LEIOMYOSARCOMA OF THE ESOPHAGUS IN A PATIENT WITH CHAGASIC MEGAESOPHAGUS: CASE REPORT AND LITERATURE REVIEW

SHEILA JORGE ADAD, RENATA MARGARIDA ETCEBEHERE, ELCY MIKA HAYASHI, ROSEMARY KIYOKO ASAI, PATRÍCIA DE SOUZA FERNANDES, CAIO FLAVIO CASTRO MACEDO, AND EDUARDO CREMA
Faculty of Medicine, Triângulo Mineiro, Uberaba, Minas Gerais, Brazil

Abstract. Leiomyosarcoma constitutes approximately 0.5% of the malignant neoplasias of the esophagus and its association with megaesophagus has not been described. We report on a case of a woman with dysphagia that was slowly progressive from the age of 19 due to chagasic megaesophagus. The woman was subjected to cardiomyotomy at the age of 49. She presented a rapid worsening of the dysphagia due to leiomyosarcoma at the age of 61, and was subjected to subtotal esophagectomy with cervical esophagogastroplasty. She developed pulmonary and hepatic metastases 14 months after surgery and died six months later.

Chagasic megaesophagus, like idiopathic achalasia or megaesophagus, is related to an increased risk of epidermoid carcinoma of the esophagus.1-5 However, we are unaware of any studies showing an association between megaesophagus and leiomyosarcoma. We report herein a case of chagasic megaesophagus who developed leiomyosarcoma of the esophagus.

CASE REPORT

The subject was a 61-year-old woman (housewife) who had been living in rural conditions in central Brazil. She stated that she did not smoke or drink alcoholic beverages. She had a history of dysphagia from the age of 19 that became accentuated with time and was referred to as chagasic. After a diagnosis of chagasic megaesophagus was made, she was subjected to cardiomyotomy at the age of 49 and showed a distinct improvement. She maintained an unchanged state until two months before her last hospitalization, a time when the dysphagia became aggravated to a point where she had difficulty even in ingesting liquid alimentation, which was accompanied by significant weight loss and anemia. Results of serologic examinations for Chagas’ disease were positive using three different techniques (complement fixation, immunofluorescence, and hemagglutination). Endoscopic examination revealed a vegetating lesion obstructing the passageway through the distal third of the esophagus, which showed dilation. A diagnosis of malignant neoplasia was confirmed by biopsy. Thoraco-abdominal tomography and abdominal ultrasound did not reveal metastases. She was subjected to subtotal esophagectomy with esophagogastroplasty and anastomosis in the lower cervical region.

Macroscopic examination of the surgical specimen showed a polypoid tumor occupying the distal third of the esophagus. It measured 9 × 5 × 4.5 cm, was covered by mucosa with dispersed erosions, had an elastic, off-white, striated appearance at cut surfaces, and infiltrated the wall to a depth of up to 0.1 cm of the tunica adventitia. The organ showed dilation, with a maximum circumference of 11 cm, and had an intensely thickened wall and mucosa with dispersed leukoplastic plates alternating with erosions (Figure 1).

Microscopy of the surgical specimen showed a tumor composed of predominantly elongated cells forming interlaced bundles, marked pleomorphism, giant cells, and frequent bizarre mitoses (Figure 2). When stained with Masson’s trichrome stain, the neoplastic cells stained red with occasional conjunctive fibers stained blue (Figure 3). An immunohistochemical study demonstrated that the neoplastic cells had strong positivity for muscle actin (mouse monoclonal antibody HHF35; Dako, Carpinteria, CA) and smooth muscle actin (Figure 4), and were positive for vimentin and negative for cytokeratin; positivity for type 4 collagen was seen only around individual neoplastic cells. The histologic finding relating to positivity for actin led us to a diagnosis of leiomyosarcoma. In areas without neoplasia, the histologic picture was what is usually found in chagasic megaesophagus: aganglionosis, ganglionitis, periganglionitis, neuritis, perineuritis and myositis with a predominance of mononuclear cells, especially T lymphocytes, and fibrosis in the muscular layer (Figures 5–8). Erosions were also noted, alternating with regenerating epithelium and foci of ceratization, related to the alimentary stasis. The surgical margins and peri-esophageal and cardiac lymph nodes did not show neoplasia.

The patient developed dysphagia 17 days after surgery due to substenosis of the cervical esophagogastric anastomosis, and was subjected to esophageal dilation. She did not attend follow-up but returned 14 months after the surgery, when pulmonary and hepatic metastases were diagnosed. Despite chemotherapeutic treatment, she died six months later.

DISCUSSION

Chagas’ disease is endemic in central Brazil, and predominantly affects inhabitants of rural areas, and generally those of a low socioeconomic and cultural level, independent of sex, race, or color. Approximately 13% of those with Chagas’ disease in this region have megacolon and/or megaesophagus.6 Cancer of the esophagus represents 6.5% of the malignant neoplasias of the digestive tube, of which 91.3% are epidermoid carcinomas and 8.7% are adenocarcinomas.7

An increased frequency of epidermoid carcinoma in chagasic megaesophagus has been noted, varying from 1.1% to 6.6%,4,8 whereas this neoplasia is encountered in approximately 0.5% of the population in central Brazil when not associated with chagasic megaesophagus.4 There is evidence of an association between Chagas’ disease and carcinoma of

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Figures 1–8. 1, segment of the esophagus showing a polypoid tumor in the distal third of the organ, with off-white cut surfaces of a striated appearance and infiltration of the wall. Note the increased circumference of the organ, diffuse thickening of the wall, and mucosa showing erosions alternating with leukoplasic plates due to chagasic megaesophagus. The scale ruler is in centimeters. 2, leiomyosarcoma of
the esophagus, although this is related to megaesophagus and not directly to chagasic infection. Studies indicate that there is no association between chagasic megacolon and cancer of the colon or between chagasic cardiopathy and cardiac neoplasias or neoplasias of other organs.

We have not encountered any report of leiomyosarcoma in chagasic megaesophagus or achalasia in the literature. We found only one report of leiomyosarcoma in an individual with Chagas’ disease. However, it was located in the jejunum and did not have alterations that could be attributed to Chagas’ disease in this organ and there was no megaesophagus and/or megacolon. If one considers that leiomyosarcoma is a rare type of tumor in the esophagus, representing approximately 0.5% of the malignant neoplasias of this organ, it could be concluded that the case presented here might be an incidental association. Based on the data in the literature, the predisposition of chagasic megaesophagus and/or idiopathic achalasia towards epidermoid carcinoma is due to alimentary stasis, which produces intense irritation of the mucosa and an increase in the rate of proliferation of epithelial cells, which would not affect the muscle layer. However, in chagasic megaesophagus, there is also an inflammatory process in the other layers and foci of myositis are commonly found, as well as intense hypertrophy and/or hyperplasia of muscle fibers. Therefore, it is not unexpected to find that chagasic megaesophagus favors the appearance of leiomyosarcoma. On the other hand, epithelial cells proliferate more and subject to more repair than muscle cells.

The association between leiomyosarcoma and megaesophagus seen in this case may be incidental because it appears to be the first case reported. Nevertheless, it is important to report this case so that it can be determined if this is only a casual association or if there is a predisposition for this type of neoplasia in megaesophagus.

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Authors’ address: Sheila Jorge Adad, Renata Margarida Etchebehere, Eley Mika Hayashi, Rosemary Kyoko Asai, Patrícia de Souza Fernandes, Caio Flávio Castro Macedo, and Eduardo Crema, Rua Getúlio Guará, 130, Uberaba, Minas Gerais, CEP 38025-440, Brazil.

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The circulation showing the fusocellular appearance, with hypercellularity, pleomorphism and frequent mitoses (arrows) (scale bar = 30 μm). 3. Specimens stained with Masson’s trichrome stain, showing red staining of neoplastic cells similar to that of the muscle layer of blood vessels (scale bar = 30 μm). 4. Positivity of tumor cells for smooth muscle actin (scale bar = 30 μm). 5. Myositis in the middle third of the esophagus. Note the mononuclear inflammatory infiltrate attacking the myocytes (scale bar = 30 μm). 6. Myenteric plexus with aganglionicosis and chronic intense inflammation (scale bar = 30 μm). 7. The same region in Figure 6, showing positivity for protein S-100 in nerve filaments interlaced with inflammation (scale bar = 30 μm). 8. Muscle layer with fibrosis stained blue with Masson’s trichrome stain (scale bar = 30 μm).