PO Box 2345, Beijing 100023, China
Fax: +86-10-85381893
E-mail: wjg@wjgnet.com www.wjgnet.com

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• BRIEF REPORTS •

Pathological characteristics of gastric leiomyoblastoma

Xiao-Feng Huang, Chun-Mei Wang, Bo-Rong Pan, Xiao-Wen Dai, Li Fang, Jia-Ji Yang, Hua Yu, Jun Ren

Xiao-Feng Huang, Chun-Mei Wang, Jia-Ji Yang, Hua Yu, Electron Microscope Center, Fourth Military Medical University, Xi'an 710032, Shaanxi Province, China
Bo-Rong Pan, Jun Ren, Department of Oncology, Xijing Hospital, Fourth Military Medical University, Xi'an 710032, Shaanxi Province, China
Xiao-Wen Dai, Li Fang, Department of Pathology, Chinese PLA 117 Hospital, Hangzhou 310013, Zhejiang Province, China
Supported by the Foundation of 117 Hospital, No.99008
Correspondence to: Chun-Mei Wang, Electron Microscope Center, Fourth Military Medical University, Xi'an 710032, Shaanxi Province, China. fmmuem@fmmu.edu.cn
Telephone: +86-29-83374572
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Abstract

AIM: To determine the pathological characteristics of gastric leiomyoblastoma.

METHODS: All tissues were obtained during surgery or gastroscopy. Tissue specimens for examination by light microscope were 1 cm×1 cm×1 cm in size, fixed in 40 g/L neutral buffered formaldehyde, embedded in paraffin, and stained with hematoxylin and eosin. The fresh tissues obtained for electron microscopy were 1 mm×1 mm×1 mm in size, and fixed in phosphate buffered 30 g/L glutaraldehyde, postfixed in 10 g/L osmium tetroxide and dehydrated in graded alcohol, embebbed in Epon 812. Ultrathin sections of 50 nm were stained with uranyl acetate and lead citrate and examined under a JEM-2000 EX transmission electron microscope.

RESULTS: The most important histopathological feature of leiomyoblastoma was the predominance of large, rounded or polygonal cells with characteristic perinuclear clear zone in cytoplasms. The tumor cells arranged in patch, cell junction or junctional complex could be found occasionally between cells under electron microscope. Most of the neoplastic cytoplasms were filled with myofilaments, dense bodies, and dense patches. Rough endoplasmic reticulum dilatated as lakes, and large quantities of protein secretions of intermediate electron density were found in the dilated cisternae. Intracisternal segregation could also be found. The nuclei were round or oval, and anomalous nuclei were found in part of cells.

CONCLUSION: The diagnosis of gastric leiomyoblastoma can be confirmed by electron microscopy. The clear appearance of tumor cells is due to the dilation of rough endoplasmic reticulum, not fat droplets, glycogens or mucus in cytoplasm.

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INTRODUCTION

Gastric neoplasms are common in the world, specially in China[1-8]. Gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor of gastrointestinal tract[9], although GIST may arise from any portion of the foregut to hindgut, two thirds of stromal tumors originate from the stomach[10]. Leiomyoblastoma, also called bizarre leiomyoma or epithelioid leiomyoma, is a rare smooth muscle tumor characterized by epithelioid cells with clear cytoplasms and an unknown biological behaviour. It is an unusual type of smooth muscle tumor which is biologically benign in most cases, but on rare occasions may behave in a malignant manner and metastasize[11-15]. It is most frequently seen in the gastric wall but may occasionally be encountered in the uterus[16,17], tongue[18], round ligament[19], omentum[12], vulva[20], urethra[21], intestines, mesentery, retroperitoneum, mediastinum, and deep superficial soft tissues[22,23]. Gastric leiomyoblastoma is a benign neoplasia, extremely uncommon and potentially malignant, arising from the muscular layer of the stomach[24-26]. These neoplasms form solitary, well-defined, but not encapsulated, rounded or lobulated masses which, when small, tend to be localized intramurally. Multiple tumors are rare[27-30]. The growth may take place towards the lumen, resulting in a polypoid mass and is covered by an attenuated mucosa.

MATERIALS AND METHODS

All the cases were obtained from the Chinese PLA 117 Hospital. Information of these cases is shown in Table 1. The patient population consisted of two men and three women. Their mean age was 51.4 years, ranging from 48 to 58 years at the time of diagnosis (Table 1). No relevant information of family history was found.

Table 1 Principal manifestations of gastric leiomyoblastoma

No	Sex	Age (yr)	Manifestations
1	Male	48	Abdominal dull pain, gasterorrhagia, dyspepsia
2	Male	56	Abdominal pain, abdominal mass, hemafecia
3	Female	42	Abdominal pain, nausea, vomiting
4	Female	53	Abdominal pain, vomiting, black stool
5	Female	58	Interrupted hematemesis, cupressus defecation

The cytologic samples were negative in all cases. The patients were explored surgically and neoplasms of stomach resected. All tissue specimens for examination by light microscope were 1 cm×1 cm×1 cm in size, fixed in 40 g/L neutral buffered formaldehyde, embedded in paraffin, and stained with hematoxylin and eosin. The fresh tissues obtained for electron microscopy were 1 mm×1 mm×1 mm in size, and fixed in phosphate buffered 30 g/L glutaraldehyde, postfixed in 10 g/L osmium tetroxide and dehydrated in graded alcohol, embebbed in Epon 812. Ultrathin sections of 50 nm were stained with uranyl acetate and lead citrate and examined under a JEM-2000 EX transmission electron microscope.

RESULTS

Gross anatomy and gastroscopy

All resected tumors were well-circumscribed, and three tumors were located at the antro-pyloric region (cases 1, 3 and 4), one

at the body (case 2) and one at the gastric antrum (case 5). The size was measured between 2.5 cm and 13 cm, averaging 6.8 cm. The type of tumor growth was intraluminal (1/5) or extraluminal (2/5) or mixed (2/5). An ulcerated nodular tumor, located in the anterior wall and minor curvature of the gastric antrum (case 1), was found by gastroscopy.

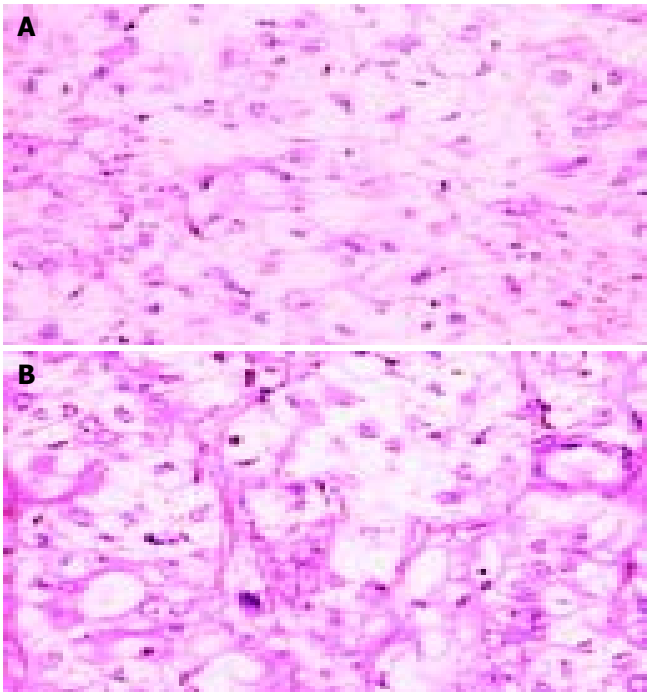

Figure 1 Round tumor cells, with clear cytoplasm, vary greatly in size and shape.

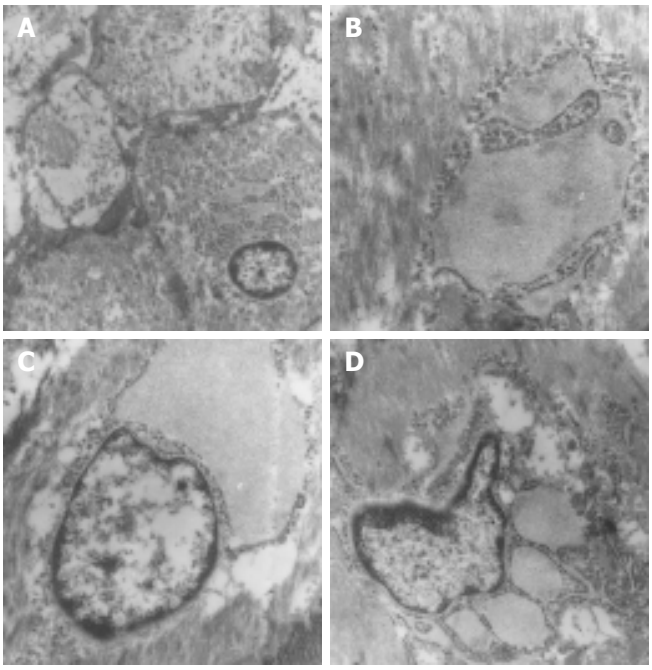

Figure 2 Ultrastructure of gastric leiomyoblastoma. A: Tumor cells with many microfilaments, B: Intracisternal segregation could also be found, C: Rough endoplasmic reticulum dilatated as lakes, and protein secretion of intermediate electron density was found in the dilated cisternae, D: Distorted nuclei were found in tumor cells.

Histopathological appearances

Round tumor cells with clear cytoplasm, varied greatly in size and shape in different parts of the same tumor (Figure 1). The cellular morphology of the muscle neoplasm was all homogenous and the frequency of mitosis was 2 mitoses in case 1 and 4 in case 5 in 10 HPFs, and some areas of fibrosis and degeneration were found in case 3. The most important feature of leiomyoblastoma was the predominance of large, round or polygonal cells with characteristic perinuclear clear zone in cytoplasm (Figure 1). The nuclei might be pleomorphic with prominent nucleoli.

Ultrastructural characteristics

Ultrastructural studies confirmed that the origin of these tumors was smooth-muscle cells, and they were fusiform and round with many microfilaments. Tumor cells arranged in patch, and the cell junction or junctional complex could be found occasionally between cells. Most of the neoplastic cytoplasms were filled with myofilaments, dense bodies, and dense patches (Figure 2 A, B). Rough endoplasmic reticulum dilatated as lakes, and large quantities of protein secretions of intermediate electron density were found in the dilated cisternae (Figure 2C). Intracisternal segregation could also be found (Figure 2B). The nuclei were round or oval, and distorted nuclei were found in part of cells (Figure 2D).

DISCUSSION

The most important ultrastructural features of leiomyoblastoma were myofilaments, dense bodies and dense patches present in most of the tumor cells. The perinuclear clear zone in cytoplasm was caused by dilation of rough endoplasmic reticulum. These characteristics proved that gastric leiomyoblastoma arised from smooth muscle cells of the gastrointestinal (GI) tract. Leiomyoblastoma was often previously diagnosed as GIST. Although the term GIST was first used in 1983 (by Mazur and Clark), the 1998 discovery by Hirota that GIST tumors could contain mutations in the c-kit gene and marked the beginning of a new understanding and reclassification of sarcomas of the GI tract. Prior to the year 2000, GISTs were classified as one of the types of soft tissue sarcoma (STS), including tumors of smooth-muscle origin (most commonly leiomyosarcoma, and also leiomyoma or leiomyoblastoma) and of neural-crest origin (eg, Schwannoma, or nerve sheath tumour).

Most tumors previously diagnosed as gastrointestinal autonomic nerve tumors (GANTs) are also now classified as GISTs and contain essentially the identical KIT mutations as GIST. What establishes GIST as a separate diagnosis from these other soft tissue sarcomas is not just the description of where the tumor is located, but also the additional factor that it is KIT (CD117) positive. Most GIST patients are also CD34 positive and desmin negative. Well, one of the best ways to identify the cancer cell type (aside from just looking at the cells under a microscope) is to determine the proteins that the cells make. Specialized tests allow the pathologist to do this, usually by determining whether the cells will bind to antibodies against the protein of interest. So, “kit-positive” means that the cells make the protein “kit”, desmin-negative means that the cells do not make the protein “desmin”.

With the development of new effective therapies for GIST, it is vitally important that patients with soft tissue sarcomas of the GI tract have their tumor slides tested for KIT (CD117) by a pathologist experienced with GIST and KIT. Some (perhaps many) patients with pathology reports that were done prior to 2001 may think they have leiomyosarcoma, leiomyoma, leiomyoblastoma, or GANT when in fact their pathology slides were never tested for KIT and they might have GIST. Once more, misdiagnosis can be a disaster. Pathology is critical. Fortunately, the pathology of GIST is now (2003) much better understood than it was in five years ago.

Another question is the origin of GIST. GISTs were previously thought to arise from smooth muscle cells of the GI tract. The discovery that GISTs could express KIT protein helps establish that GISTs do not originate from smooth muscles. The current thinking is that GIST tumors arise either from stem cells that differentiate towards interstitial cells of Cajal or directly from interstitial cells of Cajal (ICCs). The interstitial cells of Cajal are the pacemaker cells of the GI tract (they are named after a great Spanish biologist and microscopist named Cajal), they stimulate the movement (contractions) of the GI tract. These movements ("peristalsis") are the waves of contraction which force the digested food through the gut. GIST often spreads from the original (primary) site to distant locations. If this happens, these tumors are called metastases (or simply, "mets"). If GIST tumors metastasize they usually travel to the liver, or the peritoneum. Metastases to lymph-nodes and lungs are rare, but do occur. Metastasis is usually even worse than the growth of the primary one. Metastases can cripple a vital organ such as the liver. They are usually harder to treat than primary tumors. Metastases are the terrorist network of cancer, stealthily spreading to distant sites, where they can grow and do damage.

The results showed that gastric leiomyoblastoma cells did not differentiate to interstitial cells of Cajal, but differentiated to smooth muscle cells. Therefore, we think if definite smooth myocytes are found in this tumor, it should be diagnosed as leiomyoblastoma but not as GIST.

In summary, gastric leiomyoblastomas have a characteristic ultrastructure, electron microscopy may play a crucial role in diagnosis of gastric leiomyoblastoma.

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