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High rate of unnecessary thymectomy and its cause. Can computed tomography distinguish thymoma, lymphoma, thymic hyperplasia, and thymic cysts?

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ABSTRACT

Purpose: To determine the non-therapeutic thymectomy rate in a recent six-year consecutive thymectomy cohort, the etiology of these unnecessary thymectomies, and the differentiating CT features of thymoma, lymphoma, thymic hyperplasia, and thymic cysts.

Materials and methods: Electronic data base query of all thymectomies performed at the Massachusetts General Hospital from 2006 to 2012 yielded 160 thymectomy cases, 124 of which had available imaging. The non-therapeutic thymectomy rate (includes thymectomy for lymphoma and benign disease) was calculated. Preoperative clinical and CT imaging features were assessed by review of the in-house electronic medical record by 2 thoracic surgeons and 2 pathology-blinded radiologists, respectively.

Results: The non-therapeutic thymectomy rate of 43.8% (70/160) was largely secondary to concern for thymoma and was comprised of lymphoma (54.3%, 38/70), thymic bed cysts (24.3%, 17/70), thymic hyperplasia (17.1%, 12/70), and reactive or atrophic tissue (4.3%, 3/70). Among these four lesions, there were significant differences in location with respect to midline, morphology, circumscription, homogeneity of attenuation, fatty intercalation, coexistent lymphadenopathy, overt pericardial invasion, and mass effect ($p < 0.001$). True thymic cysts ranged in attenuation from −20 to 58 Hounsfield units (HU), with a mean attenuation of 23 HU.

Conclusion: The high rate of unnecessary thymectomy was due to misinterpretation of thymic cysts, thymic hyperplasia, and lymphoma as thymoma on chest CT. This study demonstrates differentiating features between thymoma, lymphoma, thymic hyperplasia, and thymic cysts on chest CT which may help triage more patients away from thymectomy toward less invasive and non-invasive means of diagnosis and thereby lower the non-therapeutic thymectomy rate.

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1. Introduction

Non-therapeutic thymectomy rates ranging from 22% to 68% have been reported in the literature [1,2]. Non-therapeutic thymectomy refers to performance of this invasive surgical procedure without therapeutic benefit on account of unsuspected final diagnoses including lymphoma, thymic cysts, and thymic hyperplasia [2] (the latter in the absence of myasthenia gravis) [3]. To our knowledge, no prior study has researched the cause of these unnecessary thymectomies or compared and contrasted the CT features of these four entities with 100% pathological proof in a single institution cohort of consecutive thymectomy patients [4].

Our study hypothesis was that lack of awareness by radiologists and surgeons of the shortcomings of CT in the evaluation of thymic cysts and thymic hyperplasia and of the differentiating CT features between thymoma, lymphoma, and these benign lesions substantially contributes to the high non-therapeutic thymectomy rate, committing many patients to unnecessary invasive surgery and its associated morbidity.

The purpose of this study was two-fold. First, to determine the primary cause of unnecessary thymectomy in our study cohort and second, to investigate whether there were any significant differences in the CT appearance of thymoma, lymphoma, thymic hyperplasia, and thymic bed cysts in our recent, 6-year consecutive thymectomy cohort which could have led the surgeon to consider other less potentially morbid and costly forms of clinical management, instead of proceeding directly to thymectomy.

2. Materials and methods

2.1. Patients and clinical data

An informed consent waiver was obtained for this IRB-approved, HIPAA-compliant retrospective study. Data base query was used to obtain the initial list of patients who underwent thymectomy between January 1, 2006 and December 31, 2012 using search terms “thymus,” “thymectomy,” “thymic cyst,” “mediastinal cyst,” and “anterior mediastinal mass” against the electronic database of all in-house surgical pathology specimens accessioned at the Massachusetts General Hospital Department of Pathology (Sunquest CoPathPlus Laboratory Information System). Additional inclusion criteria were applied to this broad search, based on review of the pathology. These criteria included whether the primary pathology involved the thymus and whether the assumed purpose of surgical excision or other tissue sampling was to target the thymus and/or anterior mediastinal abnormalities. Fulfillment of these inclusion criteria was determined through review of pathology reports and associated clinical records, when possible via the electronic medical record. On the basis of these criteria, the following types of cases were excluded from further study: cervical or other ectopic thymic tissue removed in the process of neck or other dissection, incidental thymectomy for repair of congenital cardiac or tracheal anomalies, thymectomy for management of myasthenia gravis, and histologic identification of fetal thymus during the pathologic examination of products of conception.

To ensure accurate classification of the benign cystic lesions found at thymectomy, the histopathology of all of the benign cystic lesions was re-reviewed by 2 pathologists (A.L. and A.E.K.) with 10 and 5 years of experience, respectively. Based on histologic features, the classification of these cystic lesions was confirmed or modified. In select cases, immunohistochemical stains were performed to aid classification (calretinin and D2-40; Leica Bond IHC, pre-diluted; Buffalo Grove, IL). 2/17 thymic cysts in this study co-existed with thymic hyperplasia and were counted as thymic cysts.

Preoperative clinical features (rationale for surgery, nature of surgery) of all 32 benign lesions in the original 160 cohort (not just those with available imaging) and of a similar number (34) of randomly selected (by Excel random number generator) malignant lesions or lesions with known malignant potential were assessed collectively by review of the electronic medical record (clinical and operative notes, imaging reports, and laboratory studies, including pathology reports) by two thoracic surgeons (C.D.W. and M.L.) with 26 and 10 years of experience respectively.

2.2. CT protocol

All chest CT examinations were performed on inspiration with multidetector scanners with 16 or 64 detector rows, with the vast majority on GE Healthcare CT scanners (Milwaukee WI) and with the minority on Siemens Healthcare CT scanners (Erlangen, Germany). 24/124 studies were performed without intravenous (IV) contrast; the remaining 100/124 were performed with IV contrast. Among the benign lesions, 5/10 thymic bed cyst cases and 3/10 thymic hyperplasia cases were performed without IV contrast; the rest of these cases were performed with IV contrast. Among the lymphoma and thymoma cases, 28/31 and 27/42 cases were performed with IV contrast and the rest were performed without IV contrast. The IV contrast-enhanced examinations were obtained 35 s after administration of 65 cc or 80 cc (for patient weights of less than or greater than 200 lbs, respectively) of Iopamidol 76% injection (Isovue® multipack 370, Bracco Diagnostics, Inc., Princeton, NJ) at the rate of 2.5 cc/s. Technical parameters of the scanning protocol included 120 kVp, 120–250 mAs (automatic dose modulation), pitch of 1, 2–2.5 mm collimation slice thickness, contiguous section interval, and 512 × 512 matrix.

2.3. Assessment of thymic lesional and perilesional features

Image analysis was performed by thoracic fellowship-trained radiologists, J.B.A. and S.V., with 17 and 1 years of experience respectively, who independently analyzed images of the 124 subjects on a PACS station using IMPAX® software (AGFA HealthCare, Waterloo, ON). Twenty preoperative imaging features were assessed: 1) lesion morphology, 2) presence of bipyramidal shape (latter evaluated separately from other morphologic descriptors), 3) circumscription/definition, 4) size, 5) attenuation (homogeneous versus heterogeneous), 6) region-of-interest (ROI) measurement of attenuation in the case of homogeneous lesions only, 7) presence of cystic and/or necrotic change amidst solid tissue, 8) gross fat, 9) intercalated gross fat (latter recognized as “fatty marbling”), 10) infiltrativeness, 11) calcifications, 12) midline versus off-midline location, invasiveness – 13) pleural, 14) lung, 15) chest wall, 16) vascular), and associated findings including 17) lymphadenopathy, 18) pericardial involvement, 19) pleural nodules, and 20) presence of mass effect. Any discrepant data results were resolved by consensus. Morphology was described as round/oval, saccular (resembling/behaving like a sac of fluid in response to gravity, regardless of attenuation), lobulated (wavy contour), lobulated-multinodular (multiple coalescing nodules), triangular/arrowhead, quadrilateral (overall quadrilateral shape with biconvex margins included in this category), bilobed, and amorphous. Assessment of bipyramidal morphology was made separately from assessment for other morphologic descriptors (Fig. 1). Borders of the mass were described as well-defined or not well-defined. Partially well-defined, partially ill-defined, and ill-defined lesions were all considered not well-defined, for the purpose of statistical analysis. Homogeneity versus heterogeneity of attenuation was assessed, discounting beam hardening artifact, streak artifact, and image noise from this assessment, to the extent possible. Thymic lesion attenuation in Hounsfield units (HU) was assessed exclusively in