Watchful waiting for some children with a mediastinal mass: the potential role for $^{18}$F-fluorodeoxyglucose positron emission tomography: a case report and review of the literature

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Abstract

**Background:** Benign hyperplastic thymus is a rare but important differential diagnosis of anterior mediastinal lesions. Histological and radiological criteria are used to distinguish this benign condition from other malignant diseases but have their limitations, and biopsy of mediastinal masses can be risky. We report for the first time the diagnostic value of fluorodeoxyglucose $^{18}$F positron emission tomography for patients with incidentally identified anterior mediastinal masses to avoid biopsy in some cases.

**Case presentation:** A 2 year old girl presented with new onset of emesis and constipation leading to the incidental discovery of an anterior mediastinal mass on radiograph. Chest computed tomography revealed cystic components within the mass concerning for a malignancy. Biopsy of the lesion and bone marrow aspiration and biopsy were negative but there was concern that the mediastinal biopsy may have missed the malignant component of the lesion. Hence, a positron emission tomography scan was obtained that showed mild homogeneous fluorodeoxyglucose $^{18}$F avidity within the mass similar to that of normal thymus. The diagnosis of benign hyperplastic thymus was made.

**Conclusion:** The differential diagnosis of an incidentally found anterior mediastinal mass includes malignancy, but benign lesions such as benign hyperplastic thymus must also be considered, particularly when the complete blood count and biochemical profile are normal. Fluorodeoxyglucose $^{18}$F positron emission tomography can help guide a clinician’s decision for further interventions and treatment.

**Keywords:** Mediastinal disease, Mediastinum, Positron-emission tomography, Thymus hyperplasia

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Background

Potential etiologies of anterior mediastinal masses in children include benign and malignant tumors whose incidences vary by patient age and symptoms at presentation. Benign hyperplastic thymus (BHT) is a rare condition that occurs mainly in infants and usually resolves spontaneously by 3 years of age, while it seldom occurs in older children and never in adults [1-3]. BHT is characterized by an increase in size of the thymus with normal histological architecture [1-5]. Hence, BHT must be distinguished from follicular hyperplasia in association with Graves’ disease, rebound thymus hyperplasia in cancer patients after chemotherapy, or thymoma and thymolipoma, which do not meet histological criteria for BHT and are mainly seen in adolescents and adults, respectively [1,6,7].

Diagnoses such as germ cell tumor, thyroid cancer, and lymphomas (Hodgkin and non-Hodgkin) must be ruled out during diagnostic workup. BHT spontaneously resolves over time, without specific treatment or...
surveillance; thus, prognosis and management differ from that of malignant etiologies [1,8]. Fine-needle aspiration cytology and imaging studies (e.g., chest radiograph, ultrasound, and computed tomography [CT]) are used to diagnose BHT in a minimally invasive manner but may result in inadequate biopsy specimens or inconclusive radiologic findings, requiring more invasive and potentially dangerous procedures [9-11]. In one study of 54 children and adults who underwent mediastinal biopsy, the procedure-related morbidity was 6%, and fatalities have been reported [12].

Here we describe a child whose diagnosis of BHT was based on CT-guided core needle biopsy and supported by conventional imaging and 18 F-fluorodeoxyglucose (FDG) positron emission tomography (PET) scan. PET can help differentiate BHT from other conditions associated with an anterior mediastinal mass.

**Case presentation**

A 2-year-old girl with no significant past medical history was in her usual state of health when she developed non-bloody and non-bilious emesis associated with constipation. A review of other systems was negative. She did not take any medications and family history was non-contributory. In the emergency room, she appeared well and in no acute distress, with a normal physical examination. Weight, height, and vital signs were normal for age and gender. A chest/abdominal radiograph to evaluate her constipation showed no intra-abdominal pathology but demonstrated mediastinal widening (Figure 1A). A CT scan revealed a 10.3 cm × 6.6 cm × 6.3 cm heterogeneous, right-sided anterior mediastinal mass with a single hypodense area likely representing necrosis, and compression of bronchovascular structures. Laboratory tests showed no hematologic or metabolic derangements.

The patient underwent CT-guided core needle biopsy of the lesion, bilateral bone marrow aspirates and biopsies to rule out a malignancy. Hematoxylin and eosin staining and immunohistochemical studies of the mediastinal mass biopsy showed preservation of thymic architecture, with sheets of variably mature small- to intermediate-sized lymphoid cells and few Hassall’s corpuscles, consistent with benign thymic

**Figure 1** Diagnostic imaging studies of the presented patient. (A) Anteroposterior chest radiograph reveals a large predominately right-sided mass. (B) PET image shows that activity within the mass (black arrow) is indistinguishable from that in the normal thymus (white arrow). (C) Fused transaxial 18 F-FDG PET/CT shows only low-intensity, homogeneous 18 F-FDG avidity within the mass, with photopenia corresponding to the cystic/necrotic area (white arrow).
| Differential diagnosis | Diagnostic imaging modality | Comments |
|------------------------|----------------------------|----------|
| **Normal thymus**      | Computed tomography: Quadrilateral with convex or straight margins in infants, triangular with concave or straight margins in older children | Magnetic resonance: Bilobed, convex at birth, straight during puberty, concave in old age, greater generalized T1-weighted and fast spin-echo T2-weighted hyperintensity and diminishing intermediate T1- and T2-signal soft tissue with fatty involution |
| **Benign Etiologies**  | PET scan: Homogeneous low-intensity uptake | **Age-dependent change in appearance** |
| **Benign thymic hyperplasia** | **Magnetic resonance:** Typically homogeneous low-intensity uptake | **Idiopathic** |
| **Thymic follicular hyperplasia** | **Magnetic resonance:** Homogeneous uptake. Chronic inflammatory states, autoimmune conditions, myasthenia gravis (65%-75%) | **Increased homogeneous uptake** |
| **Rebound hyperplasia** | **Magnetic resonance:** Increased homogeneous uptake | **After chemotherapy** |
| **Thymolipoma**        | **Magnetic resonance:** Resembling uptake in fatty tissue and normal thymus | **Mainly in adolescents and young adults** |
| **Malignant Etiologies** |                          |          |
| **Lymphoma**           | Homogeneous or heterogeneous, nodular, hemorrhage, necrosis, cystic components | Homogeneous low-signal on T1-weighted images, high-signal or intermixed areas (low and high) intensity on T2-weighted images | Heterogeneous intense uptake | Peak incidence in adolescence |
| **Teratoma**           | Well-circumscribed, displacing mass, calcification (80%), fat-fluid levels, cystic, heterogeneous changes in lung parenchyma, pleura, or pericardium (tumor rupture) | Hyperintense fat on T1-weighted images within fluid of low signal intensity (cystic changes), hyperintense mass on T2-weighted images | Heterogeneously avid | Tissue from germ-cell layers |
| **Seminoma**           | Large and lobular, homogenous | High-intensity mass with with septal structures in T2-weighted images | Heterogeneously avid | Most common primary solid tumor of the mediastinum |
| **Non-seminomatous tumor** | Large, lobulated, heterogeneous masses with large (>50%) areas of low attenuation, hemorrhage, necrosis | Internal heterogeneous intensities with areas of high signal intensity reflecting degenerative cystic changes on T2-weighted images. | Heterogeneously avid | Highly aggressive |
| **Thyroid carcinoma**  | Well-defined, smooth or lobulated, tracheal deviation, contrast-enhancing, calcifications | Most tumors are hyperintense of markedly hyperintense on T2-weighted images | Heterogeneously avid | Ectopic thyroid |
| Reference        | Case no* | Sex | Age | Size                  | Presenting symptoms         | Diagnostic imaging          | Pathology | Course          | Comments/Follow up                        |
|------------------|----------|-----|-----|-----------------------|----------------------------|----------------------------|-----------|-----------------|-------------------------------------------|
| **Symptomatic cases** |          |     |     |                       |                            |                            |           |                 |                                           |
| Oh [17]          | 1        | F   | 15  | 15 × 10 × 2 cm, 102 g | Pulmonary infection         | Fluoroscopy, angiography    | Histology | Open resection | None                                      |
|                  | 2        | F   | 14  | 8.4 × 2.8 × 1.4 cm, 20 g | Upper respiratory infection | Fluoroscopy                | Histology | Open resection | None                                      |
| Ruco [5]         |          | M   | 5   | 950 g                  | Dyspnea                    | None                        | Histology | Open resection | None                                      |
| O’Shea [18]      |          | M   | 1   | 420 g                  | Dyspnea, lymphocytosis     | CXR FNA, histology          | Steroids, open resection | 5 months |                                            |
| Barcia [19]      | 2        | M   | 4   | 47-92 g                | Pulmonary infection        | CXR FNA, histology          | Steroids, open resection | 1 month |                                            |
|                  | 3        | M   | 1   | 47-92 g                | Pulmonary infection        | CXR FNA, histology          | Steroids, open resection | 1 month |                                            |
|                  | 11       | F   | 9   | 47-92 g                | Chest discomfort           | CXR FNA, histology          | Steroids, open resection | 1.5 years |                                            |
| Rasore-Quintino [20] |        | M   | 4   | 800 g                  | Pulmonary infection        | 99Technetium scan           | Histology | Open resection | None                                      |
| Lack [6]         | 2        | M   | 11  | 15.2 cm, 324 g         | Mild dyspnea, URI          | CXR FNA, histology          | Steroids, open resection | 9 years  |                                            |
| Lamesch AJ [21]  |          | M   | 6/12 | 230 g               | Respiratory distress     | CXR FNA, histology          | Ventilation, steroids, open resection | 6 years  |                                            |
| Parker [11]      |          | M   | 1 3/12 | 200 g              | Pulmonary infection       | CXR FNA, histology          | Steroids, open resection | 9 years  |                                            |
| Kobayashi [22]   | 1        | M   | 1/12| -                     | Respiratory distress, lymphocytosis | CXR CT, histology           | None       | Observation, steroids | Intensive care unit admission, no follow-up |
|                  | 2        | M   | 2/12| -                     | Respiratory distress, lymphocytosis | CXR CT, histology           | None       | Observation, steroids | None                                      |
|                  | 3        | M   | 4/12| -                     | Pulmonary infection, lymphocytosis | CXR CT, histology           | None       | Observation, steroids | None                                      |
|                  | 4        | F   | 1/12| -                     | Respiratory distress, lymphocytosis | CXR CT, histology           | None       | Observation | None                                      |
| Nezelof [23]     | 1        | F   | 10  | 93 g                   | Cough                      | CXR                        | Histology | Open resection | None/uneventful follow up                 |
| Judd [24]        |          | M   | 12  | 13 × 8 × 3.5 cm, 245 g | Wheezing, dysphagia        | CXR Basic laboratory tests, histology | Open resection | None          |                                            |
| Ricci [2]        | 3        | M   | 14  | 850 g                  | Dyspnea, altered LFTs, atelectasis | CXR CT, histology           | ECG LFTs, history | Open resection | 9 years                                  |
|                  | 4        | M   | 5   | 950 g                  | Dyspnea                   | CXR CT, histology           | ECG MG, LFTs, biopsy x2, histology | Open partial resection | Wound infection, osteomyelitis, lung atelectasis/1 month |
| Linegar [8]      | 1        | F   | 2/12| 220 g                 | URI, lymphocytosis, splenomegaly | CXR CT, histology           | Histology | Open resection | 3 months                                 |
| Case | Gender | Age | Initial Symptoms | Imaging findings | Diagnostic procedures | Treatment | Outcome |
|------|--------|-----|-----------------|------------------|----------------------|-----------|---------|
| 2    | M      | 3   | 18 x 10 x 6 cm, 855 g | Recurrent URI, lymphocytosis | CXR, Histology | Open resection | None   |
| 3    | M      | 6   | 1260 g | Wheezing, dyspnea, respiratory distress | CXR, CT | FNA, histology | N/A | None |
| 4    | M      | 3   | 100 g | Recurrent URI | CXR | Histology | Open resection | None |
| Lee [25] | F | 3/12 | - | Persistent URI, lymphocytosis | CT | Open biopsy, histology | Observation | 1 year |
| 2    | M      | 11/12 | 500 g | URI, lymphocytosis, mediastinal shift | CT | Histology | Open resection | None |
| Bangerter [9] | M | 1/12 | 5 x 6 cm | Acute airway obstruction | Imaging not further specified | U/S guided FNA, histology | Steroids | Death 10 months after diagnosis of unknown cause/8 months |
| Hoerl [10] | M | 5/12 | 4.6 cm AP | Choking | CT | FNA, histology | Observation | 1 year |
| Tareen [26] | M | 3/12 | - | Persisting URI | CT, CXR, US | None | Steroids, observation | 6 months |
| 2    | M      | 8/12 | - | Recurrent URI, dyspnea, tachypnea | CXR, CT | FNA, histology | Open resection | 6 months |
| Sosothikul [27] | M | 4 | - | Dyspnea, wheeze | CXR, CT | BMA, histology | Observation | Involution/1 month |
| Gow [28] | F | 6/12 | N/A | Respiratory symptoms | Imaging not further specified | Flow cytometry, histology | Open resection | 1 year |
| Piednoir [29] | M | 3/12 | - | Anesthesia related respiratory distress, incidental finding | CT | None | Observation | Involution/2 years |
| Sosothikul [27] | M | 2 | 830 g | Fever, dry cough and dyspnea | CXR, CT | Alpha-FP, beta-HCG, FNA, histology | Steroids, open resection | Reoccurrence of symptoms |
| Tan [31] | F | 9/12 | 17.5 x 11 x 5 | Upper respiratory infection | CXR, MRI | FNA, histology | Steroids, open resection | None |
| Oh [17] | F | 10 | 80 g | Incidental finding | Fluoroscopy | Basic laboratory tests, histology | Open resection | None |
| Katz [32] | M | 7/12 | 9 x 8 x 6 cm, 224 g | Incidental finding, lymphocytosis | CT, upper GI, IV, pyelography | Immunologic studies, BMA, histology | Open resection | Hypogamma-globulinemia/4 years |
| Barcia [19] | M | 4 | 47-92 g | Incidental finding | CXR, Histology | Open resection | None |
| 5    | F      | 11  | 47-92 g | Incidental finding | CXR | Histology | Steroids, open resection | 3 months |
| 6    | F      | 3   | 47-92 g | Incidental finding | CXR | Histology | Open resection | 3 months |
| 7    | M      | 4   | 47-92 g | Incidental finding | CXR | Histology | Open resection | 1 year |
| 8    | M      | 4   | 47-92 g | Incidental finding | CXR | Histology | Open resection | 2 years |
| 9    | F      | 7   | 47-92 g | Incidental finding | CXR | Histology | Steroids, open resection | 1.5 years |
| No. | Gender | Age | Size | Incidental finding | Imaging | Histology | Treatment | Follow-up |
|-----|--------|-----|------|--------------------|---------|-----------|-----------|-----------|
| 10  | M      | 13  | 47-92 g | Incidental finding | CXR     | Histology | Open resection | 4 months |
| Lee [33] | F | 2 | 19 × 12 × 4.5 cm | Incidental finding | CXR     | Histology | Oral steroids, open resection | None |
| Lack [6] | M | 14 | 490 g | Incidental finding, lymphocytosis | CXR     | Histology | Open resection | 17 years |
| Nezelof [23] | F | 5 | N/A | Incidental finding | CXR, mediastinoscopy | Basic laboratory tests, biopsy, histology | Observation | None/uneventful follow up |
| 3 | F | 11 | N/A | Incidental finding | CXR, mediastinoscopy | Biopsy, histology | Observation | None |
| Arliss [34] | M | 15 | 17 × 16 × 6 cm, 680 g | Incidental finding, lymphocytosis | CXR, CT | Histology | Open resection | 1 4/12 years |
| Ricci [2] | M | 16 | 13 cm, 250 g | Incidental finding | CXR, CT | ECG, EMG, LFTs, histology | Open resection | 12 years |
| 2 | M | 12 | 7.5 cm, 120 g | Incidental finding | CXR, CT | ECG, EMG, LFTs, histology | Open resection | 7 years |
| Rice [3] | M | 10 | 482 g | Incidental finding | MRI, BMA, histology | Open resection | None |
| Bangerter [9] | F | 5 | 3 × 5 | Imaging not further specified | U/S guided FNA, histology | N/A | 9 years |
| 6 | F | 8 | 1.5 × 1 | Imaging not further specified | U/S guided FNA, immunophenotyping, histology | N/A | 8 months |
| Current case | F | 2 | | Incidental finding | CXR, CT, PET | Core needle biopsy | Observation | |

* If number of patients with benign thymus hyperplasia and patients with other conditions is provided in report. 
CT Computed tomography, CXR Chest radiograph, ECG Electrocardiogram, EMG Electromyogram, FNA Fine needle aspiration, LFTs Liver function tests, MRI Magnetic resonance imaging, N/A Not applicable, PET Positron emission tomography, URI Upper respiratory tract infection, U/S Ultrasound.
tissue. Flow cytometry revealed T-lymphocytes with a full spectrum of orderly thymic maturation patterns, and bone marrow aspirates and biopsies showed normocellular marrow (80%) with trilineage hematopoiesis without evidence of leukemia or lymphoma.

However, the inhomogeneous area within the mass on CT imaging is not a typical finding of BHT and raised concern for a malignancy such as teratoma or lymphoma, which may present with such features (Table 1). PET-CT scan of the large anterior mediastinal mass showed areas of low-intensity, and diffuse, homogeneous FDG avidity, similar to the normal thymus (Figure 1B). Central low-attenuation areas by CT within the mass lacked FDG activity and are suggestive of necrosis (Figure 1C). The standardized uptake value of the lesions ranged from 2.3 to 2.5 MBq/kg, except for the cystic area, which had values less than 2 MBq/kg.

The diagnosis of BHT was made based on histology and lack of FDG avidity on PET scan. The patient continues routine follow up almost a year after original diagnosis with stable mediastinal mass and no further problems or complaints.

**Discussion**

As the scope of diagnostic imaging broadens, there is greater likelihood of incidental detection of anterior mediastinal masses. Lymphomas and germ cell tumors are the most common malignant tumors of the anterior mediastinum in children; whereas, thymomas seldom occur in this age group [13]. Thymolipomas may occur in young adolescents and adults and occasionally

![Flow chart for the workup of a mediastinal mass in an otherwise asymptomatic child.](http://www.biomedcentral.com/1471-2431/13/103)
children. Although their radiographic appearance may resemble BHT, thymolipomas present on MRI as mainly fatty masses with inhomogeneous areas that represent thymus tissue [14,15]. BHT is a rare but important benign condition and must be differentiated from malignant and other benign tumors.

To date, 53 patients with BHT have been reported (Table 2); 34 (64%) of them had respiratory symptoms, and imaging studies revealed a mediastinal mass. In the remaining 19 (36%) patients, the mediastinal lesion was an incidental finding. In either scenario, further diagnostic workup was warranted to rule out a malignancy; however, the implication of malignancy together with imaging findings and parental fear may have led to use of invasive interventions for diagnostic confirmation. Indeed, 79% (15/19) of asymptomatic patients underwent open biopsy and only 26% (9/34) of symptomatic patients were observed clinically without biopsy. In symptomatic patients, open biopsy can be diagnostic and therapeutic, but less invasive procedures are preferred [16].

The primary goal while assessing a mediastinal mass is to rule out oncologic emergencies (anatomic, metabolic, or hematologic) that require immediate medical attention. Workup includes patient’s history, physical examination, routine laboratory tests, and anatomic imaging (Figure 2). After excluding oncologic emergencies, further tests are needed to diagnose the mediastinal lesion.

Physiologic imaging, most often PET-CT, is recommended in the diagnostic process when uncertainty about the malignant versus benign nature of the mass persists (Figure 2) [35].

The pattern and intensity of uptake within such lesions on PET and morphologic appearance on CT can help differentiate benign from malignant etiologies [36] (also see Table 1). To accurately interpret BHT in PET studies, FDG uptake patterns in the normal thymus and pathologic entities involving the thymus need to be known [37]. Normal thymic tissue and benign conditions such as BHT after chemotherapy (so-called “thymic rebound”), comparable to our patient, demonstrate diffuse, low-intensity, homogeneous FDG avidity (Table 1) [38,39].

Malignant conditions show intense FDG avidity that is usually heterogeneous in distribution [40]. The appearance of our patient's lesion was similar to the normal thymus without foci, suggesting its benign nature (Figure 1B), [41] despite the cystic and necrotic areas within the mass [36,42]. The morphology and uptake pattern on 18 F-FDG PET are more meaningful than the SUV. There is an overlap in SUV range between normal thymus and other malignant anterior mediastinal tumor entities [43]. Although a very high SUV may be indicative of malignancy, an average SUV does not exclude malignancy [36,43].

Conclusion

In conclusion, for incidentally found anterior mediastinal masses in otherwise healthy children, we recommend that clinicians expeditiously rule out oncologic emergencies then perform a diagnostic workup. PET scans can help differentiate BHT from other more serious conditions and may spare patients invasive diagnostic procedures.

Further studies including large pediatric series are needed to evaluate the importance of 18 F-fluorodeoxyglucose positron emission tomography in patients with suspected benign hyperplastic thymus.

Consent

Written informed consent was obtained from the patient’s mother for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Abbreviations

BHT: Benign hyperplastic thymus; BMA: Bone marrow aspiration; CT: Computed tomography; FDG: 18 F-fluorodeoxyglucose; PET: Positron emission tomography; SUV: Standardized uptake value.

Competing interests

The authors declare that they have no competing interests.

Authors’ contributions

All authors have participated in study design, interpretation, and writing of the report. RN did the collection of the data, review of literature, and drafted the first version of the manuscript. JLC provided the figures and reviewed the manuscript. SCH reviewed the manuscript. MLM primarily participated in study design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

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