EXTRAMEDULLARY PLASMA-CELL TUMORS OF THE UPPER AIR PASSAGES

WITH REPORT OF A CASE

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The occurrence of plasma-cell tumors of extramedullary origin is of sufficient interest and rarity to merit the report of even a single case. Such tumors were reported in the lacrimal glands by Hannes in 1911, in epulides by Pirone in 1909 and by Kaufmann in 1922, and in the pleura by Klose in 1911. The more common site for this type of tumor would, however, seem to be the upper air passages, as indicated by published reports of 19 such growths in this location. A review of the reports shows that these tumors displayed characteristics ranging from inflammatory to malignant. Very few of them showed lymph node involvement or recurrence after removal, while the appearance of the sections only occasionally suggested true malignancy. For detailed descriptions, reference may be made to the original communications or to the summaries published by Claiborn and Ferris and by Blacklock and Macartney.

CASE REPORT

G. H. A., male, age sixty-one, of German parentage, entered the State Institute in November 1933, complaining of difficulty in breathing and the sensation of a foreign body in the throat. These symptoms had been growing progressively worse for two or more years, and for the past two months there had been a "shutting off the wind, as if the throat were closing up." This was especially marked when the patient assumed the recumbent position. The voice showed a slight nasal quality but was otherwise normal. Dysphagia was not present. The family history was essentially negative; the patient's habits were generally good. The past history showed "rheumatism" and gonorrhea some years earlier. Syphilis was denied, and there was no record of operation or injury.

Physical examination showed a well nourished man, with heart, lungs, and abdomen apparently normal. No palpable nodes were found in the axillae or groins, but one small movable node was observed in the right cervical chain. Rectal examination showed a normal prostate, and the reflexes were normal. The pupils reacted normally. Ears and tonsils appeared normal. The patient could not breathe freely through the nose. The upper jaw was edentulous, and a denture was worn. The lower molars and bicuspids were absent and the remaining teeth were carious, with gingival recession and alveolar absorption.

Special examination of the pharynx displayed a sessile tumor approximately $4 \times 3 \times 2$ cm., the surface of which was covered with a normal but congested mucosa which presented some small eroded areas with coarse folds suggesting lobulation. The tumor was situated behind the soft palate and practically filled the space between it and the posterior pharyngeal wall, to which the growth was attached. The lower pole was
barely visible through the oral cavity. The tumor was quite firm in consistency and felt somewhat like an epithelioma. Mirror laryngoscopy showed a second tumor of similar appearance, apparently arising from the right hypopharyngeal wall just above the larynx. This growth measured approximately $3 \times 2 \times 1$ cm., was pedunculated, and was freely movable except at its point of attachment. It acted as a check valve in shutting off inspiratory air currents. The larynx proper was otherwise normal.

X-ray studies of the chest showed a diffuse fibrosis in both lungs. The cardiac shadow was normal. Plates of the pharynx and larynx showed both tumors in their respective positions and failed in either case to reveal any involvement of the vertebrae. The larynx appeared normal, though the thyroid cartilage showed considerable calcification.

The Wassermann and Kahn reactions of the blood were positive ($++$). The sputum was negative for B. tuberculosis in two examinations, and the urine showed nothing unusual.

Operative removal of the tumors was effected by applying diathermy to the base and cutting with the cold snare, the tumor from the nasopharynx presenting the greater difficulty in the process. Both tumors were completely removed, and the patient made an uneventful recovery. He was discharged in three days with instructions as to antiluetic treatment.

Gross examination of the tissues showed two polypoid masses. The growth from the nasopharynx showed on section no definite invasion of the mucosa by tumor tissue, a narrow band of submucosal connective tissue separating the two areas. The tumor was grayish pink and granular in appearance and seemed to be growing from several centers. In some portions the color was darker, approaching a reddish brown. The
mass presented a broad base of attachment, and the mucosa covering it was congested, with a few small points of erosion. The second tumor, from the hypopharyngeal region, had a distinct pedicle. The mucosa covering this growth was intact and somewhat paler than normal. On section this tumor presented the same gross picture as the other. Frozen sections were made, at 8 microns, from both tissues and stained with hematoxylin and eosin.

The tissue sections made from these tumors all showed a dense growth composed almost entirely of plasma cells. In most places this growth lay definitely below the mucous membrane, being separated from it by a thin layer of fibrous connective tissue and a deposit of round cells lying directly below the squamous epithelium. In some places, however, the growth of plasma cells impinged on the covering squamous epidermal, causing sufficient pressure to produce destruction of the mucous membrane with ulceration. In the neighborhood of these ulcerated areas, hydropic degeneration of the squamous epithelium, particularly in the basal layers, was observed. While the tumor was for the most part encapsulated, in some fields the growth appeared unconfined and definitely invasive in character. The bulk of the tumor was composed of rather typical plasma cells, mostly of average size with dark staining protoplasm and eccentric nuclei. These nuclei were round or oval in contour, with a rather irregular radial arrangement of the chromatin. While the tumor was fairly uniform in appearance, some variation was noticed in the size and shape of the cells and of their nuclei. Very few giant plasma cells were seen and mitotic figures were found only after careful search of many fields. The tumor grew in fairly large sheets of solid cells supported by a fine reticular stroma. The cell islands were surrounded by heavier fibrous tissue strands and throughout numerous capillary lymph and blood vessels were observed. A definite tendency toward perivascular arrangement was characteristic. The sheet-like disposition of the cells was quite different from the more or less loose grouping found in inflammatory lesions. Many of the capillary lymph channels were dilated and filled with mucoid secretion which took the eosin stain. In most places the endothelial cells lining these capillaries remained intact and were readily seen; in others they had disappeared and the secretion lay in direct contact with tumor cells. Round-cell infiltration was definitely absent in the tumor proper and was observed only in the inflammatory areas about the ulcerated mucous membrane.

The histologic picture suggested a neoplastic growth rather than inflammatory reaction. The lack of mitosis in the plasma cells of the tumor, in contradistinction to the
frequency of such figures in the plasma cells of inflammatory lesions, and the absence of round-cell infiltration pointed to the correctness of this contention. On the other hand, from the histology the malignancy would be characterized as low, which observation was amply verified by the long duration without serious inconvenience or metastasis. Nothing in the histologic make-up was even remotely suggestive of infectious granuloma.

The patient was again seen on Dec. 20, 1933, and on Feb. 26, 1934, approximately one month and three months respectively after operation. No recurrence of the tumors was observed at either visit. Breathing was free, with no choking spells. At the time of the last visit the Bence-Jones reaction could not be demonstrated in the urine, and the long bones were all negative roentgenographically for tumor involvement. Antisyphilitic treatment had been instituted, and the blood count was normal.

We believe this tumor to be a true neoplasm. No histological signs of tuberculosis or syphilis were discovered.

**COMMENT**

Extramedullary plasma-cell tumors are comparatively rare if one may judge from the cases reported in the medical literature. To date only 20 cases, including the one here presented, have been reported in the upper respiratory passages. This type of tumor occurs rarely in females and is usually found after middle age. The major clinical symptom was nasal obstruction in 11, difficulty in swallowing in 4, epistaxis in 2, hoarseness in 2, and dyspnea in one case. These tumors arise in the nose and various portions of the pharynx, while two have been reported in the larynx, the symptoms presented being due largely to the location of the growth. Enlargement of regional nodes occurred in 5, but means little unless histologic examination can be made. Recurrence after removal was reported in 6 of the 19 cases, and 4 of the cases were regarded as being probably malignant.

There is considerable variation of opinion as to the significance of the plasma-cell tumors. Some authorities regard them as neoplastic in character; others include them in the inflammatory lesions; while still others consider them as granulomas due to a specific toxic agent. Rösse, von Werdt, and Pallestrini believed that their cases were undoubtedly of neoplastic nature and most probably malignant. Vogt
seemed not so certain in this conclusion. Boit, Wachter, Facchini and Scalas, Hückel, Blacklock and Macartney, and Claiborn and Ferris were inclined to classify their cases as benign neoplasms. Kusunoki and Frank, and also Bronzini, favored a granulomatous nature, probably due to a specific toxic agent. Borri considered his two cases distinctly syphilitic in origin. To express the wide divergence of interpretation as to the nature of such mesoblastic tumors, many names ranging from granuloma plasmacellulare (Vogt), through plasmocytoma (an expression first used by Unna), to plasma sarcoma (Facchini and Scalas) have been suggested. Dr. James Ewing, who has previously called attention to the occurrence of plasma-cell growths in the pharynx and nasal passages, has seen sections of the growth here described, and considers this tumor definitely neoplastic and invasive in character.

In our opinion the tumors in the case here presented histologically resemble true plasma-cell myelomas rather than the plasma-cell granulomas which are frequently found in the mouth. More careful study of the polypoid tumors of the upper air passages might, we believe,
<table>
<thead>
<tr>
<th>No.</th>
<th>Author and Date</th>
<th>Age and Sex</th>
<th>Symptoms, Duration, Etc.</th>
<th>Location of Tumor</th>
<th>Tumor Single or Multiple</th>
<th>Glandular Involvement</th>
<th>Pathologic Impression 1</th>
<th>Recurrence</th>
<th>Therapy</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Schirrle, H., 1905</td>
<td>40 M</td>
<td>Not given</td>
<td>Nose</td>
<td>M</td>
<td>S</td>
<td>None</td>
<td>B</td>
<td>R</td>
<td>S</td>
</tr>
<tr>
<td>2</td>
<td>Bolt, H., 1907</td>
<td>55 M</td>
<td>Increasing hoarseness for two years</td>
<td>Larynx, at false cord, in sinuses of Morgagni. Size of small cherry</td>
<td>S</td>
<td>None</td>
<td>B</td>
<td>R</td>
<td>S</td>
<td>Healed and well six months later</td>
</tr>
<tr>
<td>3</td>
<td>von Werdt, F., 1911</td>
<td>69 M</td>
<td>Difficulty in swallowing and nasal speech</td>
<td>Posterior surface uvula, freely movable. Size of walnut</td>
<td>M</td>
<td>Cervical, axillary, inguinal</td>
<td>G or M?</td>
<td>None</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>4</td>
<td>Vogt, E., 1912</td>
<td>20 M</td>
<td>Sudden onset of increasing difficulty in swallowing</td>
<td>Uvula, pharynx, tonsils, epiglottis, supraglottic structure, cervical, axillary and inguinal nodes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>S</td>
<td>Roentgen therapy without results</td>
</tr>
<tr>
<td>5</td>
<td>Kusunoki, M., and Frank, 1915</td>
<td>44 M</td>
<td>Node in left side of neck. Two years later respiratory difficulty, epistaxis, and tumors of nasopharynx. Loss of weight. Died four years after swelling of thigh, probably of same nature</td>
<td>Pen sized mass at angle of left jaw. Two years later nasopharynx</td>
<td>M</td>
<td>Cervical</td>
<td>G</td>
<td>R</td>
<td>S</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Wachter, H., 1914</td>
<td>48 F</td>
<td>Began twenty years before with hoarseness and pain in neck.</td>
<td>Floor both nasal fossae, posterior surface soft palate, left false cord. Eustachian region</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>S</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Rogers, J. T., 1920</td>
<td>42 M</td>
<td>Epistaxis of one year duration, nasal obstruction, anemia</td>
<td>Inferior border of Eustachian tube and adjoining soft palate</td>
<td>M</td>
<td>None</td>
<td>B</td>
<td>R</td>
<td>S</td>
<td>Growth removed, uneventful recovery</td>
</tr>
<tr>
<td>8</td>
<td>Facchini, J. B. and Scalas, A., 1925</td>
<td>47 F</td>
<td>Difficulty of breathing through right nose, of two years duration. No recurrence one year after removal</td>
<td>Upper and posterior portion of right nasal septum</td>
<td>S</td>
<td>Physical exam. neg.</td>
<td>B</td>
<td>0</td>
<td>S</td>
<td>Husband has had syphilis. His Wassermann reaction negative</td>
</tr>
<tr>
<td>9</td>
<td>Riehle, H., 1926 (Oppikofer)</td>
<td>54 M</td>
<td>Swelling of cervical glands and, nasal obstruction of eighteen months' duration</td>
<td>Sphenoidal sinus, roof of pharynx, and upper left nose, posterior surface soft palate, left antrum, cervical nodes</td>
<td>M</td>
<td>Cervical</td>
<td>M</td>
<td>S</td>
<td>S</td>
<td>Died three days after operation of angina and general infection</td>
</tr>
<tr>
<td>10</td>
<td>Hajek, R., 1926</td>
<td>53 M</td>
<td>Had nasal polype removed from right side two years before. Fourteen months later exophthalmos right eye and tumor size of bean in inner angle right orbit</td>
<td>Tumor of right ethmoidal cells and frontal sinus, broken through into orbit</td>
<td>S</td>
<td>None reported</td>
<td>0</td>
<td>0</td>
<td>S</td>
<td>Good recovery</td>
</tr>
<tr>
<td>11</td>
<td>Höckel, R., 1927</td>
<td>40 M</td>
<td>Partial nasal obstruction for six months, becoming almost complete</td>
<td>Nasopharynx and mucosa of posterior edge of wing of vomer</td>
<td>M</td>
<td>None</td>
<td>B Neoplasm</td>
<td></td>
<td>S</td>
<td>Cervical adenitis in youth</td>
</tr>
</tbody>
</table>

reveal the more frequent occurrence of these rare neoplasms. A varied terminology has been used to describe this type of tumor, the particular designation being largely dependent on the opinion of the observer as to its source and as to its malignancy. We have found x-ray plates taken laterally of the pharynx and larynx to be of definite value in the diagnosis of such growths and would suggest their more extensive use. Surgical removal of the tumors was done in most of the reported cases. In 6 of these recurrence was noted one or more times. Wide surgical removal with curettage of underlying bone has been suggested. In one case radium therapy, in small dosage, preceded surgical removal, while a combination of radium and x-rays is reported to have effected marked diminution in the size of the tumor in another. In the event of recurrence in our patient we would be disposed to use external irradiation followed by implantation of emanation seeds in the local growth.

Summary

1. A case of plasma-cell tumors occurring simultaneously in the nasopharynx and hypopharynx, apparently of neoplastic nature, has been described clinically and pathologically.

2. The 19 plasma-cell tumors of the upper air passages previously reported have been variously interpreted as granulomatous, inflammatory, benign, or malignant by different observers. Details of these cases are presented in tabular form.

3. We suggest that the occurrence of polypoid growths in the upper air passages, of single or multiple nature, with a history of long duration should arouse suspicion of a plasma-cell tumor. We also suggest the use of x-rays as an aid to diagnosis.

4. We believe the tumors reported to be unusual and dissimilar to most of the tumors previously reported, in that they are definitely neoplastic.

BIBLIOGRAPHY

### Plasma-cell Tumors of the Upper Air Passages—Cont.

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<th>Therapy</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>Pallestrini, E., 1927</td>
<td>63 M.</td>
<td>Right nasal obstruction and discharge, with frontal headache on same side and pain in region of first and second division of fifth cranial nerve, right side. Right moderate exophthalmos</td>
<td>Inferior half right lateral wall of nose</td>
<td>S</td>
<td>Cervical, axillary, inguinal, supraclavicular</td>
<td>M</td>
<td>Yes</td>
<td>Metastasis</td>
<td>8</td>
</tr>
<tr>
<td>13</td>
<td>Bronzini, A., 1928</td>
<td>53 M.</td>
<td>Right nasal discharge and obstruction. Sneezing. Duration four years</td>
<td>Right inferior turbinate</td>
<td>S</td>
<td>None</td>
<td>G</td>
<td>0</td>
<td>8</td>
<td>Died after nine to ten months of broncho-pneumonia</td>
</tr>
<tr>
<td>14</td>
<td>Borri, C., 1928</td>
<td>56 M.</td>
<td>Difficulty in eating solid food. Left nasal obstruction. Operation, local recurrence. Second operation and recurrence. Disappearance of lesion after anti-syphilitic treatment</td>
<td>Posterior pharyngeal wall, right tonsil, left nasal fossa</td>
<td>M</td>
<td>Cervical</td>
<td>G</td>
<td>Recurrence in nose</td>
<td>8</td>
<td>Active antiluetic treatment also given</td>
</tr>
<tr>
<td>15</td>
<td>Kaufmann, E., 1922</td>
<td>30 M.</td>
<td>Left nasal obstruction</td>
<td>Nasal</td>
<td>S</td>
<td>Not noted</td>
<td>S</td>
<td>8</td>
<td>R &amp; X-Ray</td>
<td>Marked shrinkage under radiation</td>
</tr>
<tr>
<td>16</td>
<td>Rosenwasser, H., 1930</td>
<td>34 M.</td>
<td>No note for years</td>
<td>Right intertubal area obstructed</td>
<td>S</td>
<td>Physical neg.</td>
<td>G-B</td>
<td>0</td>
<td>8</td>
<td>Seen one and one half years later. No recurrence</td>
</tr>
<tr>
<td>17</td>
<td>Claiborn, L. N., and Ferris, H. W., No. 1, 1930</td>
<td>60 M.</td>
<td>Right nasal obstruction and discharge of two years' duration</td>
<td>Right mid. meatus extending over mid. turbinate, fossa of Rosemüller</td>
<td>M</td>
<td>Physical neg.</td>
<td>B</td>
<td>R</td>
<td>S &amp; R 33.75 mc. hrs.</td>
<td>No recurrence six months later</td>
</tr>
<tr>
<td>18</td>
<td>Claiborn and Ferris No. 2, 1930</td>
<td>64 M.</td>
<td>Hoarseness and difficulty in clearing throat</td>
<td>Right ventricular band, two polyps. Naopharyngeal polyps two on posterior wall, three from naopharyngeal surface soft palate</td>
<td>M</td>
<td>None</td>
<td>B</td>
<td>R</td>
<td>8</td>
<td>Slight recurrence on three occasions in two and one quarter years</td>
</tr>
<tr>
<td>19</td>
<td>Blacklock, J. W. S., and Macartney, C., 1932</td>
<td>61 M.</td>
<td>For two years past, a feeling of something in throat, causing difficulty in swallowing. For past two months a feeling of suffocation, as if throat were closing, especially on reclining. Voice somewhat thick and nasal</td>
<td>Pedunculated tumor from right hypopharyngeal wall near right aryepiglottic fold, approximately 3 × 2 cm. Another tumor 4 × 3 cm. arising from posterior naopharyngeal wall behind soft palate</td>
<td>M</td>
<td>None</td>
<td>B</td>
<td>8</td>
<td>Given antiluetic treatment. Sputum neg. for tubercle bacilli twice. X-ray of chest shows pulmonary hilar and obliteration of costophrenic sinus with general infiltration not unlike pneumoneiosis</td>
<td></td>
</tr>
</tbody>
</table>
Pallestrini, E.: Arch. per le sc. med. 51: 175, 1927.