Elastofibroma dorsi: An Association with Hematological Malignancies

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Abstract

Background: Elastofibroma dorsi (ED), a benign soft tissue tumor, has multiple chromosomal mutations in 3q21, 1p32, 6q25, Xq and 19q13. Most of these mutations are also present in multiple hematological malignancies. However, the clinical prevalence of ED in patients with hematological or solid malignancies has not yet been reported. The purpose of this study was to investigate the association between ED and other malignancies.

Methods: In this case-control study, we identified 52 ED patients (cases) and randomly selected 150 non–ED-patients (controls) who underwent Computed Tomography (CT) at our institution between 1973 and 2015. Owing to the various malignancy subtypes, limited sample sizes, and predominance of Diffuse Large B-cell Lymphoma (DLBCL) in these cohorts, Patients were pooled into 1 of 3 categories: DLBCL, no cancer, and other cancers. The primary endpoints were the odds ratios (ORs) of no cancer and other cancers using DLBCL as a reference. The second endpoints were the ORs of affected systems using hematological malignancies as a reference.

Results: The mean age of the ED patients was significantly higher than that of the control patients (P = 0.0003). Compared with control patients, ED patients had a higher risk of having DLBCL than no cancer (P = 0.029) or other cancers (P = 0.001) and had a higher probability of having hematological malignancies than other systems’ cancers (P = 0.002).

Conclusions: Compared with patients without ED, patients with ED have a higher risk of developing hematological malignancies, especially DLBCL. This association is likely secondary to the mutations shared by ED and hematological malignancies.

Introduction

Elastofibroma dorsi (ED) is a non-encapsulated benign soft tissue tumor that classically affects the periscapular region but has also been reported to involve the olecranon process, stomach, axilla, and intestine [1]. Pathologically, ED is composed of extracellular collagen and an elastin matrix interspersed with fatty tissue strands and fibroblasts [2]. Despite its indolent clinical behavior, ED has multiple chromosomal mutations Nishio et al. [3-7] found that 33% of ED patients had genetic mutations, the most common of which were gains in [3]. McComb et al. reported that genetic alterations in 1p32 were present in 3 cases of ED Vanni et al. [6] described the same 1p32 mutation as well as mutations in 3q and 6q25 in ED patients [5]. Moreover, another report documented genetic alterations in 1p32 in 2 patients with ED; the same study described multiple genetic mutations, including 3q21 and 19q13, in the 2 patients. Most of the chromosomal mutations that have been reported in ED are also present in multiple hematological malignancies; for example, mutations in 1p32 are also present in leukemia [8-12], and mutations in 3q21, 19q13, and Xq are also present in B-cell lymphoma [13-15].

The clinical prevalence of ED in patients with hematological or solid malignancies has not yet been reported. The shared chromosomal mutations of ED and hematological malignancies suggests that these disease processes may be associated with one another. To test this observation, we
conducted a case-control study to investigate the association between ED and other malignancies.

**Methods**

**Patient Data**

The primary objective of this study is to determine the associations between ED and other malignancies. In this case-control study, we searched our institutional data registry and identified 52 patients diagnosed with and/or treated for ED (cases) from 1973 to 2015 and randomly selected 150 patients without ED (controls) who underwent CT at our institution. MD Anderson’s Institutional Review Board approved the study with a waiver of consent. We reviewed patients’ medical records and collected demographic, clinical, pathological, and radiological data. Of the 52 ED patients, 17 had pathologically proven ED, and 35 had ED detected on imaging studies for other diseases. Of the patients with pathologically proven ED, 3 were excluded because no data were available for them, as only their biopsy specimens were sent to our institution for pathological confirmation. Of the remaining 49 patients with ED, 39 (80%) had a malignant process, the most frequent of which was diffuse large B-cell lymphoma (DLBCL). Of the 150 control patients, 132 (88%) had a neoplastic disease; their most common malignancies were colon cancer and lung cancer.

**Statistical analysis**

To increase the statistical power, we applied a case-control ratio of 1:3 in data collection. Owing to the large number of different malignancy subtypes, the limited sample sizes, and the predominance of DLBCL in the cohort, patients were pooled into 3 categories: patients with DLBCL, no cancer, and other cancers. The primary endpoint was the odds ratio (OR) of no cancer and other cancers with ED status. The ORs of a basic model containing a single dichotomous covariate (ED status) were obtained. All tests were 2-sided, and p-values of 0.05 or less were considered statistically significant. Statistical analysis was carried out using SAS version 9.2 (SAS Institute, Cary, NC).

**Results**

Among the 49 ED patients, the location ED most frequently affected was the periscapular area in 47 patients (96%), followed by the gastrointestinal tract in 2 patients (4%). In addition, 24 patients (49%) had bilateral lesions, 14 (29%) had right-side ED, and 11 (22%) had left-side ED. ED was incidentally detected in 40 patients (82%), most of whom were receiving treatment for malignancy; detected in 8 patients (16%) who presented with complaints of a slowly growing mass in their back; and detected in 1 patient (2%) who presented with chronic periscapular pain. Nine patients (18%) underwent surgery to remove ED, and 8 patients (15%) were manual workers.

The ages in case and control groups were tested by 2 sample t-test with equal variances. The mean age of the ED patients (67.27 years) was significantly higher than that of the control patients (58.73 years; P = 0.0003) (Table 1). A chi-squared test showed there was no significant difference of sex distribution in case and control groups (P = 0.59) (Table 1).

**Association of ED with Other Malignancies**

Ten ED patients and 15 control patients had no neoplastic process. ED patients had 19 malignant diseases affecting 8 systems. The most common malignant diseases among ED patients were hematological malignancies, namely lymphoma, followed by genitourinary malignancies. Control patients had 56 neoplastic diseases (53 malignant and 3 benign) affecting 11 systems. The most common malignant diseases among control patients were lung cancer and colon cancer, followed by prostate cancer. Whereas only 7% (11 patients) of the 150 control patients had hematological malignancies, 22% (11 patients) of the 49 ED patients had hematological malignancies. Moreover, only 1 control patient (<1%) had DLBCL, whereas 8 ED patients (16%) had DLBCL.

Because it was the most common malignant disease among ED...
patients, DLBCL was used as the reference group in the comparison of ED patients with control patients. Compared with control patients, ED patients were at a significantly higher risk of having DLBCL than having no cancer (P = 0.029) or other cancers (P = 0.001) (Table 2).

Because blood was the most common affected system by malignancy in ED patients, hematological malignancies were used as a reference in comparison with no cancer and other systems’ cancers in both groups. When hematological malignancies were used as the reference group, ED patients had a significantly higher risk of having hematological malignancies than having other systems’ cancers compared with control patients (P = 0.002) (Table 2). Genitourinary cancers occurred at the same frequency as hematological malignancies in ED patients. When genitourinary cancers were used as a reference group, ED patients or control patients did not have significantly different risks of having a genitourinary cancer rather than no cancer (P = 0.39) or a genitourinary cancer rather than other system’s cancers (P = 0.27).

**Discussion**

We found that, compared with control patients, ED patients have a significantly higher risk of developing hematological malignancies (P = 0.002), specifically DLBCL. This finding may be explained by the chromosomal mutations that ED and hematological malignancies share.

Chromosomal instability and multiple genetic breakpoints are the salient cytogenetic features of ED [4-7]. The most commonly reported genetic mutations in ED are at 3q21, 1p31-p32-p36, Xq12-q22, 6q25, and 19p13.3-q13.3 [4-7]. Multiple translocations involving 1p32 have been reported in several types of leukemia, including acute T-cell, B-cell, megakaryocytic, lymphoblastic, and monocytic leukemias [8-12]. Moreover, chromosomal alterations at 3q21, 6q25, and 19q13 have been documented in several subtypes of DLBCL [13,15,16]. In the present study, DLBCL was the most common malignancy in patients with ED, and its incidence compared with that of other cancers was significantly higher in ED patients than in control patients (P = 0.0003). The ED patients’ mean age was 67.27 years, and 71% of the ED patients were older than 60 years. Others have posited that ED is a neoplastic process arising from genetic mutations [4-7]. The present study showed that ED patients were at significantly higher risk of having hematological malignancies, and both of them share multiple mutation. The reported mutations and increased risk of hematological malignancies in ED reflect the neoplastic nature of ED.

**Conclusion**

Our findings suggest that, compared with patients without ED, patients with ED have a higher risk of developing hematological malignancies, especially DLBCL. This association is likely secondary to the mutations in 1p32, 3q21, 19q13, 6q25, and Xq shared by ED and hematological malignancies.

**References**

10. Sagawa M. Establishment of a new human acute monocytic leukemia cell line TZ-1 with t(1;11)(p32;q23) and fusion gene MLL-EPS15. Leukemia. 2006; 20: 1566-1571.


