X-ray diagnosis of synchronous multiple primary carcinoma in upper gastrointestinal tract: a report of 59 cases

Poster No.: C-0210
Congress: ECR 2011
Type: Scientific Paper
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Keywords: Stomach (incl. Oesophagus), Conventional radiography, Digital radiography, Barium meal, Technology assessment, Socio-economic issues, Swallowing disorders, Obstruction / Occlusion, Tissue characterisation
DOI: 10.1594/ecr2011/C-0210

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Purpose

1. The incidence of multiple synchronous upper gastrointestinal cancers is increasing gradually, but for some reasons, some of synchronous primary lesions often be overlooked at the time of diagnosis. Accurate diagnosis of these synchronous primary lesions before operation is crucial because it can significantly alter clinical management. However, so far, there has not been a consensus on how best to diagnose mucosal lesions of multiple primary carcinomas in the upper GI: endoscopy or barium radiography?

2. The purposes of this study are analyze the radiological features of multiple primary carcinoma (MPC) in upper gastrointestinal tract, study its biological characteristics and evaluate X-ray examination in its diagnosis.
Methods and Materials

Patients

Patients with MPC were selected from January 1988 to December 2008 in the First Affiliated Hospital of Zhengzhou University. Of the 59 patients aged 42~85 (61.20 in average), 44 were men and 15 were women. Main clinical manifestations were choking or swallowing difficulties, some cases associated with anemia, weight loss, abdominal pain and other upper GI signs or symptoms. Specimens for pathologic confirmation of 59 cases were obtained by endoscopy biopsy alone in 13 patients, by endoscopy biopsy and surgery in 27, and by surgery alone in 19. Thirteen patients did not have surgery, either because they were not considered surgical candidates or because they chose to be treated elsewhere.

X-ray examinations

After 6~8 h of fasting, patients first received 20mg hypotonic drugs as well as anisodamine (654-2) intravenous injection. Ten minutes later, the patient swallowed 3 g aerogenic agents, and then, as fast as possible, 150 ml of resuspended barium sulfate at 200% weight for volume (w/v). Three to four spot radiographs were obtained in sequence at different levels of the esophagus, and double-contrast esophagograms were obtained with the patient in the upright LPO position. Multi-position dynamic observation of the stomach and duodenum was performed for all cases, and all patients were pathologically confirmed by endoscopic biopsy or surgery.

Imaging criteria

According to Warren and Gates multiple primary carcinomas were defined as follows:\textsuperscript{12}: (1) each lesion is histopathologically malignant; (2) each lesion is separated by the normal mucosa; and (3) each lesion is not the result of local extension or metastasis of another lesion. Multiple primary cancers may be synchronous or metachronous depending on the interval between their diagnosis. Synchronous carcinomas were diagnosed simultaneously or within an interval of about 6 months, and metachronous carcinomas were secondary cancers that developed more than 6 months after the diagnosis of primary cancers usually after treatment of primary lesions. In our series of 59 cases, all were synchronous multiple primary carcinoma.

The radiographs were reviewed retrospectively by two authors to determine the location, size, morphology and interval distance of these tumors. Lesions were classified morphologically as hyperplastic, medullary, infiltrative, ulcerative or mixed type. Pathologic records were also reviewed to determine the postoperative histological classification, depth of invasion and number of lesions being misdiagnosed in this group.
**Statistical analysis**

We evaluated the clinicopathological differences of esophageal lesions between esophageal MPC and esophageal-gastric MPC, gastric lesions between gastric MPC and esophageal-gastric MPC. Statistical analyses were performed using software from SPSS for Windows 17.0. The statistical methods including #2 test for categorical variables and t test for continuous variables. $P < 0.05$ was taken to indicate statistical significance.
Results

Characteristics of MPC

In our series of 59 cases, all were synchronous multiple primary carcinoma, and mostly occurred in males. Male/Female=2.93/1, 71.19% of the patients were older than 55 years, and average age was 61.2 years old.

Multiple esophageal carcinoma was seen in 24, and 49 lesions were found. One case with triple lesions (Figure 1), and the remaining 23 cases were double lesions (Figure 2~4). The distance between every two esophageal lesions ranged from 5~13 cm, and 8.21 cm in average. Of the 49 lesions, proliferative lesions up to a total of 23, followed by medullary type (n = 9). The size of the proliferative lesions ranged from 1.1 to 5.4 cm (average, 2.7 cm), medullary lesions ranged from 5.2 ~ 9.6 cm (average, 7.6 cm). There were 17 lesions located at the upper, 19 at the middle and 13 at the lower. The largest dimension of the first lesions (3.63 ± 1.96 cm), which were significantly smaller than second ones (5.00 ± 2.67 cm). Regarding the depth of invasion, $T_1$ lesions were more frequent in first lesions, especially in upper. The X-ray features of esophageal multiple primary carcinomas were the same as those of generally solitary ones. All cases were squamous cell carcinoma pathologically proved.

There were 27 cases with synchronous multiple esophageal-gastric carcinoma, and all were double lesions. Esophageal lesions concentrated in the middle (n = 16) and lower segment (n = 11). Of them, proliferative lesions were 11 (Figure 6a, 7a), medullary lesions were 7. While the gastric lesions were mainly located at the gastric cardia (n=16) (Figure 5b), followed by antrum (n = 7) (Figure 6b), body (n = 3) (Figure 7b) and fundus (n = 1). 17 proliferative lesions were mainly located at gastric cardia and the fundus, ulcerative type and infiltrating type were 6 and 4 respectively, mainly at the antrum. In this series, one case of esophageal lesion was pathologically confirmed as sarcoma with the size of 9.1 cm × 5.3 cm × 5.2 cm, the others were squamous cell carcinoma. Twenty-three cases of gastric lesions were adenocarcinoma, and the other four cases were squamous cell carcinoma located at the cardia. The largest dimension of esophageal lesions in EGMPC (5.56 ± 2.34 cm) were significantly larger than that of EMPC (4.33 ± 2.35 cm), and $T_1$ esophageal lesions were more frequent in EGMPC, especially in middle.

Eight patients (13.56%) were found to have synchronous multiple gastric carcinoma, all were double lesions and divided into 2 categories: main lesions (larger or advanced lesion) and additional lesions (the other lesion). The additional lesions mostly located in cardia, of them, two cases with evidence of invasion of the gastric fundus (Fig. 8). Four main lesions located in antrum, and three at gastric body. Thirteen (81.25%) cases were proliferative lesions, of which five cases were early gastric protruded lesion. All lesions were adenocarcinoma pathologically proved. The main lesions were significantly larger than the accessory lesions ($P = 0.001$). Regarding the depth of invasion, $T_1$ lesions were
more frequent in accessory lesions. especially in cardia. Moreover, the largest dimension of gastric lesions in EGMPC were significantly larger than those of GMPC ($P = 0.007$), and also significantly showed differences in the depth of invasion.

**Accuracy of pre-operative diagnosis**

A total of 119 lesions in the 59 patients with synchronous multiple carcinoma were proved by surgery or endoscopy biopsy, and preoperative upper radiographic examination detected 100 of them (84.03% sensitivity). Thus, 19 (15.97%) lesions were missed out of a total of 119 lesions. Regarding the depth of invasion, 18 (52.94%) of $T_1$ lesions were accurately found out of a total of 119 lesions during preoperative diagnostic of radiographic examination, Moreover, only 3 (3.53%) of $T_{2-4}$ lesions were misdetected. By retrospectively reviewing the missed radiographs, we found four lesions mistaken for bubbles, uneven coating of barium illusion, and two lesions in the gastric cardia and lower esophagus were misdiagnosed as invasion. Of the 19 missed lesions, 16 lesions were microscopic early stage and $T_1$ lesions. Moreover, missed gastric lesions showed a tendency to be of the flat type. The mean size of the missed lesions was $2.40 \pm 1.01$ cm.
Fig. 0: Figure 1. 64-year-old male with three esophageal lesions. The first was medullary lesion(#) located at upper, the other two were small ulcerative lesions (#) located at middle-lower segment, and all were squamous cell carcinoma pathologically proved.

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Fig. 0: Figure 2. 58-year-old male with two esophageal lesions. The first was medullary lesion located at upper, with stenosis and rough rigid margins (#); the other was proliferative nodule located at middle segment, with disruptive mucosa (#).

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**Fig. 0:** Figure 3. 63-year-old male with two esophageal lesions. The first was proliferative nodule located at upper (#), the other was medullary lesion located at middle segment (#), and all were squamous cell carcinoma pathologically proved.

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Fig. 0: Figure 4. 56-year-old female with two esophageal lesions. The first was small proliferative nodule located at middle (#), the other was medullary lesion located at lower segment (#), and all were squamous cell carcinoma pathologically proved.

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**Fig. 0:** Figure 5a. 49-year-old male with esophageal-gastric MPC. The esophageal lesion was ulcerative located at middle (#).

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**Fig. 0**: Figure 5b. 49-year-old male with esophageal-gastric MPC, the gastric lesion was proliferative located at cardia (#), with distal esophageal infiltration.

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**Fig. 0:** Figure 6a. 57-year-old male with esophageal-gastric MPC. The esophageal lesion was proliferative located at middle (#).

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**Fig. 0:** Figure 6b. 57-year-old male with esophageal-gastric MPC, the gastric lesion was infiltrative located at antrum (#).

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**Fig. 0:** Figure 7a. 46-year-old female with esophageal-gastric MPC, the esophageal lesion was proliferative located at middle.

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**Fig. 0:** Figure 7b. 46-year-old female with esophageal-gastric MPC, the gastric lesion was ulcerative located at body (#).

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Fig. 0: Figure 8. 59-year-old male with two gastric lesions. The main lesion was proliferative (#) located at cardia, with fundus infiltration; the additional one was also proliferative lesion located at antrum, with disruptive mucosa (#). All were adenocarcinoma pathologically proved.

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Conclusion

Hypotonic double-contrast upper GI examination is safer, less expensive than endoscopy, and also its accurate information about lesions morphology, location and size, can serve as an excellent technique for the screening and diagnosis of synchronous upper gastrointestinal MPC, especially in China.
References


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