

Multiple Primary Malignancies

DING Lian-an, NIU Dong-guang, SHAO Chang-chun, QU Lin-lin, SUN Li-qun, CHEN Shuang-xi

(General Surgery Department Medical College Hospital, Qingdao University 59 Haier Road Qingdao 266100)

ABSTRACT Objective: To investigate the etiology, clinical characteristics, and management of multiple primary malignancies (MPM). **Methods:** A group of 77 patients with MPM were treated in the general surgery department from May 2002 to April 2007. **Results:** These patients accounted for 1.3% of hospitalized patients (77/5768) in the general surgery department from May 2002 to April 2007. Half of them were more than 65 years old; gastrointestinal MPM accounted for 81.8% of the cases (63/77). The related factors are genetic defects, environmental factors, medical treatments (such as radiotherapy and chemotherapy), immunity defects and advanced age. **Conclusion:** The incidence of MPM is increasing in recent years. The possibility of synchronous/metachronous carcinomas should not be overlooked during treatment for cancer or when patients return for further consultation. Resection is the primary therapeutic measure for solid MPM tumors.

Key words: Multiple Primary Malignancy; Malignancy; Genetic Predisposition; Management

Chinese Library Classification (CLC): R730.2, R735 **Document code:** A

Article ID: 1673-6273 (2012)09-1738-04

Introduction

Along with the science development and advancement of human society, the life-span of human being has been prolonged, and the incidence of tumors has been increasing in recent years also. The aged people occupies more than half of the total. During tumor's diagnosis and treatment, the multiple primary malignancy was defined, and also the elderly occupies more than the half^[1-7]. What are the pathogenesis of MPM and the sole cancer? Are they the similar or alike? Are there any regular pattern of morbidity? What are the difference for principles and methods of treatments between MPM and unitary malignancy? All these problems are not unambiguous defined and are being explored actively.

Most patients suffering from MPM are older people who are often suffering from other diseases^[5-9], which adds to the difficulty of diagnosis and treatment. Unquestionably, our understanding and ability to treat MPM would be improved by studying its clinical manifestations and pathogenesis. In this article, we summarize case reports of patients suffering from MPM in our department, and review some related articles.

1 Materials and method

Clinical materials of patients with multiple primary malignancy(MPM) hospitalized in Dept. of General Surgery, Affiliated Hospital of Qingdao University Medical School from May 2002 to April 2007 were retrospectively collected. The clinical manifestations and associated factors are presented with combination of its statistics and articles review. Seventy-seven patients suffering from MPM admitted to our general surgery department from May 2002 to April 2007, including 48 men and 29 women; they ac-

counted for 1.3% of hospitalized patients (77/5768) in the general surgery department during this period. Their average age when second carcinoma was diagnosed was 67.9 years (range: 43-84 years). All the tumors was confirmed by operation and pathology as primary but not metastasis. Thirty-three were synchronous malignancy, and forty-four cases were metachronous carcinomas with an average interval time of 7.70 years (range: 9 months-30 years). (see Table 1)

2 Results

There was a total of 180 cancer foci for these 77 patients. Sixty-three (81.8%) of the cases had gastrointestinal carcinoma or gastrointestinal MPM except for 14 cases. For the 29 female patients, two had metachronous endometrial cancer combined with breast carcinoma; 1 patient had synchronous bilateral breast cancer; 6 patients had synchronous bilateral multiple primary malignancy of the thyroid; 6 patients had accessory sex organ carcinomas combined with metachronous gastrointestinal cancer. The rest 14 patients were other tumors.

Thirty-two of 33 synchronous cases were diagnosed definitively before surgery or during surgery; the remaining patient was not diagnosed until reoperation because of duodenal stump fistula and bowel obstruction after the first operation. Six cases were triple carcinomas. One patient had 4 carcinomas; this patient died from renal failure caused by perforation of the gastrointestinal tract 17 years after his first operation, and there was no evidence of recurrence. One patient had 9 carcinomas, and was operated 8 times; his first operation was 7 years ago; his last operation was considered to be radical surgery. Twenty-nine patients (37.7%) were 65 years of age or older when they were first diagnosed with cancer; 43 patients (56%) were 65 years of age or older when they were diagnosed with a second cancer.(see Table 2).

Author introduction: DING Lian-an (1958-), Male, Chief Physician and Professor of Medical School, Postgraduate Tutor,

E-mail: larryding1987@gmail.com

(Received: 2011-06-05 Accepted: 2011-06-30)

Table 1 Demographic Information of MPM Patients

Gender	Age	Average Age	No.	The Aged (%)	Synchronous Carcinoma	Metachronous Carcinoma	Average Time Interval(ys.)
Male	51~84	68.8	48	33(68.8%)	23	25	6.10
Female	24~82	58.4	29	10(34.5%)	10	19	9.73
Total	24~84	64.8	77	43(56.0%)	33	44	7.70

Table 2 Organs with Cancer

Car. type	St.	As. Co.	Re.	Sig.	Tr/De. Co.	Br.	Ut.	Sk.	Thr. (lips)	Ur. Sy.	Thy.	Am.§	S. In.	Cun.#	Lu.*	Tot.
Pri.	26	9	14	9	8	9	6	2	3	5	17	2	3	2	3	118
Sec.	17	11	8	4	6	3	1	1	1	6	0	0	1	0	3	62
Tot.	43	20	22	13	14	12	7	3	4	11	17	2	4	2	6	180

Note:1.Abbreviation: Car.-carcinoma; Tot.-total; St-stomach; As-ascending; Co.-colon; Re-rectum; Si-sigmoid; Tr-transverse; De-descending; Br.-breast; Ut-uterus; Sk.-skin; Thr.-throat; Ur.Sy.-urinary system; Thy.-throid; Am-ampullary; Cun-cunus; S.In- small intestine; Pri-primary, Sec.-secondary
2. Total 180 carcinoma foci; #-include lymphoma *- include esophagus § - include bile commen duct

3 Discussion

Multiple primary malignancy was described initially by Bill-roth in 1889^[7]. It consists of synchronous and metachronous multi-ple primary malignancies or multiple carcinomas, and is defined as non-metastasized independent carcinomas that developed simulta-neously or successively in an individual patient, whether in same organ or a different one. The gastrointestinal tract was prone to multiple primary malignancies, accounting for 0.32%-6.9% of ma-ignant multiple tumors^[1,2,4-7].

Reports vary. An article from Japan reported that 38 of 319 patents (12%) who were operated on for renal carcinoma were found to have synchronous or metachronous cancer of other or-gans ^[6]. The foci of 22 (7%) of these patients' secondary cancers were situated in the GI tract. Multiple primary malignancies are often seen in colorectal cancer, possibly due to the susceptibility of colon polyps to carcinogenesis. It was reported that multiple pri-mary malignancy accounts for 5%-7% of colorectal carcinoma and for 8-10% of colorectal cancer occurred in older patients (includ-ing those found on autopsy). Thirty percent of older patients suf-fering from colorectal carcinoma also had carcinomas of other or-gans^[5,9,10].

The initial cancers in our group mostly originated from stom-ach, colon and rectal tissues (there were 74 carcinomas in all, ac-counting for 59.2%). Cancers were considered to be synchronous if they occurred at the same time, or if the interval between the two cancers was less than 6 months; otherwise, they were consid-ered to be metachronous carcinomas. However, the diagnosis of multiple primary malignancies did not depend on the time interval between initial and later malignancies, but on histopathological examination^[5,7].

Older people accounted for more than half of carcinoma pa-tients, according to Japanese data. This conforms to our data. Old-er people who die of cancer accounted for more than two thirds of patients with cancers. It was estimated by American scholars that in 30 years, more than 50% of carcinoma patients would be older people^[5].

It can be seen from statistical data that there are some inter-esting phenomena in MPM. For example, patients with prostate cancer were less likely to have second primary carcinoma ^[7]. Pa-tients with ovarian cancer scarcely suffer from gastroenteric tu-mors. Bladder cancer in men has an inverse correlation to prostate cancer; while bladder cancer in women has a positive correlation to uterocervical cancer^[11]. Genetic instability may be higher in MPM than in single primary malignancies, according to one study^[9,10,12]. Some research discovered that early gastric carcinoma patients suffering from MPM have worse prognoses than patients with stomach carcinoma only^[13]. Research data also showed that cancer history didn't influence the management of a new carcinoma or pa-tients' life expectancies. Clinicians should not assume that a later carcinoma is the recurrence or metastasis of an earlier cancer, as this could delay diagnosis and treatment^[1,2,7,8]. Nor should they lose hope; several patients suffering from MPM in our study were cured.

At least two factors are currently recognized as contributing to the pathogenesis of MPM: genetic defects and environmental carcinogenic agents ^[12]. The former includes familial polyposis, breast cancer, hereditary nonpolyposis colorectal cancer (HN-PCC), Bloom syndrome, Fanconi anemia, etc. The latter includes upper respiratory tract or gastrointestinal tract cancers; the inci-dence of multiple primary malignancies are several times higher than ordinary people. Breast carcinoma has same characteristics;

women with cancer in one breast are 3-4 times more likely to develop a primary cancer in the other breast, especially patients who are suffering from lobular carcinoma or benign breast disease^[7,10,14,15]. More studies indicate that the coaction of genetic defects combined with environmental carcinogenic agents give rise to the increase of MPM^[16-23].

Besides genetic and environmental factors, other contributors of multiple primary malignancies may include treatment factors (such as radiotherapy and chemotherapy), immunity defects, and old age. Acute myelocytic leukemia, when initiated by radiotherapy or chemotherapy, usually emerges 1-5 years after treatment; treatment-caused solid tumors emerge 10-25 years after management^[14]. The possibility of treatment-induced cancers increases, to some extent, with the number of years survived after the treatment; when combined with the naturally increased prevalence and morbidity of cancer among older people, this can lead to increased likelihood of multiple cancers^[7,14].

Therefore, two clinical practices warrant more attention after diagnosing and treating cancer patients. The first is systematic examination. Another primary malignancy may be overlooked if other minor symptoms or signs are ignored; it is not advisable to be satisfied with finding a single carcinoma, but to examine other organs carefully in order to avoid missing a synchronous malignancy.

The second recommended practice is regular physical examinations after treatment, which should not only be directed at the primary cancer, but should include details of the patient's daily life, such as diet, exercise, body weight, changes in sleep patterns and so on. Other types of auxiliary examinations also should be considered, especially for the older people^[9,10,24].

4 Conclusion

Multiple primary malignancies are increasing, and is often seen in older people. With more diagnostic devices available, more multiple primary malignancies may be diagnosed correctly before surgery or other treatments. Surgery is the effective managing means for solid MPM.

Acknowledgements

Thanks given to Professor LI Yu-Jun of department of pathology, who gave us a great help in collecting associated data. We also thank to Mrs. HE Shu-Ling, Director of Medical Record Library, who had spent a lot of time in searching and looking up medical records for the paper.

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多原发癌

丁连安 牛冬光 邵长春 曲林林 孙立群 陈双喜
(青岛大学医学院附属医院 普通外科 山东 青岛 266061)

摘要 目的 探讨多原发癌的病因、临床特点及其诊治。方法 回顾性总结分析了一组普通外科多原发癌病人的资料 ,并结合文献进行了分析。结果 本组 77 例多原发癌 ,占同期普通外科住院病人的 1.33%(77/5768),半数以上发生于 65 岁及以上的老年人。胃肠道多原发癌占 81.8%。其发生主要与下列因素有关 :基因缺陷因素(遗传易感性)、环境因素、治疗所致(如放、化疗)、免疫缺陷、老龄。结论 :多原发癌近年呈增加趋势 ,对于肿瘤病人的诊治 ,不要忽略了同时性癌的可能 ;手术仍是多原发癌实体瘤主要而有效的治疗手段。

关键词 :多原发癌 ;恶性肿瘤 ;遗传易感性 ;治疗

中图分类号 :R730.2 ,R735 文章标识码 :A 文章编号 :1673-6273(2012)09-1738-04

作者简介 :丁连安(1958-) ,男 ,主任医师 ,教授 ,硕士研究生导师,
主要研究方向 :胃肠外科疑难症、危重症 ,腹部创伤 ,临床营养支持 ;E-mail:larryding1987@gmail.com
(收稿日期 :2011-06-05 接受日期 :2011-06-30)