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Some Considerations on Massive Stomach Bleeding Complicated with Head and Neck Cancers

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頭頸部癌に合併した胃大出血についての2, 3の考察

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過去4年間(1966~1970年)に頭頸部癌約200例の放射線治療を行った。これ等の中で、(1) 右口蓋扁桃癌(男73才, T2N3M0) (2) 舌癌(男59才, T4N1M0), (3) 舌癌(男40才, T3N2M0) 及び、(4) 右下顎歯肉癌(男70才, T4N2M0) の4例に胃潰瘍の大出血が合併した。胃出血は、舌癌(男59才)例では放射線治療中に発生(吐血400cc)した。本例は治療を中断して実施した胃切除で救命し得た。他の3例は治療終了後の全身状態、局所反応が改善されぬ時に発生し直接死因となつた。4症例の原発巣及び転移巣に対する治療効果は剖検結果により認められた。胃潰瘍はUI IVで胃角部附近或いは体部後壁に存在し進行性慢性消化性潰瘍で穿孔或いは癒着があつた。

駿河台病院の頭頸部癌剖検数(7年間)32例中3例の直接死因が胃潰瘍大出血であつた。同時期の肺癌35例には胃潰瘍大出血はなかつた。日本剖

検報(昭和42年)の調査では合併胃潰瘍の頻度の差はないが胃潰瘍の出血死は肺癌1018例中10例(0.98%), 頭頸部癌391例中15例(3.84%)で有意差があつた。

頭頸部癌では癌の治療中或いは終了後の短い間に発生していた。頭頸部癌患者の合併胃潰瘍が急速に悪化する理由は、高令者が多い、放射性口腔粘膜炎による疼痛及び食餌摂取困難等から低栄養状態になり易いこと、症状を改善するための各種鎮痛剤による胃障害の助長、鼻腔ゾンデ等の刺激もある、更に頭頸部癌病巣は他の部位の病巣と異り患者が病状を認識出来る等、精神肉体医学説も関連すると思われる。

頭頸部癌の治療では諸検査に加えるに消化管のX線検査等を実施し潜在性の胃病変の把握と局所反応が高度で全身状態が不良の時は消化管出血の可能性が有る事に注意し管理を更に慎重に行うべきである。

Introduction

During the past four years, from June 1966 to May 1970, about 200 cases of head and neck cancers were treated with high energy radiation at the Dept. of Radiology, Surugadai Nihon Univ. Hospital⁴⁾⁵⁾. Among these, we experienced four cases⁶⁾ of the massive haemorrhage from gastric ulcer complicated with above diseases during or immediately after the treatment. In the three cases of them, unfortunately the massive haemorrhage from stomach ulcer was the direct cause of death.

Therefore, we will hereon report these cases briefly and point out the importance of controlling the digestive tract during and immediately after the radiation treatment of head and neck cancers. And secondly, we will investigate if there is any relation between the massive haemorrhage from stomach and head and neck cancers.

Case Report

Case 1. Carcinoma of Tonsil (T2N3M0) seventy-three years old, male.

Past History: 34 years old, appendectomy, 37 years old, hepatitis.

Present Illness: Since Oct. 1967, he suffered from foreign body feeling and slight bleeding from the right side of tonsil.

In the middle of Jan. 1968, he visited our hospital and was diagnosed as squamous cell carcinoma of the right side of tonsil. Then he was admitted to our Department of Radiology. A total tumor dose of 7,000 rad/40 days was given with external electron beam to the both of primary lesion and metastatic lymphnodes on the right side of the neck. By this treatment the primary tumor was markedly regressed and the metastatic lymphnodes almost disappeared.

During the later part of the course of the treatment, severe radiation muco epithelitis developed and he suffered from pain and loss of appetite. Therefore, he was supplied with high-caloric semifluid diet and intravenous fluids daily. After the completion of the radiation treatment, he was discharged from the hospital.

He was re-admitted in four weeks because he suddenly vomited blood with discomfort in the epigastrium. The primary lesion and metastatic lymphnodes were controlled clinically. Blood transfusion and I.V. fluids were given. When he came to a state lull, the stomach X-ray examination was taken, and a large gastric ulcer located at the posterior wall of the body of the stomach was found. His general condition became weak and he died on the thirty-first day from re-admission.

At the autopsy a few viable cancer cells remained at the primary lesion and necrosing nests of cancer cells were found at metastatic lymphnodes microscopically. The gastric ulcer (UI-IV) was located at the posterior wall of the body and its size was 7 cm × 5 cm with penetrated to the pancreas as shown on Fig. 1.

Case 2. Carcinoma of Tongue (T4N1M0), fifty-nine years old, male.

Past History: No serious illnesses.

Present Illness: In Nov. 1966, the left margin of tongue swelling, he had a pain of the part. At the end of Jan. 1967, he was admitted to our hospital and was diagnosed as squamous cell cancer of the tongue.

The primary lesion and metastatic node were treated with external electron beam therapy. When



Fig. 1. The photograph shows the chronic penetrated gastric ulcer which was located at the posterior wall of body; Ul-IV, the bottom of the ulcer consisted of pancreas.



Fig. 2. The photograph shows the chronic stomach ulcer which was located at the posterior wall of the angle and its size 2 cm \times 1.5 cm, Ul-IV. At the bottom of the ulcer, a small destroyed artery was found.

the dose of 5,400 rad/23 days was irradiated, he had loss of appetite and a slight epigastric pain. On 11th of March, he suddenly vomited a great deal of blood (400 cc). The cause of bleeding was diagnosed as gastric ulcer. Therefore stomach resection was performed. The stomach specimen revealed that the ulcer was located at the posterior wall of the angle and its size was 2 cm \times 1.5 cm Ul-IV as shown on Fig. 2. Radiation treatment was interrupted for 30 days until 10th of April. Therefore the treatment plan was obliged to be changed unfortunately. From 11th of April, irradiation to the primary lesion and metastatic node was delivered again. In June additional irradiation to tongue was given.

Although the primary lesion and the lymphnode were reduced, his general condition became weak step by step and he died on 18th of Dec. with lung abscess. Autopsy revealed that viable cancer cells did not remain in the primary lesion and the lymphnode.

Case 3. Carcinoma of Tongue (T3N2M0), forty years old, male.

Past History: No serious illnesses.

Present Illness: He became aware of the swelling with white belag which was located in the left margin of tongue in Jan. 1968. He was admitted to our Dept. and was diagnosed as squamous cell carcinoma of tongue. The primary lesion was treated with intra oral therapy with 6 MeV electron. Daily dose of 500 rads was irradiated 2 times per week and the total dose of 7,500 rad/50 days was given. On the other hand, metastatic lymphnode was irradiated the total dose of 5,700 rad in 32 days.

By this treatment, the primary lesion was controlled clinically and metastatic lymphnode reduced distinctly. Six months later, new metastatic lymphnode developed to the margin of the irradiated field. Combining therapy with electron beam irradiation (4,600 rad/30 days) and chemotherapy (5FU 250 mg/day \times 20) was given in Oct. 1968. Although the effect of the combined therapy was poor, in Jan. 1969,

extripation of the lymphnode was performed.

In April, skin metastases appeared at the left side of the neck, therefore the electron beam therapy was delivered again. But the lesion became worse step by step and he could hardly take diet. His general condition became weak and he had a slightly epigastric pain from the end of May 1969. Then he was readmitted on 9th of June. The result of blood examination did not show anemia to make us suggest the bleeding. But suddenly he died on 10th of June vomiting a large amount of blood. Autopsy revealed that the gastric ulcer (3.5 cm \times 3 cm) Ul-IV was located at lesser curvature of the angle and perforated as shown on Fig. 3. The small intestine and the large intestine were filled with blood from gastric ulcer.



Fig. 3. The Photograph shows the chronic stomach ulcer (3.5 cm \times 3 cm) Ul-IV located at the lesser curvature of the angle and perforated.

In the primary lesion a few viable cancer cells were found and viable cancer nests were seen in the skin at the left side of the neck.

Case 4. Carcinoma of Lower Gum (T4N2M0), seventy years old, male.

Past History: No serious illnesses.

Present Illness: He felt the palpable lymphnode at the right angle of the jaw in June 1969. From the beginning of July, he suffered from pain and bleeding at the right side of the lower gum. He visited our hospital and was diagnosed as squamous cell carcinoma at the right side of the lower gum. Combination therapy with intra-arterial infusion of 5FU (total 2,450 mg in 30 days) and radiation treatment (4,000 rad/20 days) was given to the primary and metastatic lesion. Tumor was radio-sensitive, the primary tumor was controlled clinically. Metastatic lesion markedly regressed. Then on 13th of Nov. 1969 the radical neck dissection was performed to the residual node. After the operation, the patient suffered from paralysis of lingual nerve and severe muco-epithelitis in the oral tissue. He could not take diet for himself. Nasal tube nutrition was delivered. From about 5th of Dec. complaining of discomfort

in stomach, he suddenly vomited a great deal of blood on 10th of Dec. The cause of bleeding was considered due to gastric ulcer. Several treatments were given. But the bleeding could not stop. And he died on 13th of Dec. Autopsy revealed that the gastric ulcer was located at the posterior wall of the body and its size was 4 cm \times 3.5 cm Ul-IV with penetrated to the pancreas. In the primary lesion viable cancer nests could not be found microscopically.

Discussion

It is important to check up the general condition, making several kinds of examinations prior to radiation treatment. Although we have been examining blood, heart, lung, and functions of liver and kidney prior to radiation therapy, we haven't made the stomach X-ray examination except for the special cases. In our cases, the omission of the stomach X-ray examination became one of the causes of failure in controlling the general condition. Therefore the stomach X-ray examination was added to the routine examinations prior to radiation treatment. And the observations of general condition of patients were taken more carefully during and after the radiation treatment.

Thus, we experienced a case (55 years old, female) of stomach ulcer complicated with maxillary cancer. The stomach X-ray examination which was taken before the treatment revealed an inactive small ulcer located at the pylorus. Radiation treatment was given carefully. On the midway of the schedule, she gradually complained of the worse of general condition and the slight pain of stomach. Stomach was re-examined. An activated ulcer was proved and the radiation therapy was interrupted for a few weeks. During these periods, the ulcer was getting better. And the radiation therapy was given again, and a good result could be got.

It is generally recognized that some kinds of diseases such as burn²⁾ and brain diseases⁹⁾ can yield the gastric ulcer. Furthermore not a few erosions or gastric ulcer occur during or after the steroid therapy^{7,8)}. In these cases, the massive haemorrhage such a large amount 500 cc–1,000 cc is relatively rare.

The Frequency of the Complicated Gastric Ulcer

About the massive haemorrhage from stomach complicated with the head and neck cancers, six cases were reported by Sato¹⁰⁾ in Japan. He had investigated for five years on autopsy that among the causes of death in seventy-six cases of head and neck cancers, six cases (8%) were due to the unexpected bleeding from stomach after the operation combined with radiotherapy or chemotherapy. In many cases which stomach bleeding occurred, the primary sites of the cancer were found on hypopharynx and oral regions. In our Surgadai Nihon Univ. Hospital, 32 cases of head and neck cancers were autopsied during these eight years from June 1963 to Sept. 1971. The direct causes of death in these cases were almost by the primary tumor or metastases or the both of them. But three cases (10%) out of the above 32 cases died due to the massive haemorrhage from the gastric ulcer with perforation.

On the other hand, 35 cases of primary lung cancer were autopsied at the same period. On this investigation, the direct cause of death in these was not owing to the massive haemorrhage from gastric ulcer, but cancer death or pneumonia.

In order to clarify the above tendency, we studied further as follows. On the paper of the magazine "Annual of the Pathological Autopsy Cases in Japan"¹¹⁾ issued in 1967, we investigated the number of the cases of gastric bleeding or perforation complicated with head and neck cancers and lung cancers. As the results of our investigation on this literature, autopsies on lung cancers were reported in 1,018 cases

and among these the massive haemorrhage from gastric ulcer realized as the direct cause of death was seen no more than in ten cases (0.98%). On the other hand, as the results of 391 cases of head and neck cancers, we could count 15 cases (3.84%) of the massive haemorrhage from gastric ulcer as the direct cause of death. But there were no differences on frequency of the complicated ulcers between head and neck cancers and lung cancers.

It proves that in comparison with lung cancers and head and neck cancers, gastric ulcer complicated with head and neck cancers grew worse rapidly and sometimes massive haemorrhage or perforation occurred subsequently. The mortality by the stomach bleeding complicated with head and neck cancers is higher than one of lung cancers. This difference revealed statistically with 5% significance.

Considerations on the Complicated Gastric Ulcer with Head and Neck Cancers

The development of stomach ulcer was explained by Harry Shay¹¹⁾ as follows. "The development of a chronic peptic ulcer is determined by the algebraic sum of two groups of forces acting on the gastrointestinal mucosa, the one defensive¹¹⁾ and the other aggressive¹¹⁾. Peptic ulcer develops when the summation of their action is resolved in favor of aggression and does not develop if the defensive mechanisms are adequate to cope with aggression, regardless of the degree of gastric acidity." "Defensive" and "Aggressive" have several factors of their own. We considered that there were any relations between these causes of the gastric ulcer and the patients who had head and neck cancers, especially during or immediately after radiotherapy.

In many cases who were given radiation therapy, irradiation to the normal oral mucosa and the salivary glands could not be avoided. Particularly, when the primary lesion was large and neck metastasis was also irradiated, severe radiomuco epithelitis occurred. The patients maybe suffered from pain and had loss of appetite. The general condition became rapidly weak and the infectious disease might occur. The condition of worse nutrition caused the reduction of resistant power of the stomach mucosa¹²⁾. To improvement of this worse condition, method of nasal nutrition is often used. But gastric tube may injure the stomach wall.

In this period, radiomuco epithelitis may also cause increasing in the toxic histamin as burn. To relieve the pain, analgesic drugs are given to usually. But it is well known that analgesic drugs¹⁷⁾ or steroid¹⁸⁾ make the erosion on the mucosa of stomach and it may subsequently grow ulcer. In our cases steroid was not used.

Arterio-sclerotic¹²⁾ changes of the stomach artery has been considered as the cause of the ulcer. In the pyloric region and the lesser curvature of the body, artery of mucosa is narrow and bending, furthermore they have a few anastomosis. For these reasons, stomach ulcer occurs in these regions with high incidence. The presence of the sclerosis easily causes the mechanical obstruction of the artery and subsequently the ulcer occurs. These phenomena are seen in aged groups much more than in younger groups. In our 5 cases, the massive haemorrhage occurred in aged patients except in one case of a forty-year-old patient. In aged groups, the patients have a few specific symptoms of the stomach ulcer. On the contrary, the frequency of stomach bleeding is higher and its quantity is also more. This fact is very important when we treat aged patients with head and neck cancers.

Generally speaking, peptic ulcer is the most numerous and simplest cases in the several psychosomatic diseases. The results of our study revealed that serious gastric ulcer complicated with head and neck

cancers was much more in number than lung cancers. From the psychosomatic point of view, as the patients with head and neck cancers can easily recognize the symptoms of his own, their psychological trouble is a great deal. Then the above mention is seemed to be applicable to this theory.

Anyway there is the high probabilities that the new ulcers and the recurrence of healing ulcers complicated with head and neck cancers may occur by the action of several factors related to one another and they grow into severe conditions rapidly.

Therefore, prior to the radiation treatment, the stomach X-ray examination should be taken. And the observation of gastrointestinal tract must be taken carefully as well as head and neck lesions, while the radiation reactions are severe and the general condition becomes weak.

Summary

We reported four cases of the massive haemorrhage from stomach ulcer which suddenly developed during or immediately after radiation treatment on cancer in head and neck. In three cases of them, the massive haemorrhage was the direct cause of death. In the course of radiation treatment, a careful attention to the upper G-I tract should be paid, especially in case whose reaction to irradiation would be severe and who developed marked debilitation. From these experiences, we decided to add the stomach X-ray examination prior to radiation treatment. We revealed that there is a higher probability of combining head and neck cancers with serious stomach ulcers than lung cancers.

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