

CASE OF INTRANASAL EPITHELIOMA.—CURED BY
EXCISION AND RADIUM.—LITERATURE.

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Mrs. S. B. R. (white), age 42 of Toccoa, Ga. Patient consulted the writer on account of some soreness and stopping of the left nasal cavity which had been present for several months.

History. Patient was of an unusually strong and healthy looking physique. Weight 160 pounds. Had never had any severe illness nor chronic complaints which necessitated the consultation of a physician. No history of any malignant disease in her family. Her only complaint was susceptibility to colds in the head.

Present History. For the last three months has had some irritation and some stopping of the left nasal cavity. This was accompanied by scabby condition and an occasional bloody discharge. She had been able to see a small growth just within the external opening on the outer side which was evidently increasing in size.

Examination. No external swelling or congestion. No enlargement of the cervical or submaxillary glands. On inspection just within the left nasal cavity could be seen a small growth at the anterior end of the inferior turbinate close to the mucocutaneous margin. It was dry and about the size of a bean, slightly scabby, sessile in form with a slight tendency to bleed if touched. The patient gave no history of nose bleed. To all appearances the growth gave every indication of being a fibrous papilloma. Under cocaine anesthesia the growth was very easily removed with the cold wire snare and the raw surface cauterized with the electrocautery. There was very little hemorrhage.

The growth was submitted to Dr. John Funke, pathologist, who gave the following report:

"Specimen consists of a reniform mass 1.2 by 0.6 by 0.4 cm. which is reddish grey in color and rather firm.

Microscopic Examination. The sections are surrounded by a stratified layer of squamous epithelium which at one point is clearly destroyed by a very small ulcerated area. Extending from this area for a short distance the superficial portion of the epithelial stratum is undermined. The structures underlying the ulcerated and undermined area are infiltrated with cells which for the most part are arranged in plugs, but some are in long strings. These cells are polyhedral in shape, are about the size of the cells occupying the lowermost portion of the epithelial stratum. They stain well, especially the nucleus. The protoplasm is granular and rather scanty.

The stroma is abundant, stains rather feebly and contains a few blood vessels.

Diagnosis. "Basil cell epithelioma."

Subsequent History. The patient returned in one week's time, showing no signs of reaction and nothing more upon the surface than would be expected from the removal of a benign growth. A sedative ointment had been given to be used in the nasal cavity.

Nov. 16th, 1919. Three weeks later the patient was again seen. There was considerable irritation inside the nose, accompanied by scabbing and bleeding. The patient said she felt very uncomfortable. She was then referred to Dr. O. D. Hall for radium treatment. I saw the patient at intervals during the radium treatment, but only for observation. The radium was used as follows, being placed just inside the nasal cavity and properly screened.

Nov. 15th, 1919. 50 milligrams. Time 2 hours.

Dec. 15th, 1919. Same amount. Time 4½ hours.

Feb. 11th, 1920. Same amount. Time 2½ hours, making a total of 450 milligram hours.

Jan. 15th. Examination shows a complete disappearance of the growth, smooth surface, and only slightly scabby condition.

Oct. 22nd, 1920. Nasal cavity looks normal and patient told to report at the slightest indication of discomfort in the nose.

A letter from the patient May 15th, now 19 months since operation indicates there is no further trouble.

Contrary to the opinion of several observers, my own experience leads me to conclude that radium is much more effective in epitheliomata than in other forms of malignant growths.

In 1919, before the American Ophthalmological Society, I reported two cases of epithelioma of the eyeball, where exenteration of the orbit followed by the use of radium produced a complete cure up to the present, six years in one and eleven years in the other.

In 1916, the writer reported a case of epithelioma of the pharyngeal wall treated by complete excision with the electric cauter, and which has remained cured up to the present date. Radium was not used, but in epitheliomata accessible for complete excision, especially by electrocautery, results will nearly always be favorable. This has been frequently demonstrated in the removal of skin epitheliomas in the region of the face or from skin surfaces.

The cure of epitheliomata is entirely a different proposition, however, when they are located in a vascular region like the ethmoid or have their origin in a closed cavity like the antrum maxillary. Thorough eradication is practically impossible, but it is in just such cases that radium does its best work.

The splendid results shown in Boston last year by Drs. Barnes and Greene in the combined use of surgery and radium in malignant growths of the head certainly leads us to be far more optimistic in our views than has heretofore been the case.

I take the liberty of presenting a bibliography of the literature bearing on the treatment of nasal epitheliomata, especially in regard to the results obtained by the use of radium. No doubt this is far from being complete, but if other observers will add to this series, we may begin to have more exact statistics.

RADIUM IN THE TREATMENT OF EPITHELIOMA OF THE NASAL CAVITIES.

CASE REPORTS.

Adam² reports a case of endothelioma in which the tumor filled the right half of the nasopharynx, appearing to grow from the eustachian orifice. Two radium applications were

made on November 29, 1915, and January 12, 1916; 50 mg. of radium screened by 1 mgm. of gold was applied for twenty-three hours at the first treatment, and for eleven hours at the second. At the time of the report, August, 1916, the parts seemed normal. Sufficient time has not elapsed to establish a permanent cure, but the result is certainly better than could have been obtained by surgical interference. (Sonnenschein refers to this case as epithelioma.)

Botey⁵ treated two cases of endonasal epithelioma with radium with poor results. In both the growth progressed and the patients died.

Delavan⁶ in his report on radium in the treatment of the growths of the upper air passages, at the Memorial Hospital, includes three tumors of the "nasal mucosa," treated by radium. Two of these had advanced recurrent lesions. (The nature of these tumors is not indicated.) In the third case, a recurrent epidermoid carcinoma of the posterior portion of the nasal septum, occluding both nasal passages, an excellent result was obtained by removing the growths with a snare and treating their bases with radium. There was no recurrence in three months.

"The difficulties of making accurate applications of radium to the nose are very great, unless the lesion is an early one and situated low down." These cases are also reported by Janeway in his book.¹¹

Hill⁹ reports one case of epithelioma originating in the left antrum, extending into the nasal cavity, the ethmoid cells and nasopharynx, treated by radium; 100 mgm. of radiobromide was inserted through a breaking down area over the hard palate into the antrum; 50 mg. into the same cavity by the inferior nasal route; a small tube of 20 mg. in the ethmoid region; a fourth tube of 50 mg. in the nasopharynx. A 48 hour exposure was made, as the growth was fungating. The growth cleared up within a few days, but apparently had invaded the cranial cavity, as the patient died "shortly afterwards" from intracranial pressure.

In general, Hill says that radium is worth trying in any malignant growth of the nose and throat "which is considered hopelessly outside the range of radical excision by the knife, provided always that an adequate amount is available,

and that the primary growth is accessible and not too far advanced and extensive, that the secondary adjacent growths and more remote metastases are not a contraindication, and provided also that the general health of the patient is fairly good." If an extensive growth is treated and reacts well, a massive dose of toxins may cause not only general malaise and fever, but "a very definite toxemia."

Generally speaking, round cell sarcomas and most endotheliomas react rapidly and consistently well to radium; spindle celled sarcomas and fibrosarcomas react fairly; squamous epitheliomas and carcinomas "are far more uncertain in the way they react to radium. It may be asserted, however, that some epitheliomas in the nose, throat and gullet do react beneficially to radium, in striking contrast to those of the tongue and of the vulva."

In the case reported the author calls attention to the fact that the tumor—through an epithelioma—reacted immediately "after the manner of a round celled sarcoma." There is usually, he says, a longer latent period in carcinoma.

Kelly¹² reports one case of epithelioma of the nasopharynx, the tumor being attached to the roof and resting on the palate, hiding the entire right posterior nares and all but the outer segment of the left posterior nares. Nasal fossæ normal. It caused nasal obstruction and a severe hemorrhage. On January 27, 1915, 50 mg. of radium was screened with 2 mm. of silver and covered with 2 mm. of rubber was applied for twenty-four hours. This caused ulceration of the palate and fauces for a week. On March 10th, the tumor had shrunk so that the nose was free, but a small rounded mass was still present on the roof of the nasopharynx. Radium was again applied in the same dosage as before. On May 14th and June 2d there was no sign of the growth, but the site of origin was covered by an adherent crust of mucus. Underneath was an apparently healthy surface. A third radium treatment was given on June 2d. Last examination on February 22, 1916. Still crusting behind the right choanal arch, but the underlying surface was healthy, and there was no sign of recurrence.

Kofler¹³ reports on the treatment by radium of three lymphosarcoma and eleven carcinoma of the nose, mouth and throat.

The results were better in the carcinoma than in the sarcoma. One of these was a basal cell carcinoma filling the right side of the nose, originating from the region of the infundibulum. Operation of Langenbeck, followed by application of radium. Patient in good health and free from recurrence at last report. (Operation in October, 1912; report published early part of 1913, exact date not given.)

New¹⁶ reports results from the use of radium in 211 neoplasms of the nose, throat and mouth at the Mayo Clinic.

In cases suitable for surgical treatment, radium alone is not used, he says.

Of the 211 tumors, 9 were intranasal epitheliomas and 5 epithelioma of the nasopharynx. In regard to the results, New says, "it is too soon to report end results in this group."

Of the results in nasal epithelioma he says that: "Operative measures in the treatment of epithelioma of the nose are usually of little value. Radium frequently clears up the ulceration and discharge and scars down the growth, giving the patient much relief, and sometimes accomplishing more than this." No further detail in regard to results is given.

The author's general conclusion is: "The immediate results of the treatment of neoplasms of the nose, throat and mouth with radium are, as a whole, very encouraging. Many patients previously operated on with a recurrence following are now treated with radium and the neoplasm disappears, giving months or years of relief, with no surgical mortality. The patients are made much more comfortable than they would be with an operation. The number of patients that will be permanently cured of a true malignancy with radium is probably very small relatively, but the number of inoperable cases that are markedly relieved and receive months or years of comfort is quite large. We do not, however, recommend the treatment by radium of any neoplasm that is surgical. In such cases the patient should have the benefit of both surgery and radium. The use of radium has entirely changed the prognosis in neoplasms of the nose, throat and mouth."

Schmeigelow²⁰ reports twelve cases of malignant tumors of the nose, pharynx and oral cavity treated by radium in 1918 and 1919. Three patients died; one (epithelioma of the right tonsil) from metastasis in the liver; one (cancer of the left

tonsil) from recurrence in the pharynx with ulceration and hemorrhage; one (nasopharyngeal sarcoma) from septic abscess without recurrence or metastasis of the tumor. In one case (epithelioma of the soft palate and left tonsil), the tumor disappeared, but the patient suffered from a radium burn, probably due to a faulty radium tube. In another case (cancer of the tonsils) the tumor did not recur, but the glands were involved and continued painful in spite of both radium and Roentgen treatment.

In the other patients of this series, results were excellent, without recurrence in a year or over. One of these cases was an epithelioma of the nasopharynx in a woman 70 years old. The tumor was located on the posterior wall of the nasopharynx. Three radium tubes (30 mg.) of radium were applied through the nose for 24 hours on June 26, 1919; this was followed by immediate improvement, but two subsequent treatments were given as a preventive on July 31st and October 11th, although the tumor had entirely disappeared, and the tissue appeared entirely normal. Clinically the cure was complete at the time of the report (June, 1920).

Schmeigelow says that Lederman and Kuznitzky¹⁵ report one case of advanced squamous celled epithelioma of the nasopharynx which improved under Roentgen treatment, but was entirely cured by mesothorium and radium. Their original report is not available.

II.—CASES OPERATED.

(Including only a few cases operated. See also notes with reference for results with operation.)

Beck³ includes in his report on malignant disease of the upper respiratory tract, 7 cases of intranasal carcinoma, including the accessory sinuses; 3 cases operated; 5 followed up to recent date. All died.

Dougherty⁷ reports two cases of epithelioma of the frontal sinus, both operated. One patient died several weeks after the operation from purulent meningitis; the other died two months after operation from extension and ulceration of the growth.

Ferreri⁸ states that epithelioma of the nasal fossæ is undoubtedly rare. His table of cases shows 1 epithelioma of the antrum of Highmore, cured by operation; 1 case of rhino-

pharyngeal epithelioma inoperable, death; 5 cases of epithelioma of the nasal fossæ and diffuse epithelioma of the nose, of which one was cured by operation, the others were inoperable; 1 epithelioma of the left maxillary sinus, not operated. One epithelioma of the roof of the mouth was treated by radium; the patient died. This is the only case of epithelioma included in the report in which radium was used.

Thomson²³ reports two cases operated, using Moure's operation. Case 1. Endothelioma of the ethmoid and antrum: Moure's operation; no recurrence in 5½ years. Case 2. Epithelioma of the left maxillary antrum; Moure's operation; no recurrence after 3½ years.

III.—GENERAL CONCLUSIONS IN REGARD TO THE VALUE OF RADIUM IN THE TREATMENT OF EPITHELIOMA.

Boggs⁴ makes no mention of epithelioma of the nasal cavities specifically, but says in regard to radium treatment of epithelioma in general:

"Primarily epithelioma is not a surgical disease, because, in order to remove all the cancerous cells, it is nearly always necessary to remove too much healthy tissue. The permanency of the end-results, in the past few years in many thousands of cases, has shown that radiation far surpasses any other method.

"Radium is the best form of radiation locally on the lesion and in regions where glandular metastases are likely to take place. Radium used over glandular centers or junctions with complete roentgen treatment over the tributaries, is far superior to the most complete and often unnecessary dissection."

"Each year," he says, "there is a smaller percentage of surgeons removing epitheliomas. I do not mean to say that surgery is never indicated, but I believe that it is seldom, if ever, indicated in primary cases."

Janeway¹⁰ in his 1918 article says that at the Memorial Hospital they "have been encouraged to treat a rather large number of operable cancers of the mucous membranes" with radium. "The remarkable improvement in some of the cases treated palliatively has not alone stimulated this attempt, but more especially the favorable result obtained on many early cancers in patients refusing operation, or in whom operation was contraindicated for other reasons. Two facts have been

demonstrated by this experience; first, within the time limits in which we have been working, single applications were often sufficient to cause apparent complete retrogressions; and second, in the larger lesions, where this favorable result was not obtained, the lesion has become more of an operable one than it was before treatment."

The cases reported by Janeway in this article do not include any malignant growth of the nasal cavities. See report under Delavan's name in section on case reports.

Lannois, Saignon and Moutet,¹⁴ in their report on radium therapy in tumors in otorhinolaryngology, report 13 cases treated by radium. These include six tumors of the nose and sinuses, and four tumors of the nasopharynx, but all of these were sarcoma, none epithelioma.

In general, they say that nonepithelial tumors are much improved, often completely cured by radium, but that results are not so good in epithelioma, especially ectodermic epitheliomas containing epithelial pearls (globe corné) are very slightly influenced by radium.

Pancoast¹⁸ reports several cases of sarcoma and carcinoma of the tonsil and one case of sarcoma of the left turbinates and antrum. No case of epithelioma of the nose or nasopharynx.

His general conclusions are:

"In the treatment of inoperable malignant growth, originating in cavities such as the mouth, throat and ear, radium therapy is an extremely valuable adjunct, for the reason that it can usually be applied directly to the growth, which is more or less inaccessible to direct roentgen ray exposure. This alone is not sufficient, and the growth should also be attacked from every possible direction by cross firing, either by radium or roentgen rays or both. Any near by area in which metastasis is likely to occur should also be exposed.

"Sarcomatous growths, especially in the tonsillar region, are more amenable to treatment than carcinomas.

"It would be best to continue treatment for some time after the apparent complete disappearance of the growth."

Sonnenschein²² in his paper on radium in the treatment of malignant tumors of the nose and throat says little definite in regard to epithelioma of the nasal cavities as distinguished

from other malignant tumors. The specific cases mentioned by him are reviewed elsewhere in this report under the authors' names.

In his table he includes 41 malignant tumors of the nose and sinuses in which radium was "the main form of treatment employed"; of these 13 were apparently cured, 2 were free from recurrence for one year or more, 14 were improved, 12 unimproved. Of 12 cases of malignant tumors of the nasopharynx treated by radium all were apparently cured. This table does not differentiate between carcinomas or sarcomas. Some writers, Sonnenschein says, "merely speak of 'malignant disease' of certain tissues or structures so that it is impossible to differentiate in the table."

From the study of the subject presented in this article he comes to the conclusion that:

"The future of radium therapy seems very bright, particularly in reference to applications in tumors of the nose and throat; but great caution is advisable in statements regarding actual cures. It is important to watch for recurrences during a period of from two to five years.

"Radium is probably of great value before, and certainly after operations. It is very efficient in relieving pain, hemorrhage, discharge, etc., in many inoperable cases.

"Sarcomas are especially responsive to radiation; the carcinomas yield much less readily, and the squamous type of epithelioma is scarcely amenable to radium at all.

"Radium has many advantages as compared with roentgen rays, especially for application in the nose and throat.

"The diagnosis of the malignant cases should be made by a competent laryngologist, and the radium applied either by him or in cooperation with a radiologist. Only in this way will correct statistics and reliable results be obtained, with greatest benefit to the patient and the safest guide to the profession."

Wickham and DeGraiss²⁴ say that "the value of radium in malignant tumor of the mucous membrane is incontestable, but varies according to the region and the nature of the tumor—sarcoma being by far the most amenable to treatment."

Their cases reported do not include any malignant tumors of nasal cavities.

Barnes reports a series of malignant tumors of the nasal accessory sinus treated by operation and radium. For the operation the Moure incision is made in the cheek, and "every particle of tumor tissue, all necrotic or soft bone" removed. Wherever possible, it is desirable to remove a small margin of normal tissue. A triangular flap of integument, "having its base in the upper incision and its apex at the lower limits of the antrum," is removed from the cheek, leaving a permanent opening into the operative cavity, so that any tendency to recurrence may be observed. The deformity following this is not great. The cavity is lightly packed with gauze, in the center of which a radium emanation tube "of appropriate strength" is placed. The tube remains in place about two weeks, being reinserted at each dressing. As the tube loses one-sixth of its radiating strength every 24 hours, it is practically inert at the end of convalescence. Three or four later radium treatments are given at weekly intervals as a preventive measure. Marked reaction of the tissues should be avoided in these treatments.

In the series reported by the author there were six carcinomas, one small round celled sarcoma and one fibrosarcoma. With the exception of the last named, all were of long standing and involved both the ethmoid and the sphenoid. Three (all carcinomas) were operations for recurrences, and one (sarcoma) had had an enucleation of the eye one year before, further operation being abandoned on account of the extent of the growth. Neither sarcoma shows any sign of recurrence (14 and 26 months after operation). Of the carcinomas, three patients have died, one has extensive recurrences, two are well with no sign of recurrence 25 and 17 months after operation respectively. One of the deaths was postoperative, due to septic meningitis. The carcinoma in this case involved all the sinuses except the frontal.

The author believes that in these massive tumors of the sinuses "radium without operation is useless." However, "thorough operation combined with immediate radiation through a wide opening in the face which for purposes of observation is allowed to remain permanently, will give, I believe, better results than we have been accustomed to consider possible."

Guichard reports two cases of epithelioma of the nasal fossa that invaded the sinuses, the orbit and, in one case, the cranial cavity. No treatment is reported in one case. The other case was operated and given several X-ray treatments. The treatment was successful and the patient remained in good health. (Operation in August, 1919; report published March, 1920.)

In a later article (October 10, 1920) Lannois and Saignon review their work on radium treatment of tumors of the ear, throat and nose, but report no new cases. In their work they employ Dominci radium tubes; they use doses of 25 to 160 mg., left in place for 6 to 24 hours, occasionally for 36 hours, exceptionally for 48 hours.

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