given liver extract and on the last report the hemoglobin was 14.2 gms., the red cell count 4,600,000. It should be pointed out that this high hemoglobin and red cell count had been present on previous occasions when she was thoroughly treated with liver.

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Comments

It is notable that this patient had no gastric history whatever. Further questioning after the discovery of the x-ray findings elicited no complaints, referable to the stomach. This is characteristic of patients with benign polyps and the lesions found were certainly benign in origin, although malignant degeneration had already occurred.

The sequence of events noted above, namely; atrophic gastric mucous membrane with pernicious anemia to benign polyps to adenocarcinoma is beautifully brought out in this case. While the tumors were easily diagnosed roentgenologically, they were in a relatively early stage. It should be noted that the gastroscopic examination was negative. It is such cases which give some hopes for cure of carcinoma of the stomach. One such case found on routine roentgen examination thoroughly justifies the numerous negative examinations which attend such a routine procedure.

Unfortunately, this project has been far from successful. Owing to a variety of causes, the patients with pernicious anemia have not appeared for roentgen examination as frequently as they should and none of the cases discovered in this manner can be considered early cases of carcinoma or of benign tumors. Yet we have now observed three cases in our own clinic which were discovered only because of this routine procedure and a similar enterprise at the General Hospital has yielded similar results. The failure to take advantage of this routine procedure and the disastrous results which occur are illustrated in the following two cases.

Case Report

a male aged 73 was first seen June 1, 1934 complaining of loss of sensation and other evidences of neurological changes. He was apparently well until Christmas of 1933 when changes in the hands began. There were no other symptoms. On neurological examination, the evidences of a subacute combined degeneration was found. No free hydrochloric acid was found in the stomach with histamine. The hemoglobin was found to be 63 per cent with 2,470,000 red blood corpuscles and 3,800 leukocytes. The diagnosis of pernicious anemia was clearly established from the smears and by other means. Liver therapy was commenced with a prompt and excellent response. The hemoglobin rose to 90 per cent and was maintained at 75 to 90 per cent throughout the treatment. The neurological findings improved.

Gastro-intestinal x-ray study was done July 6, 1934 in accordance with the usual routine and a small paraesophageal hernia was found. There was no other evidence of pathology in the stomach or duodenum. On May 4, 1942 he reported to the Clinic complaining of general fatigue, but no other symptoms. It was thought that he might have had somewhat inadequate therapy.

Because of the routine procedure, he was sent to x-ray for examination of the gastro-intestinal tract and an extensive carcinoma of the cardiac end of the stomach was found. He was admitted to the hospital July 4, 1942 and on July 10th an operation was undertaken. An inoperable carcinoma of the cardiac end of the stomach attached to the pancreas was found and it was impossible to do even a palliative procedure. On July 30th he was discharged.

The hemoglobin dropped thereafter and on October 6th was lower than at any previous time. He now shows evidences of cachexia and has marked anorexia.

Comment

The absence of definite gastric symptoms despite an extensive tumor is notable. In this patient, the observance of the routine most probably would have revealed the tumor at a much earlier stage, although it may well have been inoperable from the beginning.

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Case Report

, a male aged 70 was first seen August 5, 1938 complaining of edema of the ankles, weakness and dyspnea. The gastro-intestinal history was negative except for some nausea and vomiting following the taking of medicine for his edema. He had a slight degree of ascites. On neurological examination he had a definite loss of vibratory sense and diminution in the reflexes of the upper and lower extremities. On laboratory examination a hemoglobin of 36 per cent was found with a red count of 1,350,000 and 6300 leukocytes with anisocytosis, poikilocytosis and polychromasia and on repeated examinations similar findings were obtained. Reticulocyte count was found to be 2 per cent. The gastric expression showed no free hydrochloric acid with histamine.

A consideration of the neurological findings and of the blood findings indicated the diagnosis of pernicious anemia. Liver therapy was instituted with a prompt and satisfactory response. After administration of reticulogen, the neurologic findings improved greatly. The hemoglobin rose to 83 per cent and was maintained there quite constantly through this period of time. On August 12, 1938 roentgen examination of the stomach and duodenum was done as a routine procedure and appeared to be negative. On February 5, 1940 the roentgen examination was repeated as a routine procedure. There were some changes found on the greater curvature of the stomach, nodular defects appearing in the middle third suggesting the possibility of polyps. Gastroscopy was suggested and was done on February 28, 1940 and reported as essentially negative.

At this time blood was occasionally found in the stool and this corresponded with sudden drops in the hemoglobin, which were otherwise unexplainable.

The gastroscopy was repeated April 16, 1940. Atrophy of the mucous membrane was reported, but no other evidence of pathology. No polyps were seen.

An increase in the amount of liver produced a rise in the hemoglobin to 88 per cent, which was maintained. The patient had no complaints whatever. On March 20, 1941 he developed a gross hematuria, the cause of which was never determined. Later, under liver therapy, his hemoglobin rose to as high as 96 per cent.

On November 27, 1941 he reported some gastric distress which was thought to be associated with the medication for when he took salts this was completely relieved. No x-ray examination was ordered. Reexamination of the gastric contents after histamine showed no free hydrochloric acid.

January 22, 1942 he complained of some indigestion, but insufficient to arouse any apprehension. Because of the routine procedure the examination of the stomach was done on January 27, 1942 and an extensive polypoid carcinoma of the stomach was found involving the upper third chiefly, but extending practically down to the pylorus. Considerable ulceration was also present. A few days later he had a severe hemorrhage from

the stomach and on February 19th his hemoglobin had dropped to 63 per cent.

He was admitted into the hospital April 10, 1942 and, after blood transfusions, surgery was undertaken on April 17, 1942. An extensive carcinoma with metastasis to the colon, lymph nodes and liver was found. Palliative resection only could be done, but approximately 95 per cent of the stomach was removed. He left the hospital April 28, 1942 in fairly good condition. He died early in August, 1942. The tumor in the stomach measured 10 cm. along the greater curvature, was of the bulky type and microscopically showed adenocarcinoma.

Comment

Re-examination at six months' intervals would very likely have discovered this tumor at least 18 months earlier, at which time surgery might conceivably have been successful. No doubt the earliest stages of the lesion were present when he was examined in February, 1940. Unfortunately, the negative gastroscopy on two occasions, combined with the uncertainty of the roentgen diagnosis led to a false sense of security. Had roentgen examination been done again in April, 1940, at the time of the second gastroscopy, it is possible the diagnosis could then have been established.

Since this program was instituted at the University Hospitals we have no examined on one or more occasions 38 cases in which the diagnosis of pernicious anemia was reasonably certain. In this group three cases of carcinoma and two cases of benign polyps of the stomach have been discovered. We have also reviewed the records of an additional 74 cases of pernicious anemia seen during the past nine years in which gastro-intestinal x-ray examinations had been made. In this group five cases of carcinoma and one of benign tumor of the stomach were found. The total group is 112 cases with 8 per cent carcinomas and 2.6 per cent benign tumors.

At the Minneapolis General Hospital we have reviewed 118 cases in which the diagnosis of pernicious anemia was reasonably certain and in which either gastro-intestinal x-ray examination, gastroscopy, or autopsy was done. In this series there were three cases of carcinoma and three cases with apparently benign tumors of the stomach. If we group both series together the incidence of tumors of the stomach in cases of pernicious anemia is found to be 7.8 per cent.

It is interesting and probably significant that of the nine carcinomas seen at the University Hospitals, seven were of the polypoid type and four showed evidences of benign as well as malignant mucosal tumors when the stomach was examined by the pathologist.

We have no comparable series of patients, without obvious gastric symptoms, in which roentgen examination was done. Ericksen and I did study 4236 cases in gastro-intestinal x-ray examination had been done, but these were all on patients with symptoms sufficient to cause them to be referred to the x-ray department. In that series approximately 5 per cent of the patients showed carcinoma of the stomach and .6 per cent showed benign tumors. Such a series is obviously not comparable because a high percentage of these patients had obvious carcinoma when sent up for x-ray examination. Others had ulcers which eventually were demonstrated to be malignant, while in the series here under consideration the vast majority of the examinations were made as a matter of routine. The only comparison that is of any great significance is that between the percentage found in these cases on routine examination and the morbidity in the general population. If the figures quoted above of .3 per cent in individuals over the age of 40 are used for comparison, it is perfectly clear that the incidence of carcinoma of the stomach and benign polyps of the stomach in pernicious anemia is vastly greater.

The number of cases examined is too small for any conclusive demonstration. Furthermore, it is apparent that there is some selectivity in these two groups. What is needed in such a study is an

absolutely routine examination made semi-annually regardless of symptoms. In the small series of 38 cases in which this was accomplished five tumors were discovered, an extremely high incidence. We hope to carry on this study in a larger number of cases over a period of years and the results should be more definite. Further statistical studies will then be made to determine more accurately the actual difference in incidences.

Conclusions

1. There appears to be a distinct relationship between carcinoma of the stomach and pernicious anemia which is more than co-incidental.

2. Although it has not yet been definitely proved, its relationship may well be based upon atrophic gastritis, which is a predisposing factor to both diseases.

3. Carcinoma of the stomach should be suspected in patients with pernicious anemia if the slightest gastric symptoms are exhibited.

4. The routine roentgen examination at semi-annual intervals of patients with pernicious anemia is a fruitful procedure and is well worth while. If it were used routinely some salvage might well be accomplished in patients with carcinoma of the stomach.

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V. GOSSIP

Lieutenant Al Hayes has written to Obstetrician and Gynecologist Emil Holmstrom as follows: Al is located in some distant place as he speaks of a voyage which was uneventful even though crowded with 6 in a cabin instead of the accustomed 2. Excellent meals nullified previous weight reducing attempts. The food was served in a regular dining room with approximately the same service as was provided pay passengers in the past. After preliminary roughness, smooth sailing enabled Al to get a great deal of reading done. Much of his reading had to do with the countries through which he was passing (National Geographic Magazine). A riotous time was had by all at the Neptunus Rex ceremony. Lazy days on deck were spent watching the flying fish, an occasional shark, and porpoise schools at play. He spoke of the musical demonstration provided for their arrival. At first he was in a large city but later on he was moved to a remote spot. The description of his surroundings sounds like a Hollywood location. Spring is there. One of the difficult problems is getting accustomed to new currency. There is also the change in diet largely occasioned by available food stuffs. He is full of questions as to conditions back here. After reading his letter, most of us should be ashamed for our negligence in writing letters to those who have gone away....He wishes all of us a Merry Christmas and a Happy New Year, which is another indication of the times, as Christmas presents are now arriving in advance of the anticipated holiday rush. Word has been sent to the various associations which ordinarily meet during the holidays to cancel or postpone the meetings because of anticipated transportation difficulties. Word has been received that a group of 25 medical officers will be assigned to the University of Minnesota for training in clinical pathology during the winter quarter. The speed with which the University has been going on a war time basis will be sharply accelerated by the registration of 18 and 19-year olds. The military authorities have a plan for caring for students in the University after they are inducted into the armed forces. The details of the plan are not as yet known to the rank and file. As might be anticipated many rumors are going about including those concerning the selection and supervision of medical students by military authorities. This will probably eliminate the indifferent student and the one who is using attempts at studying medicine as a means of escaping servi e.. ..Dr. Milton Levine, former bacteriologist, University of Minnesota Hospitals, now chief bacteriologist, Cook County Hospital, Chicago, and associate in bacteriology, University of Illinois, was back for 2 days last week to teach at the course at the Center on blood and blood substitutes. He contributed a great deal on transfusion reactions to a group of 75 representatives of 68 institutions in Minnesota, Wisconsin, Iowa, North and South Dakota, and Nebraska. The interest in this subject is indicated by the registration response noted above. The private hospitals are greatly interested now because of the large number of patients being served. The Rh factor is of special importance in their increased obstetric services...There will be another Kenny treatment course for physicians December 14-19 at the Center for Continuation Study. This will be followed by a recess for 3 months in instruction for physicians (only) in this method. Did you hear the Cavalcade of America featuring Sister Kenny and our boys this week? The part of Sister Kenny was played by Madeline Carroll and the parts of Drs. Cole, Pohl and Knapp by individuals who gave a different interpretation of our orthopods than we have. Dr. Pohl was a quavering old gentleman whose words dripped through a long gray beard. Dr. Knapp appeared to be an individual of uncertain age. There was no doubt about Dr. Cole who seemed to be the most natural of the three (very snappy). When Sister Kenny went on she and Madeline Carroll had much in common with their throaty, British voices. Everyone is waiting for the movie cameramen as they come to tell the story of the origin and development of the Kenny treatment in Minneapolis....Unless plans miscarry, a one week course in internal medicine for the American College of Physicians will be given January 25-30, 1943.....

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