CASE REPORT

Individualized Treatment and Palliative Care for A 90-Year-Old Patient with Primary Gastric Diffuse Large-B Cell Lymphoma: 4 Year Follow-up and Inspiration

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Abstract A 90-year-old man was diagnosed with primary gastric diffuse large B-cell lymphoma (PGDLBL) by PET/CT examination, gastroscopy, biopsy and histopathological analysis at a regular physical check in April, 2016. The patient received R-CO chemotherapy (rituximab, cyclophosphamide, and vincristine) and radiotherapy subsequently, with enteral nutritional treatment through 3-cavity nasogastric tube due to development of pyloric obstruction. To satisfy patient's strong desire of eating by himself, we performed surgery of exploratory laparotomy and Roux-en-Y gastric bypass (RGB) to relieve pylorus obstruction. Postoperatively, the patient resumed oral feeding, supplemented by nasogastric tube feeding at 1350 - 1550 Kcal daily. He is now 94 years old with fairly well nutrition and normal communication. The outcome of 4 year follow-up suggests that nutritional treatment and palliative medicine are important for improving prognosis and life-quality of very elderly patients with end-stage tumors apart from the effective chemotherapy, radiotherapy, and surgery.

P RIMARY gastric lymphoma represents about 5% of all malignant gastric tumors, while diffuse large-B cell lymphoma (DLBL) which is the most common extranodal type, accounts for about 50% - 55% of all primary gastric lymphoma.^[1,2] The incidence of primary gastric diffuse large B-cell lymphoma (PGDLBL) is increasing, which can be pri-

mary or secondary to disseminated lymphoma.^[1] The common symptoms of PGDLBL are epigastric pain, appetite loss, weight loss, bleeding, vomiting, or palpable mass. At present, the most common treatment is rituximab combined with chemotherapy of cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP).^[3,4]

Although number of very elderly patients with DLBL increases as the elderly population increase, studies on treatment for elderly patients are limited.^[5,6] Particularly, no standard treatment can be adopted for PGDLBL patients over 90 years old who are usually in poor physical situation, or with various concomitant

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chronic diseases. We report a 90-year-old patient with PGDLBL who received comprehensive treatments of chemotherapy, radiotherapy and surgical operation due to the disease and complications. To our best knowledge, this patient appears to be the oldest PGDLBL patient who has survived for over 4 years after comprehensive treatments.

CASE DESCRIPTION

A 90-year-old Chinese man complained of intermittent epigastric discomfort and appetite loss for 2 months at a routine physical check-up in April, 2016. Physical examination: body temperature 36.0°C; weight 94 kg; height 173 cm; pale complexion and conjunctival pallor, suggesting mild anemia. The abdomen was soft, no-tender, no-distended, no palpable mass. Neither lymphadenopathy nor hepatosplenomegaly was detected. Mild edema was observed in the legs and feet. Lungs, cardiovascular and neurological examinations were unremarkable. Laboratory test results are shown in **Table 1**. Chest CT revealed a solid mass of 1.4 cm in the lateral middle lobe of right lung, which was larger than that of two years ago. As a result, he was admitted to the hospital with suspected diagnosis of early-stage lung cancer. The medical history included coronary heart disease, frequent ventricular premature beat, hypertension, impaired glucose tolerance, chronic kidney disease (stage 3) and moderate anemia, etc. He declined needle aspiration biopsy of the lung tumor. The positron emission tomography (PET)/CT was performed, and the lesion in the lung revealed to be mild hypermetabolic, but a remarkable hypermetabolic mass in the gastric antrum was found (**Fig. 1**). Therefore we performed upper gastrointestinal endoscopy and found an ulcer lesion of gastric antrum (**Fig. 2**). Biopsy was performed and the pathological diagnosis was PGDLBL, Stage I , A (with no fever, night sweats, or weight loss) according to the Lugano staging system^[7] and the International Prognostic Index (IPI);^[8] immunohistochemical staining revealed CD20(+++), CD3(+), CD68(+), CKpan(-), EMA(-), Ki-67(80%), P53(+), pax-5(+), CD10(-); the bone marrow aspiration pathology was negative. Helicobacter pylori infection test was negative.

Considering his advanced age and renal dysfunction, the initial treatment was a daily combination of rituximab 300mg, cyclophosphamide 200mg, and vincristine 0.5mg (R-CO), which was administered for

consecutive 5 days per month. After 2 cycles of chemotherapy, the patient developed abdominal distension and vomiting which gradually aggravated. Abdominal CT and gastrointestinal angiography suggested gastric retention and pylorus obstruction, which was possible caused by tumor progression. Therefore, the patient received additional dexamethasone 5mg, and local radiation therapy of 36Gy/time for 20 times were administered in the 3rd and 4th chemotherapy course. The patient refused to take gastroscopy when the entire radiation and chemotherapy completed in September 2016.

At this time, the body weight dropped to 70 kg because of pyloric obstruction and fasting. Nutritional assessment of NRS-2002 score was above 3 points. So he received enteral nutrition treatment with a 3-lumen (gastro-duodenum-jejunum) feeding tube, supplemented by parenteral nutrition in the following few months. The daily caloric requirement was 1750 Kcal (25 Kcal/kg×70 kg). In order to prevent intestinal discomfort, the initial nutrition plan was as follows: short peptide enteral nutrition 500 - 750 mL/d, divided into 3 times, slowly dripped through jejunum tube; parenteral nutrition 1350 - 1450 mL/d, intravenous drip of amino acids, or multivitamins or fat emulsion, etc. The actual daily calories and total liquid input were 1130 - 1250 Kcal/d and 1850 - 2200 mL, respectively. The nutrition treatment regimen was gradually transitioned to: short peptide enteral nutrition 1000 - 1250 mL/d at a rate of 110-120 mL/hr continuously pump through jejunum tube; parenteral nutrition 850 - 1190 mL/d. The actual daily calories and total liquid input were 1350 - 1525 Kcal/d and 1850 - 2450 mL/d, respectively. The patient's condition stabilized gradually.

One year later, PET/CT scan indicated decreased local metabolism of the gastric lymphoma lesion. At this time point, the nasogastric tube need to be replaced for having been used for 7 months. The patient strongly desired to eat with mouth rather than continuously using feeding tube despite of pylorus obstruction. After coordinated consultations among surgeons, oncologists, hematologists and gerontologists, a surgical plan of exploratory laparotomy combined with Roux-en-Y gastric bypass (RGB) was proposed. The 91-year-old man underwent operation under general anesthesia on March 30, 2017. Intraoperative exploration revealed no adjacent infiltration, no enlarged lymph node; the pylorus tumor caused obstruction and was 5 cm x 6 cm in size. The tumor was not resected for its large volume and being prone to bleeding; gastrojejunostomy

was performed. The operation was successful without obvious delayed gastric emptying and severe post-operative complications. Trans-oral feeding resumed gradually after the operation. Most of the food was semi-fluid diet, such as egg custard, rice soup, yogurt, fruit juice, nutrition powder, etc. The daily intake was about 2500 - 2700 mL for about 1550 Kcal of both nasogastric tube and oral feeding. His body weight ranged between 72 - 75 kg; BMI index: 24.1-25.1; nutritional assessment of MNA-SF every 3 months: 10-11 points, at risk. He was able to exercise outdoors in a wheelchair and communicate emotionally with his wife, adult children, doctors and nurses. He experienced pulmonary infections caused by choking for several times, and all recovered after a few days of antibiotic treatment. Chest CT showed no further changes in the previous solid mass of the right lung. In the process of treatment, the wishes of patient's own and his family members were fully considered by doctors.

Considering the advanced age, the patient and his family refused to undergo gastroscopy and other invasive examinations, and PET/CT examination was not performed again. Routine physical examinations were performed regularly every year. At present, the patient is 94 years old under care of a medical attendant and

his family, being satisfied with quality of life, in fairly well nutritional state despite mild anemia. He has normal cognitive function and good emotional interaction with family members and medical staff.

DISCUSSION

Generally, the prognosis of elderly patients with DLBL is poor, which is associated with increased incidence of toxicity by medicine therapy, reduced remission rates, increased recurrence rate, and higher mortality from cardiovascular disease other than lymphoma itself.^[9,10] Tumors with P53 (+) may progress extremely rapidly and have a poor prognosis, so therapy should start as soon as possible. Rituximab is a chimeric monoclonal antibody targeted against the CD20 antigen. Rituximab administered with concomitant chemotherapy has been considered as a standard therapy for DLBL.^[4,11]

In the current case, this elderly patient with PG-DLBL is characterized of poor prognosis for P53 (+), extremely old age, accompanied with a variety of chronic diseases, including coronary heart disease, pulmonary tumors and renal function impairment, etc. Doxorubicin was removed from the standard treatment

Table 1. Nutrition-related laboratory indexes at different time of a very elderly patient with primary gastric diffuse large B-cell lymphoma

Laboratory indexes	On admission (2016.4)	Pylorus obstruction (2016.9)	Current (2020.4)
Weight (kg)	94	70	75
BMI (kg/m ²)	31.4	23.4	25.1
Red blood cells($\times 10^{12}$ /L)	2.7	2.7	2.6
Fecal occult blood testing	+	±	-
Hemoglobin (g/dL)	8.4	9.0	9.4
Serum creatinine (μ mol/L)	126	123	102
eGFR (mL/min $\cdot 1.73m^2$)	49.6	51.1	62.8
Alanine aminotransferase (U/L)	9	10	9
Aspartate aminotransaminase (U/L)	22	19	21
Total protein(g/L)	55.5	49.5	54.9
Pre-albumin (mg/L)	248	193	188
Albumin (g/L)	36.5	32.4	36.2
Total cholesterol(mmol/L)	4.6	3.0	3.7
Low density lipoprotein (mmol/L)	3.2	1.9	2.6
Triglycerides (mmol/L)	0.9	1.3	1.4

BMI, body mass index; eGFR, estimated glomerular filtration rate.

Figure 1. The PET-CT images detecting a gastric mass of a 90-year-old man.

(A) Increased up-take of a mass at gastric antrum (white arrow), $SUV_{MAX} = 3.4$, which demonstrated pathologically as primary gastric diffuse large B-cell lymphoma; (B) follow up PET/CT showing decreased metabolism of the gastric antral mass, $SUV_{MAX} = 1.8$, no metastatic lymphadenopathy observed.

Figure 2. Endoscopic, histopathological and immunohistochemistry findings of a primary gastric diffuse large B cell lymphoma of a 90-year-old man.

(A) Endoscopy revealed an ulcerative mass of the gastric antrum. The mucosal tissue was hard and easily to bleed. (B) Histopathological finding showing large-sized atypical lymphoma cells with minimal cytoplasm arrayed irregularly with expansive appearance, consistent with gastric large B-cell lymphoma ($\times 200$); (C) Immunohistochemical staining demonstrated CD20 positive cells and the diagnosis of diffuse large B-cell lymphoma ($\times 200$)

of R-CHOP due to its cardiac and renal toxicity. However, the chemotherapy regimen of R-CO (rituximab + cyclophosphamide + vincristine) didn't work well, the tumor progressed and patient developed pyloric obstruction, which probably was due to inadequate chemotherapy; another cause might be neurotoxicity of vincristine. Therefore, dexamethasone was added to the chemotherapy regimen(R-COP) to increase efficacy and to reduce the side effects of vincristine.

On the basis that radiotherapy combined with chemotherapy was reported to have slight benefit to PGDLBL patients in several clinical trials,^[12-14] we adopted local radiotherapy consequently for 20 times. With the adjusted R-COP regimen and supplementary radiotherapy, the patient's vomiting, abdominal distension and other symptoms of digestive tract obstruction were relieved. PET/CT suggested that the systemic chemotherapy and radiotherapy had inhibited the growth of the tumor.

Due to pyloric obstruction, the patient received enteral nutritional support treatment through a 3-cavity nasogastric tube with short peptide enteral nutrition supplemented by parenteral nutrition. Short peptide nutrition can protect the intestinal barrier and promote intestinal peristalsis and nutrient absorption. It can also reduce the incidence of reflux, abdominal distension, diarrhea and other gastrointestinal complications. The nutritional support treatments were demonstrated effective for the facts that the health state of this extremely old patient with malignant gastric tumor gradually improved.

The patient has survived for 4 years by far. The outcome of this extremely old patient with end-stage disease benefits greatly from palliative medicine, nutritional supporting therapy, and comprehensive treatment with chemotherapy, radiotherapy, and surgical treatment.

In the process of treatment, the wishes of the patient and his family were fully considered. As the

patient strongly desired to eat through mouth, we had to consider operation to relieve obstruction. Surgery has no longer regarded as the standard treatment for PGDLBL, and only reserved for management of complications, such as bleeding, obstruction, perforation.^[1, 4] So we performed palliative surgery, and the patient gradually returned to oral feeding after the operation.

In the whole course of medical care, regular nutrition assessment and proper adjustment of the corresponding nutritional support routes, i.e., enteral and parenteral nutrition, played important role in improving the outcome and life quality of the patient.

Patients at advanced age usually accompanied with various chronic diseases with organ functional impairment, even multiple tumors. Clinical practice usually lacks evidence in very elderly patients, and treatment decisions have to be made on patient's individual condition in addition to the relevant practicing guidelines. The outcome of this very elderly patient suggests that individualized therapy should not only focus on tumor, but also carefully consider the side effects caused by treatment. In addition, physical and psychological influences from therapeutic measures also affect the quality of life and determine the prognosis of the disease. Therefore, individualized comprehensive treatment is often crucial to prolong life expectancy and acquire a good life quality.

Palliative medicine emphasizes on the comprehensive physical, psychological and social care for the end-stage patients in aims of improving life quality of patients and their family members. For elderly cancer patient, palliative care has particular value and needs more understanding and acceptance by doctors, patients, and their families.^[15-17] The treatment of very elderly patients with chronic diseases or end-stage tumors should transfer from "disease-centered" to "patient-centered" model, provide approaches to prevention, early identification, impeccable assessment, and management of pain, care about the physical, psychosocial and spiritual conditions of patients and their families, help them to get through the life-threatening illness, thereby to reach peaceful, comfort, and dignified lives.

Consent

Written informed consent from the reported patient was obtained.

Conflict of interests

None.

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病例报告

个体化及缓和医疗用于 90 岁胃原发弥漫性大 B 细胞淋巴瘤患者：4 年随访结果及启示

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摘要

本文报道一名 90 岁患者于 2016 年 4 月年度例行体检时，通过 PET/CT、胃镜和病理 + 免疫组化确诊胃原发性弥漫性大 B 细胞淋巴瘤。患者接受了利妥昔单抗、环磷酰胺、长春新碱（R-CO）化疗以及后续的放疗。之后患者发生幽门梗阻，遂放置三腔鼻 - 胃肠管给予肠内营养。为了满足患者经口进食的强烈愿望，我们进行了剖腹探查和胃 - 空肠吻合术（RGB）以解除幽门梗阻。术后患者恢复了经口进食，并辅以鼻饲饮食，每日热量 1350-1550 Kcal。患者目前 94 岁，营养状态中等，认知正常。本例 4 年诊疗及随访结果提示，除了有效的化疗、放疗以及外科手术治疗之外，营养照护和缓和医疗对改善超高龄晚期肿瘤患者的预后及生活质量也非常重要。

关键词：胃原发肿瘤；弥漫性大 B 细胞淋巴瘤；超高龄；营养支持；缓和医疗

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