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

Bronchial Adenoma

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William A. O'Brien, M.D.

I. LAST WEEK

Date: January 22, 1943

Place: Recreation Room - Powell Hall

Time: 12:15 - 1:15 P.M.

Program: "Osyeomyelitis"
Clarence Dennis

Discussion
Wesley Spink
W. G. Clark
Leo Rigler

Attendance: 123

Gertrude Gunn,
Record Librarian

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II. MEETINGS1. ANATOMY SEMINAR

Saturday, January 30, 1943, at 11:30 p.m. in room 226, Institute of Anatomy. "Histology of the dental pulp and periodontal membrane, with special reference to the cells of 'defense' of these tissues", C. H. Morningstar.

2. PHYSIOLOGY-PHARMACOLOGY SEMINAR

Tuesday, February 2 at 12:30 in 214 Millard Hall. "The Prostrate Gland", Frederick Scott.

3. BACTERIOLOGY SEMINAR

Thursday, February 4 at 4:30 in 214 Millard Hall. "Accessory Growth Factors of Bacteria", Margaret Houlton.

IV. BRONCHIAL ADENOMA

Thomas Lowry, M.D.

1/43

Introduction

The topic of bronchial adenoma seems to me well suited for discussion at a meeting such as this, for the condition demands the cooperation of several departments for its proper investigation and treatment. The patient usually comes first to the internist. The latter immediately enlists the aid of the roentgenologist. The bronchoscopist and the pathologist are then called on and in some instances the final treatment may be the task of the thoracic surgeon. The cases to be presented have been seen in the various departments mentioned and I wish, before going further, to thank Dr. Rigler, Dr. Wangenstein, Dr. Leven, Dr. Boies and his staff, as well as Dr. Bell and his associates, for their indispensable help.

Benign adenoma of the bronchus is a disease relatively new to clinical medicine. With the exception of a few case reports, the now considerable literature of the condition has all appeared during the past eleven years. Within that period, the more general use of bronchoscopy has been largely responsible for the increasing frequency with which bronchial adenoma is recognized; and the rapid advance of thoracic surgery has made possible (at least in many instances) effective treatment of what was formerly only a pathological curiosity. My purpose, after reviewing briefly the earlier work on the subject, is to present four of our own cases all of which have so far been treated bronchoscopically by local removal, and to outline the difficulties confronting us at present in the diagnosis and management of this tumor.

Historical

Prior to 1932, adenoma of the bronchus was not clearly distinguished as an entity. Occasional cases were discovered at necropsy. As bronchoscopy became more frequently employed (at first, in this country, through the influence of Jackson and his school), these tumors were found during life and a few were locally removed through the

bronchoscope. Some were considered to be carcinomata; and, indeed, because of their peculiar cytological features, many adenomata continue to be difficult of microscopic identification even by pathologists familiar with them. Others were called "vascular adenoma", "adenomatous polyp", or were thought to be inflammatory polypi with epithelial metaplasia.

In 1932, Wessler and Rabin established adenoma of the bronchus as an entity by their review of 12 cases with analysis of the clinical and pathologic characteristics of the disease. They felt that these tumors were benign but that malignant degeneration could and probably did occur. The general experience since the appearance of their report has indicated that distant metastasis occurs extremely rarely, if ever, in proven cases. About 150 instances of bronchial adenoma have been recorded in the literature since 1932, and it is now well recognized as a clinical entity having several distinctive characteristics.

I should like now to present some illustrative cases.

Case Reports

Case 1. The first patient, a 36 year old American housewife, was seen in the Out-Patient Clinic in August 1940. She presented a history of cough for two years, productive of thick purulent sputum, varying in amount from one ounce to one-half cup in twenty-four hours. This had not been foul, but there had been hemoptysis of two ounces or so of bright red blood on four or five occasions during the two-year period. She had not lost weight and had had no fever as far as she knew. Examination of the chest showed slightly diminished expansion of the right side of the thorax. There were decreased breath and voice sounds over the lower third of the right lung posteriorly. No rales were heard and there was no impairment of resonance on percussion. The remainder of the examination was negative. Routine urine and blood examinations showed no abnormalities.

Her x-ray revealed increased density in the medial portion of the lower right

lung field. This was interpreted as probably indicating an area of atelectasis or "drowned lung" in the medial segment of the right lower lobe. A bronchogram was made and showed obstruction of a branch of the right lower lobe bronchus with a rounded filling defect in the lipiodol shadow. At bronchoscopy, done by Drs. Robert Priest and L. R. Boies, a pedunculated, polyp-like mass was seen. This was smooth, movable and covered by glistening mucous membrane. Biopsy revealed adenoma of the bronchus, and, at a subsequent bronchoscopy, the mass was removed in toto. It was attached by a long pedicle.

Three months later, the patient had gained seven pounds and was coughing much less, but still raised one-half ounce or so of purulent sputum per day. A bronchogram in April 1941 showed filling of several saccular bronchiectatic pockets distal to the point of obstruction which were not reached by lipiodol injection before removal of the adenoma.

This patient went through a normal pregnancy and was delivered in July 1941. Since then her symptoms have continued to be mild, consisting of a slight cough with less than 5 cc. of purulent sputum daily and no hemorrhages. Bronchoscopy in April 1942 showed recurrence of the adenoma in the right lower lobe bronchus. Lobectomy was refused and therefore tissue was again removed locally.

When last seen in November 1942, the patient was in good health, had maintained her weight, and her symptoms were still in abeyance.

Case 2.

The second case was studied in more detail. It presented a more difficult problem. The patient was a 29 year old single waitress, admitted to the University Hospital in May, 1940. She had had a febrile illness three months earlier, said to be pneumonia involving the left lower lobe. At that time she was hospitalized for three weeks. Following this, she had felt well but a dry cough had persisted and during the month prior to admission she

had noted anorexia and daily afternoon fever with a weight loss of over 20 pounds. The week before entry she had a small hemoptysis. There was no history suggesting aspiration of a foreign body. On examination we found an acutely ill young woman, with a fever of 101.6°, pulse 140, respirations 24. There was evidence of obstruction of the left main bronchus, with dullness, diminished expansion and diminished breath sounds over the whole left lung. The mediastinum was displaced to the left. The significant laboratory finding was leucocytosis of 23,000 with 88% polymorphonuclears. The diagnosis was obstruction of the left bronchus with atelectasis and infection of the distal lung. X-ray showed density through the lower half of the left lung and, as you see, the planigram established the nature of the obstruction with virtual certainty.

Bronchoscopy was done by Dr. Leven and the tumor was visualized as a smooth round pink mass in the left main bronchus. Following gentle instrumentation, it bled freely and seemed to disappear from view, so that no tissue could be obtained. Following the procedure, the entire left bronchial tree became occluded by blood clot and a "drowned lung" resulted. The patient became very ill, with temperature of 105°. Bronchoscopy was repeated for removal of the clot but this only started fresh bleeding and the attempt was abandoned. As the clot absorbed, she improved gradually and the lung cleared. She left the hospital about five weeks after admission. At that time, the tumor was much smaller and the obstruction correspondingly relieved.

The patient gained weight rapidly after leaving the hospital and had very little cough. Only occasionally was there a small amount of purulent sputum. The only symptom was dyspnea on moderate exertion. She was followed in the Out-Patient Department until February 1941. The situation did not change appreciably. It was felt that the tumor should be removed if possible before it grew sufficiently to occlude the bronchus

again. Accordingly, the patient was re-admitted and at this time the bronchial mass was removed through the bronchoscope by Dr. Leven. Only slight bleeding and no untoward reaction occurred. In this patient there is undoubtedly much permanent lung damage in the form of bronchiectasis and fibrosis. At present, rales are audible throughout her left lung. Further observation will be necessary to decide whether radical surgery methods will be required to manage this residual bronchiectasis. However, at present she has no cough and very little sputum and has gone through two winters without difficulty. Therefore, at present the symptoms hardly justify a pneumonectomy.

Case 3. This was a 32 year old married white garage mechanic, admitted in August 1941. He had had pneumonia four times between the ages of 10 and 31. For one year a cough had been present, productive of one cupful daily of purulent sputum which was sometimes blood-streaked and slightly fetid. Examination showed a well-developed and well-nourished man. There was reduced expansion of the right hemithorax. On percussion, dullness was elicited over the lower half of the right lung posteriorly, with diminished breath sounds, a few coarse rales and a transient expiratory wheeze in this area. Examination was otherwise normal. The laboratory findings were within normal limits.

X-ray of the chest showed consolidation in the right lower lobe with some evidence of atelectasis. Bronchoscopy revealed a smooth rounded pink mass obstructing the right lower lobe bronchus, which bled easily and proved to be an adenoma. It was removed locally and subsequent bronchography showed extensive bronchiectasis in the previously obstructed area.

The patient's symptoms disappeared in one month. He has been seen periodically since and his cough has not recurred. A checkup bronchoscopy in April 1942, eight months after removal of the growth, showed no recurrence and a lipiodol study done over a year after the procedure showed the bronchus to be unobstructed. Ordinary

roentgenograms of the lung have remained practically clear but persistent rales in the right lower lobe testify to the presence of the bronchiectasis shown by bronchography. The patient's improvement was so striking that the surgical staff decided to defer the lobectomy which had been planned to follow bronchoscopic extirpation of the adenoma.

Case 4. The last case is that of a 39 year old house wife admitted in June 1942. Thirteen years previously she had been told she had a "spot" on her right lung. However, she remained free of symptoms until 1933 when she developed a chronic cough. This persisted with some intermissions and was associated with frequent small hemoptyses which were apt to occur at the time of her menstrual periods. For two years there had been increasing dyspnea and a feeling of substernal pressure. Examination showed a well-developed, well-nourished woman. There was marked restriction of motion of the right thorax, with an inspiratory thrill and harsh breath sounds, suggesting almost complete obstruction of the right bronchus.

X-rays showed what appeared to be an upper mediastinal mass, but on bronchoscopy a typical adenoma was found in the right main bronchus just below the bifurcation. It now appears that the mediastinal mass is merely the extra-bronchial portion of this neoplasm.

The proximity of the lesion to the carina precluded lobectomy or pneumonectomy in this case and, therefore, local extirpation was performed by Dr. Leven, part of the tumor being removed in June 1942 and a further portion in November 1942. Bronchoscopy January 14, 1943, showed the bronchus to be open. No further growth of the tumor could be noted, although only two months had elapsed and this patient will be closely followed.

Since the first partial removal of this neoplasm seven months ago, the patient has had no cough, wheeze or dyspnea. At long intervals she raises

1 or 2 cc. of blood-streaked sputum. She has gained a small amount of weight and feels entirely well.

Incidence

Bronchial adenoma is not a common tumor but its incidence is probably greater than has been supposed, amounting to between 6 and 10 percent of all primary bronchial neoplasms. However, since the

majority of bronchogenic carcinomata advance beyond the operable stage before a diagnosis is made, adenomata make up a considerably greater percentage of the curable tumors. Churchill recently stated that 25 percent of resectable bronchial growths belonged to this group.

The age and sex incidence of adenoma are in sharp contrast to those of carcinoma of the bronchus, as shown in Table I. These facts together with the clinical features to be discussed are strongly in favor of the view that the two are essentially different tumors.

BRONCHIAL NEOPLASMS

	ADENOMA	CARCINOMA
AGE	80% under 40	90% over 40
SEX	70% females	85% males
APPEARANCE	Smooth, pink, oval or lobulated; often pedunculated. Bronchus not fixed. Troublesome bleeding on biopsy.	Irregular, yellowish or grey; often ulcerated; bronchus infiltrated and fixed. Bleed readily but not profusely.
CLINICAL	Attacks of suppuration intermittent with long healthy intervals.	Suppuration or atelectasis usually progressive. Steady downhill course.
BRONCHIECTASIS	Frequent, due to chronicity of course.	In-frequent; course usually too rapidly progressive.
TYPE OF HEMOPTYSIS	Often profuse, with sudden onset and abrupt cessation.	Usually only streaking, which is often continuous.

Pathogenesis

There has been a good deal of dispute about the origin of bronchial adenoma. Some of the earlier workers believed that stasis of bronchial secretions might cause inflammatory polypi and that epithelial metaplasia then occurred and produced the final pathologic picture. This concept has been generally abandoned and it is now agreed that the adenoma is a true tumor, inflammatory changes in the lung being secondary to it rather than responsible for it. We have no good evidence as to the cell type giving rise to these neoplasms but the most commonly accepted view is

that they originate from the duct epithelium of the bronchial glands. The fact that these ducts traverse the bronchial wall beyond the cartilaginous rings is given as one reason for the frequent extra-bronchial extension of these growths.

Pathology

Bronchial adenomata occur in the larger bronchi. It has been said that they do not arise in branches of less than 10 mm. diameter, but such a sharp limit can probably not be applied to

all cases.

Grossly the adenomas are smooth, round or oval, pinkish tumor. The intra-bronchial portion most frequently is polypoid and may be pedunculated. In some instances, however, it is relatively flat and attached by a broad base. There is often extension through the bronchial wall with the formation of an extra-bronchial mass which may be larger than the intra-bronchial portion. A recent article reviewed nineteen cases in 90 percent of which extra-bronchial growth was present.

Microscopically, the adenoma is usually covered by epithelium which frequently undergoes metaplasia to the squamous cell type. Beneath the epithelium is a layer of loose connective tissue. This is often very vascular and is the origin of the profuse bleeding so commonly encountered in the condition. The neoplastic cells are rather small, cuboidal or polygonal in shape and uniform in size. They usually grow in sheets or cords and look rather undifferentiated. However, their nuclei are very uniform and mitotic figures are uncommon.

There is still a good deal of argument as to whether these lesions are benign or of low-grade malignancy. They are locally invasive and frequently recur after local removal. One recent paper reported two cases in which distant metastasis was said to have occurred, but the report is not very convincing. At present, the consensus of opinion is that the bronchial adenoma is not malignant in the clinical sense. No case is on record in which a patient has died of metastasis, even though some of these tumors have been known to exist for twenty-five years and more. They grow very slowly and the symptoms and signs

to which they give rise are largely produced by the complications of a long-standing and slowly progressive bronchial obstruction.

Clinical Features

The clinical history in bronchial adenoma is of great importance. Usually there have been recurrent episodes of pulmonary infection characterized by cough, purulent sputum, fever, often pain (when pneumonia with pleural involvement has occurred). Hemoptysis is a prominent symptom, being encountered in about two-thirds of the cases. The bleeding is often profuse and repeated. It tends to start and stop abruptly. In women, hemorrhage from the adenoma often accompanies a menstrual period. The patient ordinarily has a cough and this may or may not be productive, depending on the stage of the disease and extent of bronchiectasis or pneumonitis present. Wheezing, due to partial bronchial stenosis, is often a complaint and if the obstruction is marked and involves a large bronchus, dyspnea may be severe.

The physical signs vary depending on the degree of bronchial occlusion and the amount of pulmonary suppuration. Table 2 summarizes these changes. An early lesion may give no physical signs or there may be a localized coarse rhonchus over the lobe whose bronchus is involved. If pneumonitis is present, dulness, rales, and tubular breath sounds may be found. (The latter are usually reduced in intensity because of obstruction of the airway.) In the late stages the signs are those of total atelectasis. A few cases may at some stage exhibit obstructive emphysema. Most of them develop bronchiectasis, which is of a severe grade in the more advanced cases.

MECHANICAL EFFECTS OF BRONCHIAL TUMORS

STAGE	EFFECT ON BRONCHUS	MANIFESTATION
Early	No obstruction	-
	Irritation of mucosa	Cough
	Erosion of mucosa	Hemoptysis
Moderately	Partial obstruction	Dyspnea
		Wheeze - often localized. Impaired bronchial drainage: Pneumonitis Fever, purulent sputum Later - bronchiectasis
Far advanced	Obstruction partial in inspiration, but total in expiration.	Obstructive emphysema
	Total obstruction	Total atelectasis, usually with suppuration.

Roentgenologic Features

Until fairly recently the x-ray gave us chiefly circumstantial evidence about these tumors. That is to say, that a patient exhibiting recurrent pneumonia in the same lobe with intermittent atelectasis and some bronchiectasis was suspected of having a bronchial adenoma. Lipiodol studies were then our best roentgenologic means of diagnosing the disease. An occluded bronchus at the end of which a smooth rounded filling defect appeared in the lipiodol shadow was often very suggestive evidence of adenoma.

In the past three years or slightly more, the use of body section roentgenography has been very helpful in identifying and following these cases, since films made with this technic often may outline clearly both the intra- and extra-bronchial portions of the growth.

Bronchoscopy

Final diagnosis is ordinarily accom-

plished by bronchoscopic visualization of the adenoma. Its gross features, the lack of infiltration and fixation of the bronchial wall so common in carcinoma, are extremely important in reaching a correct conclusion as to the nature of the tumor. Biopsy is frequently helpful and incidentally is often accompanied by free bleeding. Because of the difficulty of identifying these neoplasms microscopically from the small amount of tissue obtained in a biopsy, we have often had conflicting reports from the pathologist. It may be difficult or impossible for him to exclude carcinoma. It is our feeling, therefore, that a diagnosis of bronchial adenoma must be based on the entire clinical picture including the x-ray and gross bronchoscopic findings, and that, if all these features are in accord, a report of microscopic malignancy from a biopsy should not be accepted as proof of cancer.

Clinical Course and Treatment

The natural history of these

tumors is that of a slowly progressive bronchial obstruction and often extends over many years. One case is on record in which symptoms due to a bronchial adenoma apparently were present for 53 years. As has been stated, all or certainly nearly all, these lesions are benign as far as metastasis is concerned. However, their effects upon the lung may be extremely damaging or even fatal. Severe grades of bronchiectasis, suppurative pneumonitis, lung abscess, and empyema are common sequelae. It is obviously important, since the tumor itself is benign, to recognize and treat it, if possible, before fatal or permanently incapacitating damage has been produced.

Attempts at treatment have been in three general directions:

1. Local bronchoscopic removal. This has been done in all our cases and there seems to be reason to believe that the method has advantages under certain circumstances. Early cases, in which damage to the lung is not extensive and the patient can be carefully watched for recurrences, are suitable. Patients who refuse pulmonary resection or in whom the position of the growth makes this impossible (e.g. case 4) also will fall in this group. All patients who are to have lobectomy or pneumonectomy should be subjected to local removal first, if it is feasible, to permit good preoperative drainage of the diseased lobe and thus reduce the operative risk.

Most authors now feel that the majority of cases, because of the high incidence of local recurrence and extra-bronchial extension, will require pulmonary resection. A recent article stated that this was the method of choice in 90 percent of cases. In my opinion, this has still to be proved. There has as yet been no report of a careful follow-up study of cases such as ours without resection over a period of years, with repeated local removal when indicated.

2. Radiation. This method has been given a limited trial. Results in general have not been satisfactory as these tumors are apparently not especially radio-sensitive.

3. Pulmonary Resection. Lobectomy or pneumonectomy will undoubtedly be necessary in a large number of cases, particularly where local removal is not feasible or is unable to relieve the symptoms of secondary bronchiectasis. Most authors now feel that, in carrying out resection, the tumor should be regarded as benign and the procedure therefore limited to lobectomy if possible in order to reduce the operative risk. A recent report records 19 bronchial adenomata, of which 7 had been treated by resection: 3 pneumonectomies with 1 death; 4 lobectomies with no deaths. All the living patients secured satisfactory results.

Conclusion

In conclusion, I should like to point out the importance of early diagnosis. A patient who has frequent unexplained hemoptyses or recurrent pneumonia in the same portion of a lung is a candidate for bronchial adenoma and should be bronchoscoped. Similarly, the presence of a localized bronchiectasis with repeated atelectases suggests the possibility of this diagnosis. If these tumors can be removed early, extensive suppurative lesions will not develop.

I agree with current opinion that pulmonary resection will often be indicated; but not all these cases are suitable for removal of a single lobe, and the mortality, when pneumonectomy is necessary, is still considerable. I doubt whether 90 percent of them will need radical surgery. Our four patients are all well and doing their usual work without having had it, and thus far their lesions have not progressed so as to require anything more extensive than local bronchoscopic treatment.

Clinical evidence supports the concept that bronchial adenoma is an entity distinct from carcinoma. The management of each case is an individual matter; broad and sweeping rules for therapy should not be laid down.

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V. GOSSIP

The days pass rapidly with many visitors on the campus. Nearly 80 physicians are here this week to attend the special course in internal medicine at the Center for Continuation Study. The willingness of these men to eliminate the lag between development in the teaching center and practice at the bedside is evident on every hand. Good questions, good discussions, and active interest. Their evenings are free to go downtown, to visit a laboratory, or to sit in on a discussion group. The choice is made of four or five subjects. Practically all preferred the scientific evening to the night off. One

is given new faith in human nature by such acts. The gratitude of these men and women who come long distances to hear our faculty is expressed on every hand. Monday morning was one of our cold days and still they made the effort to be on time for class as practically every one was in his place at the appointed time. It would be an interesting world if all students were equally diligent. Minnesota Medicine is celebrating its 25th anniversary as the official publication of the Minnesota State Medical Association and allied groups. The journal is full of interesting articles on progress in various fields with many personal touches concerning our progress in the state. Unless I have been misinformed Minnesota Medicine is second only to the New England Journal of Medicine among the state journals as a quoted publication in medical writing. An article in Minnesota Medicine has an excellent chance of being read by a student of the subject. Featured manuscripts in this issue include internal medicine, radiology, thoracic surgery, neurosurgery, orthopedic surgery, clinical pathology, anesthesiology and others. Minnesota is becoming well known as a place where new fields of medicine receive prompt and studious attention. The rank and file in our profession do not hesitate to change their ways when a better plan is suggested. They look to the voice of authority and more to the authority of facts. Without realizing it we have become critical of suggestions unless the idea can be demonstrated objectively. Most interesting in this regard is the story of early experimentation by Minnesota physicians with tuberculin as a therapeutic agent. Instead of giving it to their patients to see what would happen they carefully selected cases in pairs using the alternates as controls. E. L. Tuohy, who traces the development of internal medicine in Minnesota is kind to his friends. He shows the effect of the clinical viewpoint in pathology on the development in medicine. The same can be said of radiology. He mentions many by names as contributors to this program. The story in obstetrics

naturally gives credit to the excellent leadership of J. C. Litzenberg. It is believed that Minnesota will again not only have one of the low maternal mortality rates in the nation, but probably the lowest. It is good to stop from time to time and reflect on our journey. We must not be too satisfied. When Northrop Memorial Auditorium was built, a suitable inscription for the front of the building was sought. A committee selected the present motto which implies that we have a three-fold function--education, service, and research. The medical unit of the University of Minnesota more than lives up to this ideal. The psychologists tell us that Americans have three peculiarities. We will not fight until the chip is knocked off, we dislike to see a larger opponent pick on a smaller one, and third, we love to brag about ourselves and about our accomplishments. We are a new country and we had to impress our people in Europe that we made a wise choice in coming here. When we came to this country

we had to convince the people who stayed at the coast that we had made a wise choice in moving farther west. Minnesota is close to New England in many ways. Many of our early settlers were from New England. Medicine here took on many of the characteristics of the mother state. In North Dakota which has an extraordinary profession it is close to McGill and Edinburgh largely because of the Canadian physicians who settled there. North Dakota's medical profession has long been one of the most exclusive registration groups. I do not know of any group of doctors who so earnestly desired to be informed of changing concepts and better ways of doing things. Our neighbors in western Wisconsin, northern Iowa, and eastern South Dakota, eastern Nebraska, Manitoba, and Saskatchewan make up a group of physicians of essentially the same medical culture. Maps showing post office addresses of physicians who have come to the University of Minnesota in the last 7 years are studded with pins from this area.