

Esophageal carcinoma in patients with spinal cord diseases: a report on two cases and one patho-physiological hypothesis

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ABSTRACT

Two patients developed esophageal cancer: one patient had cervical poliomyelitis and the other one sustained cervical spinal cord penetrating injury.

The possible association between spinal cord disorder and the late appearance of esophageal cancer is discussed.

Key words: esophageal carcinoma, spinal cord

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Patients with chronic spinal cord damage, tend to develop various complications in the gastro-enterological tract: fecal impactions, constipation, hemorrhoids, peptic ulcer disease, (rarely) diverticulosis, rectal carcinoma or volvulus, hiatus hernia, and gastroesophageal reflux. Dysphagia may occur in those who were ventilated, had a tracheostomy, whose spinal stabilizing instrumentation is protruding anteriorly, or in whom naso-gastric tube was inserted for a long time.

To the best of our knowledge, there are no reports suggesting any association between spinal cord damage (SCD) and esophageal carcinoma.

We present herewith two case reports: one patient developed this neoplasm at the age of 65, 47 years after contracting poliomyelitis, and the other, at the age of 55, 32 years after being shot at C4 resulting in a complete traumatic spastic tetraplegia.

Poliomyelitis and esophageal carcinoma

Case 1: was born in 1930 and died in 1997. In 1948, he had contracted acute paralytic poliomyelitis, which eventually made him tetraparetic. He walked unaided with a waddling pattern. He enjoyed physical – sportive activities and achieved a respectable academic career. In 1967 he had contracted pneumonia and underwent surgical repair of an inguinal hernia. He had suffered from chronic diaphragmatic hernia (gastritis, heartburn) which was explained by diaphragmatic weakness due to his old poliomyelitis. He never smoked. During the last four years of his life, he had complained of many symptoms suggested by himself and by his physicians as “post polio-syndrome” (PPS): fatigue, weakness, functional deterioration, arthralgia, myalgia difficulties in walking, and progressive kyphosis. During the last year, he complained on swallowing disorder –dysphagia, and some reduction in his bodyweight. Gain, these signs were attributed to the “diaphragmatic hernia” and the PPS. When these signs had worsened, the diagnosis finally was made: inoperable esophageal carcinoma. Apparently, the “old chronic” post-polio signs and symptoms “masked” the newly appearance of the cancer, and caused a marked delay of its diagnosis.

There is a vast literature about the PPS [1-6]. Is an immunological proneness to infection in PPS, predispose these patients to development of cancer?

Are chronic “oncogenic” viral infections responsible for this association?

Besides PPS, we are aware of the appearance of new functional decline among those with chronic “stable non-progressive” disabilities [7].

The historical case report of President Roosevelt is worth mentioning: Ditunno, & Herbison wrote on FDR’s diagnosis, clinical course and rehabilitation from poliomyelitis [8].

“FDR, War President of the United States and the only Chief Executive in history who was chosen for more than two terms, died suddenly and unexpectedly at 4:35 PM today at Warm Springs, Ga., and the White House announced his death at 5:48 o’clock. He was 63. The President, stricken by a cerebral hemorrhage, passed from unconsciousness to death on the 83rd day of his fourth term and in an hour of high-triumph...” [9].

His death was not sudden and not really unexpected. Two articles discussed this matter [10,11]: obviously, the President with an old paralytic poliomyelitis syndrome, suffered also from overweight, hypertension, cardiac failure, recurrent respiratory infections, which are not so rare phenomena in these patients. On 28 April 1944 suspected “acute cholecystitis” was treated with codein. In Yalta Meeting, 3-10, February 1945, his general condition apparently deteriorated: weight loss, cardiac failure, anemia, fatigue, bronchitis crushing headaches, and death due to “massive cerebral hemorrhage.” Did he die eventually from metastatic melanoma? Above his eyebrow, we can easily observe a nevus. However, we would like to put forward another hypothesis: we have described a few patients who developed 30-40 years after contracting paralytic poliomyelitis, spinal cord tumors (12-13), and we had published a hypothesis how this could occur [14]. This association was never ruled -out. Reviewing the history of poliomyelitis [15] one can learn the peculiar historical occurrence and epidemiology of this disease, the late appearance of complications (PPS) or the rare incidence of sensory deficit [16] or malignant hypertension [17]. We may only speculate what kind of malignancy eventually leads to FDR’s death. The enigma of the PPS and the probable association of late appearance of various tumours, still interest researchers [18-21].

Spinal Cord Injury and esophageal carcinoma

Case 2: was born in 1945. During The Six Days war, June 1967, he sustained a cervical gunshot wound, leading to a complete spastic tetraplegia below C4. The esophagus was not directly injured. He was discharged after one year from the rehabilitation ward and was totally dependent on others in all ADL (activities of daily living). He obtained an academic degree and worked with the aid of sophisticated electronic accessories, until his last illness. During the years, he underwent hemorrhoidectomy, suffered UTIs and gastritis with reflux esophagitis, and depression. We had described in “Paraplegia” this

case among other tetraplegics who developed the phenomenon of “silent unusual sepsis” [22].

On December 1998, he was admitted to the Rehabilitation Center because of dyspnea, loss of appetite, dysphagia, anemia, pressure sores, palpable supra-sternal mass and sleep disturbance. After a thorough investigation, an esophageal carcinoma was found. Lung function was reduced comparing to his previous one. Radiological investigations revealed: right shoulder osteoarthritic changes, bone absorption around the sternoclavicular joint, at C6/7 small syrinx, bilateral pleural effusions, hypodense mass in the hepatic hilar area, and the esophageal carcinoma which invaded the sternum. Esophageal biopsy showed reflux esophagitis and squamous-cell carcinoma. Gastrostomy was performed. He refused of any “heroic” surgery and only conservative treatment was given including local irradiations and chemotherapy.

DISCUSSION

These two cases have demonstrated the possible association of cervical SCD (due to poliomyelitis or trauma), chronic reflux esophagitis and gastritis and late development of fatal esophageal carcinoma.

Esophageal reflux (GERD) syndrome, or Barrett's syndrome, may lead to esophageal carcinoma [23]. Engel et al [24], identified several risk factors for esophageal adenocarcinoma, gastric cardia adenocarcinoma, esophageal squamous-cell carcinoma and noncardia gastric adenocarcinoma: a few known risk factors account for a majority of esophageal and gastric cancers. These results suggest that the incidence of these cancers may be decreased by reducing the prevalence of smoking, gastroesophageal reflux, and being overweight and by increasing the consumption of fruits and vegetables.

A 69-year-old Japanese man undergoing total gastrectomy for multiple Gastric ulcers at age 46 was found endoscopically to have multiple esophageal cancers in the upper, mid, and lower esophagus [24]. He underwent total esophagectomy combined with laryngectomy, pharyngectomy, and lymph node dissection using the large bowel for reconstruction. The resected esophagus had multiple cancers, including well-differentiated adenocarcinoma, poorly differentiated adenocarcinoma, and small-cell carcinoma. This case is indicative of the high and totipotential carcinogenic risk of Barrett's epithelium and the relationship between duodenal content reflux and esophageal carcinogenesis after total gastrectomy.

The incidence of esophageal adenocarcinoma has risen rapidly in the past two decades, for unknown reasons. Engel et al. [25] tried to determine whether gastroesophageal reflux disease

(GERD) or the medications used to treat it are associated with an increased risk of esophageal or gastric cancer, using data from a large population-based case-control study. Cases were aged 30-79 years. History of gastric ulcer was associated with an increased risk of the noncardia gastric adenocarcinoma. Risk of esophageal adenocarcinoma increased with frequency of GERD symptoms; ever having used H2 blockers was unassociated with esophageal adenocarcinoma risk. Risk was also modestly increased among users of antacids. Neither GERD symptoms nor use of H2 blockers or antacids was associated with risk of the other three tumor types. Individuals with long-standing GERD are at increased risk of esophageal adenocarcinoma, whether or not the symptoms are treated with H2 blockers or antacids. Hamoui et al. [26] examined expression levels of several genes important in carcinogenesis and compared expression levels with alterations in esophageal acid exposure. Their data provide among the first reported correlation of genetic changes and increased esophageal acid exposure in patients with gastroesophageal reflux symptoms. The changes in gene expression occur before any metaplastic changes in the tissue are apparent, and may in the future be useful in predicting which patients will progress through a metaplasia-dysplasia carcinoma sequence. While patients with Barrett's oesophagus develop oesophageal adenocarcinoma more frequently than the general population, it has controversially been suggested that GERD itself is a more important determinant of risk. In order to assess the validity of this suggestion, Solaymani-Dodaran et al [27] examined the risk of oesophageal cancer in patients with Barrett's and with GERD compared with the general population in a community-based cohort study.

It was found that Barrett's oesophagus increases the risk of oesophageal cancer approximately 10 times and oesophageal adenocarcinoma approximately 30 times compared with the general population. There is only a modestly increased risk of oesophageal cancer in patients with reflux who have no record of Barrett's oesophagus. Their findings, therefore, do not support the suggestion that gastro-oesophageal reflux disease itself predisposes to cancer.

Wu et al. [28] reported that hiatal hernia, in combination with other reflux conditions and symptoms, was associated strongly with the risk of esophageal adenocarcinoma. These associations were more modest in gastric cardia adenocarcinomas. A significant and positive association between body size and history of hiatal hernia/reflux symptoms also was observed.

Among 567 consecutive spinal-cord-injury patients, eighty-seven episodes of gastrointestinal complications developed in 63 (11%) patients: paralytic ileus, gastric dilatation, Wilkie syndrome

[30], peptic ulcer disease, and pancreatitis [29]. In the chronic stage, these patients tend to suffer from fecal impactions, constipation, hemorrhoids, peptic ulcer disease, hepatitis, rarely diverticulosis or volvulus, hiatus hernia, and gastroesophageal reflux. Dysphagia may occur in those who were ventilated, had a tracheostomy, those whose spinal stabilizing instrumentation is protruding anteriorly, or in whom nasogastric tube was inserted for a long time.

"Endoscopic study of the upper gastrointestinal tract was performed in 40 patients in the chronic stage of spinal cord injury [31]. Of these, 37 patients were analyzed for endoscopic abnormalities, symptoms, and physical findings. Nineteen patients (51.4%) had abnormalities by endoscopy. There were 11 gastric erosions, two gastric ulcers, and six cases of congestion or submucosal hemorrhage. An attempt to find clear diagnostic clues in terms of symptoms or physical signs was unsuccessful. Anorexia and nausea were early symptoms to which we should pay attention. The results do not permit an assessment of the relation of various possible causative factors and these gastro-duodenal lesions. The study does call attention to the high incidence of gastro-duodenal lesions in these patients."

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