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Leiomyosarcoma: A rare soft tissue cancer arising from multiple organs

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ABSTRACT

Leiomyosarcoma (LMS), a smooth muscle connective tissue tumor, is a rare form of cancer which accounts for 5–10% of soft tissue sarcomas. This type of cancer is highly unpredictable. LMS is a resistant type of cancer and can remain in the dormant state for long time. It can recur in the later stages of life. LMS has been reported in different animals including humans. A wide literature search was done. The PubMed database was used to search for journal articles on the occurrence of LMS in different organs from 1950 to 2016. LMS has been reported to be associated with different organs, including esophagus, stomach, intestine, anus and uterus. In this article, an attempt has been made to review the studies based on occurrence of LMS with respect to the organs affected and frequency of publications. Finding the organ-associated occurrence of LMS may be useful in assessing the overall risk and formulating future cancer preventive strategies.

1. Background

Sarcoma refers to a cancer that arises from transformed cells of mesenchymal origin. These tumors are most common in the bones, muscles, tendons, cartilage, nerves, fat, and blood vessels. Leiomyosarcoma (LMS) is a type of soft tissue sarcoma (STS) and is referred to as malignant smooth muscle tumor. STS occurs throughout life[1] and can develop in muscle, fat, blood vessels or any of the other tissues that support or protect the organs of the body. STS spans a wide range of differentiation including adipocytes (liposarcoma), peripheral nerve tissues (malignant peripheral nerve sheath tumor), smooth (leiomyosarcoma) or striated muscle (rhabdomyosarcoma), vascular tissues (angiosarcoma), and other origins (such as undifferentiated pleomorphic sarcoma). Due to the rarity and complexity of STS, large population-based studies are required to elucidate its incidence and the potential contributing factors.[2] It has been proposed that tumor size, tumor necrosis, and vascular invasion are strong and reliable factors that can be used to improve prognostic accuracy in STS.[3]

LMS is one of the more common types of soft tissue sarcoma to develop in adults. It should not be confused with leiomyoma, which is a benign tumor originating from the same tissue. LMS is an extremely rare type of cancer and can be very unpredictable. It can remain dormant for long periods of time and recur after years.[4] LMS is not very responsive to chemotherapy or radiation, thus is considered a resistant cancer type. Furthermore, the best way to get rid of it is to remove it surgically in the early stages. LMS can arise in any type of organ. Cutaneous LMS originates from the pilo-erector muscles in the skin, gastrointestinal LMS arises from smooth muscle in the GI tract or from a blood vessel and uterine LMS comes from the smooth muscle in the uterine muscular layer. At most other primary sites—retroperitoneal extremity (in the abdomen, behind the intestines), truncal, abdominal organs, etc.—leiomyosarcomas appear to grow from the muscle layer of a blood vessel (the tunica media). Thus a leiomyosarcoma can have a primary site of origin anywhere in the body where there is a blood vessel. Due to its rare occurrence and unpredictability, this short review focuses on the reports available on the occurrence of LMS, its association with different organs, capability of metastasis and potential genetic biomarkers.

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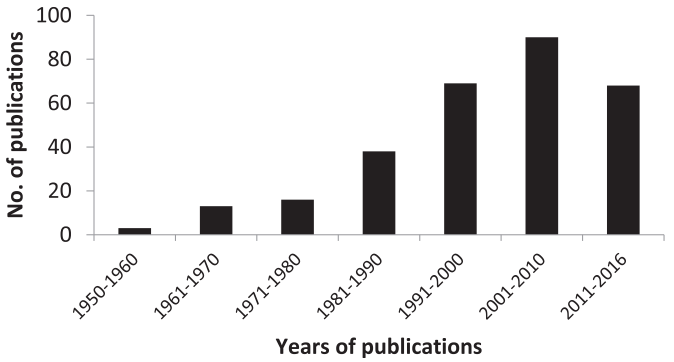

Fig. 1. Number of publications on occurrence of LMS of different organs from 1950 to 2016 (Studies taken from PubMed database search; N = 297).

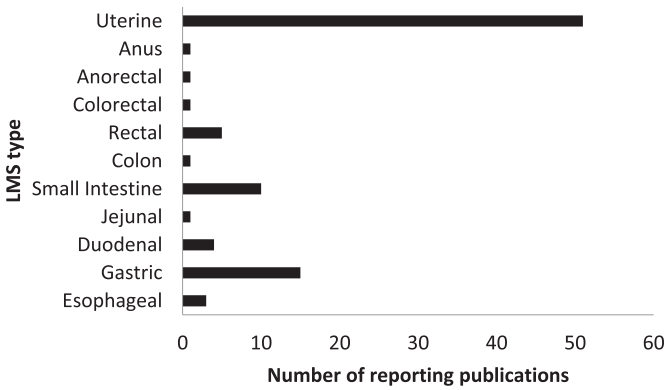

Fig. 3. Comparative number of reports on different LMS types (N = 93).

2. Literature search

A computerized literature search was done for identifying relevant studies. Articles on the occurrence of LMS in different organs were searched from 1950 to 2016 using the PubMed database. Abstracts of all the selected papers from the search were thoroughly studied and manuscripts were identified for full-text review. Different keywords and various combinations of terms related to the topic of research were used. Finally, the references at the end of the papers were also reviewed to identify any papers that were missed. Fig. 1 shows the number of publications by year (N = 297; Search from 1950 to 2016).

3. Occurrence of different types of LMS

3.1. Epidemiological studies

LMS has a low incidence rate. Hung et al.[2] reported an age-standardized incidence rate (ASR) of 1.63 per 100,000 persons. Many epidemiological studies on STS have reported the occurrence of LMS.[2,3,5–8] Most of the epidemiological studies on STS have been conducted in western countries and limited data is available for Asian countries.[2] In Taiwan, 292 LMS cases (0.075%) out of a total of 3843 primary STS cases were reported, yielding a crude rate of 0.14. ASRs for males and females were found to be 0.12 (150 cases) and 0.11 (142 cases), respectively.[2] Another study from Karachi, Pakistan reported a total of 7 LMS cases (0.072%) out of a total of 96 STS cases with ASR of 3.3 and 2.1 for males and females, respectively. The most common histological tumor was rhabdomyosarcoma.[5] Similarly, a U.S.-based study reported 104 LMS cases (29%), in addition to liposarcoma (n = 40; 11%), synovial sarcoma (n = 12; 3%) and 27 histologic subtypes (n = 207; 57%).[9] Toro et al.,[8] while showing the incidence patterns of STS, found 23.9% LMS cases out of a total of 26,758. The study also found 40% of the total LMS cases among women to be uterine in nature. Ferrari et al.[1] presented LMS as the most common type along with Kaposi sarcoma and fibrohistiocytic tumors out of a total of 48,012 STS cases. In the same line, Rydholm et al.[10] also reported LMS as the most common histologic group among the 278 STS cases.

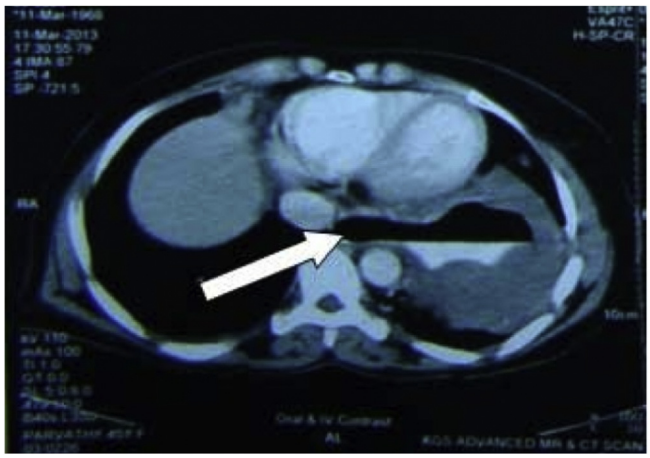

Fig. 2. CECT abdomen showing large mass in left lower thorax arising from distal esophagus. Centre of the mass was ulcerated and it was communicating with the esophageal lumen (Reprinted from Reddy et al.[12] DOI: https://doi.org/10.17659/01.2013.0100).

3.2. LMS of esophagus and stomach

Leiomyosarcoma is a rare tumor that accounts for 0.5% of esophageal sarcomas. Lise et al.[11] reported leiomyomas and LMS of the esophagus in 1972. A paper presented two cases of LMS of esophagus in a 45-year-old lady and a 52-year-old gentleman who presented with dysphagia, and whose LMS was confirmed by immunohistochemistry.[12] The lady presented normal routine biochemical and hematological parameters. Fig. 2 represents the CECT abdomen showing a large mass in the left lower thorax arising from the distal esophagus.

Miettinen et al.[13] reclassified a total of 68 stromal/smooth muscle tumors by current histologic and immunohistochemical criteria and found 3 LMSs, 17 gastrointestinal stromal tumors (GISTs) and 48 leiomyomas (LMs). All tumors were from the lower third of the esophagus, and the most common complaint was dysphagia. Similar to esophageal LMS, LMS of the stomach has also been reported[14–19] (Fig. 3). In 1948, Marvin and Walters[14] presented a case of multiple LMSs of the stomach and reviewed 16 cases. Later in 1953, Crile and Groves[15] reported 5 cases of massive LMSs of the stomach. In 1987, nuclear DNA patterns were studied by flow cytometry in LMS and benign smooth muscle tumors of the stomach.[17] In this study, paraffin-embedded tissue samples were used for determination of DNA ploidy by flow cytometry on surgically resected gastric smooth muscle tumors, including 44 LMSs. The DNA histograms of the 44 LMSs showed 20 cases (45%) of DNA diploid pattern, 14 cases (32%) of DNA tetraploid/polyploid pattern, and 10 cases (23%) of DNA aneuploid peaks. In the patients with LMS, the DNA ploidy pattern was significantly correlated with survival ($p < 0.001$), as were tumor grade ($P < 0.001$) and tumor size ($p < 0.05$). Both benign and malignant gastric smooth muscle tumors with DNA tetraploid/polyploid patterns were significantly

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