CASE REPORT

Plummer-Vinson Syndrome Complicated by Gastric Cancer:
A Case Report

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Abstract. Plummer-Vinson syndrome has been brought to attention as a precancerous lesion of hypopharyngeal and cervical lesions of the esophagus, but that involving the stomach is uncommon. We report a case of Plummer-Vinson syndrome with gastric cancer. A brief literature review of this disorder is presented, and possible causes in this unusual case are discussed. (Keio J Med 39(2): 106–111, June 1990)

Key words: Paterson-Kelly syndrome, iron deficiency anemia, sideropenic dysphagia, glossitis

Introduction

Plummer-Vinson syndrome is associated with dysphagia, iron deficiency anemia and glossitis as its main symptoms. This syndrome is also called Paterson-Kelly syndrome or sideropenic dysphagia, and much attention has been paid to it as a precancerous condition leading to hypopharyngeal and/or cervical esophageal cancer.

We encountered a patient who complained of remarkable oral mucosal symptoms at the first visit and was subsequently diagnosed as having this syndrome complicated by gastric cancer.

Case Report

The patient was an 81-year-old female. She visited the Department of Dentistry and Oral Surgery, School of Medicine, Keio University, on August 19, 1987, for contact pain in the tongue and at the angles of the mouth. The family background was unknown, except for the presence of spoon nails in her elder sister, cousin and nephew. She had no antecedents of special note.

In June, 1983, she experienced contact pain in the tongue and lips (especially at the angles of the mouth) but did not undergo any treatment. She also found spoon-like changes in her finger nails. She then visited a clinic of otorhinolaryngology, was diagnosed as having glossitis and was treated with vitamins. However, her condition did not improve, and in June, 1985, she visited the oral surgery department of another university, and was treated with topical application of steroid ointment for three months. However, because of lack of improvement, this treatment was discontinued.

In August, 1987, she visited the oral surgery department of a hospital, and was referred to our institute for further treatment on August 19, 1987.

Physical findings

Systemic findings: The patient had a poor constitution, weighing 38.5 kg. Her nutritional condition was poor, and the conjunctiva of the eyelids was pale. Finger nails were spoon-like without luster (Fig. 1). Body temperature was 35.8°C, blood pressure was 150/68 mm Hg, and heart rate was 86 beats/min. The submandibular and cervical lymph nodes and the thyroid gland were not palpable. Heart sounds were normal and the lungs were clear on percussion and auscultation. The liver and spleen were not palpable.

Findings in the oral cavity: Filiform papillae and fungiform papillae were found to be remarkably atrophied. The so-called red bald tongue was noted. The lips and angles of the mouth were eroded. The patient complained of severe contact pain and hypogeusia. She had neither maxillary teeth, nor mandibular teeth, and wore a full set of dentures but the pain was too severe to use these well (Figs 2 and 3).

Xerostomia was not so severe, but she complained of dysphagia.
Fig. 1  Nail deformation seen at the first diagnosis
Note the spoon-like nail without luster.

Fig. 2  Finding on the tongue at the first diagnosis
Appearance is so-called red bald tongue with strong redness and severe atrophy of papillae.

Fig. 3  Initial finding on the lips
Redness and erosion is seen.

Examinations

*Laboratory findings:* Peripheral blood examination demonstrated a red blood cell (RBC) of $342 \times 10^4$ cells/μl, hemoglobin (Hgb) of 5.1 g/dl, hematocrit (Ht) of 20.4% and a mean corpuscular volume (MCV) of 60 fl. Peripheral blood smear revealed anisocytosis and a few poikilocytes (3%).

Blood chemistry revealed iron deficiency, the serum iron level being 9 μg/dl, total iron binding capacity 453 μg/dl, unsaturated iron binding capacity 444 μg/dl and ferritin level 1 ng/ml. However, liver and renal functions, enzyme levels and electrolyte levels were found to be within the normal range.

In fecal examination, occult blood reaction was strongly positive (3+) as measured both by orthotolidine and guaiac methods.

From the above findings, the patient was diagnosed as having Plummer-Vinson syndrome and was transferred to the Department of Internal Medicine of our hospital for an upper gastrointestinal radiographic series. *Gastrointestinal x-ray findings:* A web was noted on the lateral image and a horizontal pellucid band, on the frontal image (Fig. 4). It was suggested that a gastric cancer was located on the posterior wall of the gastric angle and diverticulum at the duodenum (Fig. 5).
Endoscopic findings: A tumor was found on the posterior wall of the gastric angle. This tumor was diagnosed as Borrmann type 3 gastric cancer (it was demonstrated to be adenocarcinoma by histopathological examination of biopsy specimens taken during this endoscopic examination). Slight mucosal atrophy was noted in the area including the esophagus and whole stomach, but there was no organic changes corresponding to the esophageal web (Fig. 6).

Course of disease

Oral administration of an iron preparation (iron sulfate 210 mg/day) and local application of dexamethasone ointment were started from the first visit. Twenty-one days after initiation of treatment, the pain and loss of taste were remarkably improved, but, because of epigastric discomfort probably due to iron sulfate intake, sodium ferrous citrate was used thereafter at 3 tablets/day (150 mg as iron). Fifty days after the initiation of treatment, RBC, Hgb, Ht, mean corpuscular volume, serum iron, total iron binding capacity, unsaturated iron binding capacity and ferritin were all returned to normal. Mild erosion was found at the lips and the angles of the mouth as clinical signs, but atrophy of the papillae of the tongue was improved and the dysphagia disappeared.

Seventy-one days after her first visit, subtotal gastrectomy was performed. Histopathologically, a moderately differentiated tubular adenocarcinoma infiltrating the sub-serosal tissue was confirmed involving (P<0.01) (Fig. 7).
α). After operation, the patient was treated with steroid ointment alone without iron preparation. One hundred ten days after operation, the erosion of the lips and angles of the mouth disappeared, atrophy of tongue papillae was remarkably improved and the spoon-like nails normalized. Hematological parameters were all within normal range (Figs. 7 and 8).

**Discussion**

In 1912, Plummer\(^1\) reported that there were some cases of dysphagia associated with severe anemia which had been regarded as a kind of hysteria or neurosis of unknown cause. Subsequently, Vinson\(^2\) reported that this type of dysphagia has three characteristic manifestations: anemia, dysphagia and atrophic glossitis, and Kelly\(^3\) and Paterson\(^4\) pointed out the high incidence of hypochromic anemia in this disease. Since then, the syndrome associated with these symptoms has been called Plummer-Vinson syndrome or Paterson-Kelly syndrome.

This syndrome is characterized by three main symptoms — atrophic changes in the mucosa of the oral cavity, pharynx and esophagus, dysphagia and hypochromic anemia. Other oral symptoms are associated such as angular cheilosis, early loss of teeth, glossitis, etc., as well as other various signs such as esophagism, cardiospasm, web formation, achlorhydria, nail deformation, splenic tumors, dermatitis seborrhoeica, hyperkeratosis, conjunctivitis, keratitis, blepharitis, and visual disturbances, which may also occur as complications. The syndrome is before considered to result mainly from iron deficiency anemia,\(^5\) but as Winder\(^6\) reported that serum iron level was normal in 68% of 109 patients with this syndrome, it seems that some other diseases of different nature are included. However, there have been various arguments concerning the pathogenesis of this syndrome.

The syndrome has been reported to occur frequently in women aged 30 to 50 years.\(^2,6\) In Japan, some cases in males have been reported by Fukumoto et al.\(^7\) and Kumazawa et al.\(^8\) On the other hand, the cases reported by Okamura et al. (16 cases)\(^9\) and Suzuki et al (40 cases)\(^10\) all involved females aged 45.1 and 48.4 years on average, respectively. Our case involved a female who had the disease at the age of 77 years.

In general, iron deficiency anemia is considered to occur with frequency in 20- to 40-year old females who have chronic blood loss and who need increased intake of iron,\(^11,12,13\) but there are also many women who do not have the syndrome in spite of the presence of anemia. Besides, the fact that it was found in our aged patient suggests the existence of other factors triggering the syndrome other than iron deficiency. Kakizaki et al.\(^14\) reported that anemia was improved with intake of iron preparations, glossitis and chelitis were not improved, and with vitamin B\(_2\) mucositis was healed.

Iron is an essential metal ion in the human body. Especially, the supply of iron and vitamin B\(_2\) is indispensable to maintain sufficient amounts of enzyme for the oxidation and reduction of cytochrome. Deficiency of these substances renders the regeneration of mucosal cells impossible, the epithelium becomes thin,\(^15,16\) and as a result, epithelization is disturbed.\(^17\) Insufficient supply of iron from foods, insufficient absorption due to achlorhydria and loss of blood through such processes as menstruation may be mentioned as possible causes of iron deficiency. Our patient was a postmenopausal woman having no unbalanced diet, nor any particular antecedents. However, she was found to be a strongly positive for occult blood in fecal examination at her first visit, and this suggested that bleeding due to gastric cancer was one of the possible causes of iron deficiency anemia. It is generally thought that chronic iron deficiency of ten years or more exists as an underlying disease behind the occurrence of the syndrome. In our case, it was unknown when bleeding from gastric cancer had first occurred. It seemed rather reasonable to think that the case was complicated with gastric cancer after occurrence of the syndrome. In addition, we should take the possibility of genetic predisposition into account, because the patient’s elder sister, cousin and nephew also have spoon-like nails.

Patients with Plummer Vinson syndrome usually complain of dysphagia and anemic symptoms and first visit otorhinolaryngologists or internists. Some complain of oral symptoms like in our case. Regarding dysphagia, many reports query whether it precedes or follows anemia, and whether its cause is a functional or organic disturbance. At first, hysteria or spasm of the upper esophagus was thought to cause dysphagia and then anemia and nutritional disorder were thought to be triggered.\(^1,2\) Subsequently, it was thought that iron deficiency or anemia leads to mucosal atrophy in the digestive tract, ulcerous changes or cracks may occur at the inlet of the esophagus as trauma from the intake of solid foods, and then a web is induced, which results in organic stricture, and this may finally cause dysphagia.\(^18,19\)

However, Seaman et al.\(^20\) and Nosher et al.\(^21\) denied the relationship between esophageal web and the syndrome. Okamura et al.\(^9\) mentioned that the cause of dysphagia might not be an organic lesion, but might rather be the result of decreased extensibility of the esophageal wall due to iron deficiency.

In our patient, a web was found on both lateral and frontal x-ray images of the esophagus. This web seemed to correspond to the “true web with horizontal pellucid band” of Pitman’s classification,\(^22\) and the fact that no particular organic lesion was found at the location of the web is consistent with the report of Okamura et al.\(^9\)
Much attention has been paid to Plummer-Vinson syndrome as a precancerous condition. Ahlbom\(^2\) reported that 70% of 150 patients with oral, pharyngeal and esophageal cancer had Plummer-Vinson syndrome. Wynder\(^6\) surveyed premonitory symptoms of upper esophageal cancer in 472 patients and reported that, in 10% of patients with Plummer-Vinson syndrome, the syndrome developed to cancer. Richards,\(^24\) Lyndvall,\(^25\) Videback,\(^26\) Simpson,\(^27\) Owen\(^28\) and Larsson\(^29\) discussed the relationship between the syndrome and hypopharyngeal cancer or cervical esophageal cancer.

In Japan, Suzuki\(^30\) pointed out the association with hypopharyngeal or cervical esophageal cancer in 4 (10%) of 40 patients with Plummer Vinson syndrome and a close similarity between the syndrome and these types of cancer in terms of sex ratio, incidence of esophageal web and serum iron deficiency, and concluded that the presence of the syndrome is clinically significant as a premonitory symptom of hypopharyngeal cancer in women. Sakurai et al.\(^30\) and Hayashi et al.\(^31\) reported cases of Plummer-Vinson syndrome associated with tongue cancer. To our knowledge, there have been no cases associated with gastric cancer.

In Plummer-Vinson syndrome, the mucosa of the digestive tract atrophied by chronic iron deficiency anemia becomes susceptible to damage by mechanical stimulus. As reported by Tomioka et al.,\(^32\) Gotfredsen\(^33\) and Markson\(^34\) the syndrome may be associated with autoimmune disease, which suggests that a reduction in immunity participates in the syndrome. As no immunological examination was performed in the present study, we cannot discuss the syndrome from an immunological viewpoint for our patient. However, we believe it important for the diagnosis of Plummer-Vinson syndrome to perform screening to determine whether cancer is located at the mucosa of the digestive tract, and to carry out immunological examination in addition to examination for etiological factors of anemia.

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