A Case Report of Primary Tracheal Cancer from Leprosy
Autopsy series with a Review of the Literature

Akiko OBARA, Nobuo HARADA, Shigeo MATSUMOTO
(National Leprosarium Oku-Komyoen)
Masanori KITAICHI
(Chest Disease Research Institute, Kyoto University)
Mutsuhiro FURUTA
(Kyoto National Hospital)

(Received for publication: January, 9, 1984)

Abstract: Tracheal cancer is noted for its low incidence. We encountered a case of tracheal cancer, supposedly related to prolonged use of a metal tracheotomy tube in Oku-Komyoen, a leprosarium. During the past 21 years, there were 181 autopsy-cases in the leprosarium, out of which 39 cases (21.5%) showed malignancy. This ratio is not far different from the incidence of general malignancies. It is peculiar, however, for us to experience such a rare disease as tracheal cancer in our small autopsy series of leprosy patients. Our article reports this rare case of primary tracheal cancer with a review of the literature.

Pathological reports of laryngo-tracheal tracts of leprosy patients are rather limited in the category of leprosy pathology such as severe lepromatous infiltration of the laryngeal mucosa or laryngeal edema both of which need an emergency tracheotomy. Since quite effective antileprosy drugs have become available in leprosy treatment, these kinds of pathological findings have been removed from the leprologists. A case of tracheobronchopathia osteochondroplastica was reported by Furuta et al in 1982. After that case, no other leprosy autopsy case reports of tracheal pathological changes were made.

Case report

Our case is a 68 year old Japanese male, an arrested lepromatous leprosy case. His disease was noticed in 1941 when no definitely effective antileprosy drugs were available yet in Japan. His disease got progressively worse and in 1950 he needed tracheotomy for severe laryngeal lepromatous infiltration with edema. Tracheotomy was performed and a tracheotomy metal tube was applied. The patient was selected as a case to be treated with Promine, which had just been introduced into Japan and treatment with it was very limited. On administration of Promine, the patient’s disease responded so well to it that in regular annual examinations he became bacillary negative from 1964 till his death. The laryngeal change of the patient

*Address for reprint: Dr. Akiko Obara Oku-Komyoen, National Leprosarium, Mushiake, Oku, Oka
yama, Japan Zip 701-45
caused by lepromatous granuloma disturbed the motion of his vocal cords, so that his voice got husky and he felt difficulty in coughing up sputum through his mouth when he repeatedly suffered from bronchitis. He was anxious about the removal of the tracheotomy tube because he coughed out sputum through it with less difficulty. The clinical record noted that the orifice of the tracheotomy fistula got inflamed and erosive early in 1962, 20 years before his death. Surgical treatment for closure of the fistula was discussed but his vocal cords were stiff and the space between the cords was too narrow to function in coughing up the sticky bronchial discharge through them. However, he enjoyed a rather uneventful life in the leprosarium afterwards containing heavy smoking of 30 strong cigarettes per day without filters. He attended NT clinic once or twice daily for washing the metal tube and then reapplied it. In February 1982, the patient visited a doctor for an abnormal feeling on breathing and a feeling of general weakness. His disease was treated as a nonspecific upper respiratory inflammation by an internist, and an otorhinorallyngologist checked him on the internist's request. In July 1982, five months after the initial signs of tracheal cancer, the patient died. Before his death he suffered severe respiratory distress three times of short duration for intervals of several days.

Autopsy revealed tracheal cancer (Fig. 1).

Pathological findings were as follows: There was a tracheotomy tube fistula on the anterior wall of the trachea. The tumor was seen just at the orifice of the fistula, invading the entire lumen and circularly extending down 6 cm toward the tracheal bifurcation. The color was grayish-yellow. Its surface was rough, granular and uneven. The consistency was firm. The tumor was covered with bloody mucus (Fig. 2). Microscopically, the tumor was a well differentiated squamous cell carcinoma with neither metastases nor invasion into other organs. The lungs, liver, spleen, kidneys, adrenals and the pancreas were congested. The bone marrow was anemic and there were some tuberculous granulomata in the bone marrow (Fig. 3). There were residual lepromata in the hepatic parenchyma (Fig. 4). The peripheral nerves were markedly destroyed and degenerated by leprosy. The lymph nodes showed various pathologic changes reflecting the complex history of this patient's disease. They showed depletion of both B and T cell areas (Fig. 5) and there were residual lepromata and old tuberculous foci. There were some multinucleated giant cells (Fig. 6), some of which contained lipid-like substances which seemed to be phagocytosed.

Discussion

The incidence of primary tracheal cancer has been reported by several authors. According to Salm's description(1), Ranke (1962) said he experienced only one case out of 139,000 autopsies. Keeney (1837) experienced one out of 15,000 autopsies. Figi (1930) mentioned that he encountered five tracheal cancers among his 470 laryngeal cancer cases. Other reports(2-7) gave the same low incidence levels as quoted above. The incidence of bronchial cancer has continuously increased in a remarkable speed but tracheal cancer has been very slow. There have been 181 autopsy cases in Oku-Komyoen since the institute resumed autopsies in 1962. There was a 6 year intermission again after resumption of autopsies from 1971. The cause of death in all
Fig. 1 Macroscopic view of the tracheal tumor, arising from the site of tracheotomy and extending near the tracheal bifurcation. It grew annularly along the total circle of the tracheal wall.

Fig. 2 Histologically the tracheal tumor is a well differentiated squamous cell carcinoma. HE stain, ×100

Fig. 3 Granulomata in the bone marrow, showing a multinucleated giant cell and suggesting a tuberculous etiology, HE stain, ×100

Fig. 4 A leproma in the hepatic parenchyma, HE stain, ×100

Fig. 5 A cervical lymph node shows prominent depletion of both B and T cell areas. HE stain ×100

Fig. 6 There are multinucleated giant cells in the lymph nodes. Some of the giant cells contain lipid-like substance which seemed to be phagocytosed, HE stain ×100
the cases was surveyed and only two cases died with cancer of the upper respiratory tract, one was laryngeal cancer and the other was tracheal cancer as reported in this article.

As for sex, according to Salm's description\(^1\), reporters agreed with the higher incidence in males; Culp (1938) said 63% of the total number were males, Olsen (1939) said the male to female ratio was 2 : 1 and Moersch reported 4 : 1 were males. Morrison mentioned a marked predominance in males also. Our case was also male. The ratio seemed to be getting equal, supposedly reflecting an increase of female smokers, if smoking is one of the major etiologic factors in development of cancer.

As for age, it is rare to see tracheal cancer in the younger generation; few below 30 years of age. According to Salm's description\(^1\), the average age of onset was reported as 50 (Moersch, 1954), 51 (Dalby and Jones, 1961) and in the 6th decade (Salm, 1964)\(^1\). Morrison\(^2\) said the peak of age distribution fell between 50-60 years of age. These are calculated on the basis of the total number of tracheal cancer cases which included cribriform adenocarcinoma, possibly identical with adenoid cystic carcinoma, commonly affecting young adults. Excluding this type of carcinoma, the peak of age distribution of onset drops between 50-60 years of age. Our case was 68 years of age at his death.

As for the location of primary tracheal cancer, the lower trachea near the tracheal carina was the most common site (Dhand, 1981)\(^7\). The upper portion followed it and the middle portion was the rarest site. The site near the major bronchi was the most acceptable predilection for cancer in the trachea. The recent statistical survey, however, shows the reverse of the most predisposing site from the lower into the upper portion, based on the data after 1947 (Salm, 1964)\(^1\). The posterolateral wall, junctional border of the cartilagenous and fibrous membrane, was pointed to as the site of predilection. Our case showed the macroscopic tumor at the site of the tracheotomy tube on the anterior wall instead of the posterolateral wall. Salm\(^1\) quoted from Strauss' article (1922) that the lymphatic drainage of the trachea runs horizontally from anterior to posterior. In our case, the cancer originated at the site of the tracheotomy in the anterior wall, and seemed to have spread circularly with ease on the lymphatic drainage from the anterior to the posterior wall, though it is rare that the cancer occupies annularly the total tracheal segment.

Histologically, primary tracheal malignant tumor are classified into five patterns by Salm\(^1\), though there are different classifications by the other pathologists, 1) squamous cell carcinoma, 2) adenocarcinoma, 3) cribriform adenocarcinoma (possibly identical with adenoid cystic carcinoma), 4) small celled (oat-cell) anaplastic carcinoma and 5) carcinosarcoma. Of these types, many of reporters agreed that squamous cell carcinoma was the commonest. There have been sophisticated discussions on classifying these malignancies as in other neoplasmas, based on the cell origin, cytological and histological morphology and so on. Our case showed pearl formation, on which basis we classified it as squamous cell carcinoma together with other typical histological features.

As for metastasis, the metastatic sites reported formerly are regional lymph nodes, lungs, skeletal, gastrointestinal tract, liver, spleen, pancreas, kidneys, the trachea itself, pericardium, abdominal lymph nodes, heart muscle and valves, brain, adrenals, pleura and axillary lymph...
nodes, prostate and skin. Our case showed no metastasis.

As for secondary malignancy from other parts of the body to the trachea, according to McKenzie and several other reporters, the larynx, esophagus, thyroid and bronchi were mentioned as primary sites. Metastasis from distant organs as from the colon, breast and uterus were mentioned but these metastases were quite rare.

Furuta et al reported secondary malignancy of the trachea in a case of Kaposi’s sarcoma seen in a leprosy patient, of which the primary lesion was in the scalp.

Exact etiologic factors are still to be studied. All of the articles reporting on and discussing about tracheal cancer pick up smoking as the most probable etiologic factor. Smoking is also regarded as a major background factor in the pathogenesis of lung cancer which has increased strikingly in incidence though the incidence of tracheal cancer, on the other hand, is increasing slowly. This discrepancy between the incidence of these two tumors on the same etiologic factor is likely to be due to the structural difference between them. The trachea was a much wider lumen and its ciliary activity to remove irritative substance is much more vigorous in the trachea. That is why, supposedly, the incidence of tracheal cancer is much lower than bronchial cancer and increases slowly. Our case had a quite abnormal condition in smoking. He was a very heavy smoker, though the smoking index was not clearly known. In this case, the smoke passed through a very narrow space between the metal tracheotomy tube and the tracheal mucosa. It means the tobacco factor stimulates the tracheal mucosa much more strongly and stays longer in the narrow space with much less active cilia movement to remove the irritating substance. The tracheotomy tube had been cleansed once or twice daily and reapplied with abnormal friction upon the mucosa. This friction had been regularly and repeatedly given to the mucosa every day for 32 years. The number of friction stimulations may be over twenty thousand times during 32 years.

From the viewpoint of immunodepression of the lepromatous leprosy patient, microscopic findings of the lymph nodes show sparses T cell areas without normal follicle formation in the B cell areas, suggesting poor immunological defence mechanisms did not function effectively. His antineoplastic system did not protect the body from promoting the stage of his cancer. Some other initiating factors mentioned are some oils used in machine operation, irradiation therapy of thyroid disease, and prolonged exposure to toxic gas during the production of poison gas bombs. Our case had no contact with these etiologic factors.

We conclude that heavy smoking, mechanical stress repeated for a long time, a narrow space for the smoke to pass with depressed ciliary motion and immunodepressive condition as aging work together to establish this rare tracheal cancer.

Summery

A very rare case with tracheal squamous cell carcinoma is reported. The case appears to be related to prolonged use of a metal tracheotomy tube, a severe smoking habit and an exhausted immunological defence mechanism based on his long-standing lepromatous leprosy.
Acknowledgement

Our gratitude is expressed to Dr. C. F. Clark, Japan Baptist Hospital, Kyoto, for his advice in preparing the manuscript.

References

らい患者剖検例中にみられた原発性気管癌の一症例および文献的考察

小原安喜子 原田 离雄
松本 繁雄
(国立療養所鳥取光亮園)
北 市 正 則
(京都大学胸部疾患研究所)
古 田 睦 廣
(国立京都病院)

頻度の低い原発性気管癌の一剖検例を経験したので報告する。症例は男子、死亡時68歳、鈍性のらい罹患症例。1933年、らいの診断を受け、1941年らい療養所に入所した。山仕事で、喫煙を好む。1950年、喉頭らい病変のため呼吸困難を来たし気管切開が行われた。病理学的所見によりかい歯症疑う。1964年以降、胃検査は死亡時まで検出を続けた。気管切開孔は死亡時の20年前後より発展・炎症がみられたが、喉頭部の発育性変形があり、呼吸と咳嗽出のため、気管切開孔の外科的閉鎖が見送られた。使用された金属カニューレはその後32年間洗浄のための着脱を毎日1〜2回行っていた。1982年2月、呼吸の異常と全身状態の異常を訴えて来診し、月に死の転機をとった。剖検により気管切開孔より気管分岐部に直径6cm位の長さで気管内腔全周を占める腫瘍病変をみた。腫瘍は、灰黄色、表面に細かい凹凸のある腫瘍で一部白苔状となっている。組織学的には癌性変を形成している高度分化扁平上皮癌であった。骨髄には顕微鏡的に肉芽腫形成があり、多核巨細胞が出現している。肝内には顕微鏡的らい病変の残存を見た。リンパ節はT-B型新鮮、古い結核結節、脂肪様細胞を処理しているとみられる多核巨細胞の出現等多彩な像を示す。事実、腫瘍の線維化は著明である。

考察：原発性気管癌は極めて頻度が低い。文献によると男子、60歳代、多喫煙者に発生が多い。本例は男子、68歳、多喫煙者であると共に、金属カニューレを使用した気管切開の手術を繰り返した部位より発生し、カニューレ使用時間の延長を含む喫煙を多く常用し、喫煙成分の刺激増強、刺激の局所滞留があると思われる。また、リンパ節所見から、基礎疾患であるL型らいの経過中に免疫系の機能低下があったことが示唆され、上皮細胞の機能化その進展を示し観察機能が不充分であったことも、この稀な癌の成立にかかわりがあるものと思われた。

この研究に関する費用の一部は、国立療養所、治療研究費によって賃負われました。ことに謝意を表します。