

Ectopic Cervical Thymic Tissue

Diagnosis by Fine Needle Aspiration

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● Cervical thymic masses are congenital lesions that result from aberrant thymic migration during embryogenesis. Although most of these masses are asymptomatic, they may cause debilitating symptoms secondary to encroachment on adjacent aerodigestive structures. Preoperative diagnosis of ectopic thymic tissue is rare; most cases are clinically misinterpreted as branchial cleft remnants or cystic hygromas. Definitive diagnosis has relied on histopathologic examination in nearly all reported cases. However, the invasiveness of open incisional or excisional biopsy carries the risk of surgical and anesthetic complications. Inadvertent surgical thymectomy may result in cell-mediated immune deficiencies in infants and young children. The utility of fine needle aspiration is gaining wider acceptance in the diagnostic evaluation of neck masses. We describe an infant with an asymptomatic cervical thymic mass diagnosed by fine needle aspiration.

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The thymus is a primary lymphoid organ in infancy and early childhood. It initially appears early in fetal life and plays a critical role in the development of cell-mediated immunity. Ectopic cervical thymus is rarely reported, because thymic vestiges often remain asymptomatic and unrecognized by clinicians. Most of these lesions arise as a consequence of migrational defects during thymic embryogenesis. Since 1901, approximately 90 cases of aberrant cervical solid and cystic thymic lesions have been reported in the literature and were identified at either surgery or autopsy.^{1–3} Nearly two thirds of all reported cases were identified in children younger than 10 years.⁴ Ectopic thymic tissue in the neck is rare in patients older than 20 years. Surgical excision has the potential risk of rendering a child athymic and prone for developing immune dysregulation and immunodeficiencies. We report a case of nodular cervical thymic tissue in an infant diagnosed by fine needle aspiration (FNA).

REPORT OF A CASE

A 12-month-old, white, male infant was referred to the Pediatric Otolaryngology Clinic for evaluation of a persistent mass on

the left side of the neck. At birth he was noted to have very subtle left neck swelling in the submandibular area, which was interpreted to be prominent skinfolds and increased subcutaneous fat. His family history, perinatal history, and delivery were unremarkable. The patient was managed expectantly, since he continued to gain weight and thrive without dysphagia or respiratory compromise. Although asymptomatic, the cervical lesion persisted and developed a vaguely nodular texture with associated non-discrete swelling of the left upper neck. On review of a magnetic resonance imaging scan performed at 9 months of age, a solid, homogeneous mass located posterior to the submandibular gland and encroaching on the parapharyngeal space was noted (Figure 1).

On physical examination, fullness of the left submandibular area was noted without evidence of a discretely palpable mass. The overlying skin was normal, and no tenderness was evident. There was no apparent lymphadenopathy. His tonsillar fossae appeared normal, his uvula rose symmetrically, and structures of the midline section of his neck were unremarkable. The patient's hemogram, serum calcium level, and serum electrolyte levels were all within normal range.

A computed tomography-guided FNA was performed with a 22-gauge spinal needle. The unenhanced computed tomographic image demonstrated an oblong, solid mass that measured approximately 3 × 0.5 cm and was located lateral and superficial to the left submandibular gland. The mass was isodense with muscle, and although it compressed adjacent structures, it was noninvasive and distinct from surrounding cervical and periparotid lymph nodes. Cystic features were not radiologically apparent. Review of the aspiration material showed predominantly small, round, monomorphic lymphocytes, which on cell block material demonstrated an organoid pattern that was compartmentalized by fibrous trabeculae. In addition, several nests of cytokeratin-positive epithelial cells that formed Hassall corpuscles were scattered throughout the lesion (Figure 2). There was no cytologic evidence of a neoplasm. A portion of the aspirate was submitted for flow cytometric analysis, which demonstrated a lymphocyte population of almost entirely immature T cells that coexpressed CD4 and CD8 and showed positivity for the early T-cell markers CD1a and TdT (Figure 3). Together, the cytomorphologic and cytometric findings were diagnostic of ectopic cortical thymic tissue. The patient tolerated the procedure well. He remains asymptomatic with no change in the mass after 4 months of follow-up observation.

COMMENT

The primordial thymus begins to appear early in the sixth week of fetal life. It develops primarily from the ventral wing of the third pharyngeal pouch on each side of the most cephalad portion of the foregut. Lesser more rudimentary portions of the thymus are derived from the

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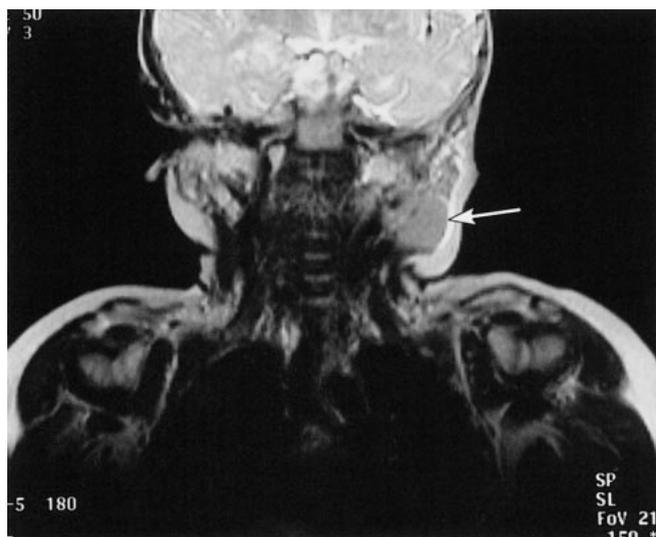


Figure 1. T2-weighted image with fat suppression demonstrates a homogeneous mass (arrow) in the left submandibular space, extending toward the left parapharyngeal space.

fourth pharyngeal pouch. The proliferation of endodermal cells within the outpouchings gives rise to paired solid structures. By the seventh week of gestation, the thymic primordia lose their connections with the pharyngeal wall and join in the midline. A mesenchymal capsule surrounds the developing thymus and maintains the organ in close association with the parietal pericardium. Together, these structures descend to their final anatomic positions in the anterior mediastinum. The medial-caudal migration pathway forms the thymopharyngeal tract, which runs from the angle of the mandible to the manubrium of the sternum bilaterally. Normally, this tract involutes by the completion of development; however, thymic vestiges may persist anywhere along its course. Lymphocyte invasion occurs at 10 weeks of gestation, whereas subsequent endodermal regressions form the Hassall corpuscles. Growth and development of the thymus continue after birth until puberty. The thymus later involutes and undergoes fatty replacement, rendering it difficult to recognize in adults.

Cervical thymic anomalies may occur as a consequence of an arrest in the medial-caudal migration of thymic primordia or sequestration and persistence of thymic vestiges along the course of the thymopharyngeal tract.^{5,6} It is often difficult to make the distinction between these 2 mechanisms. In the case of an undescended thymus due to migrational arrest, only half of the normally bilobed thymus is present in the mediastinum. However, a normal chest radiograph, which lacks the absence or diminution of a thymic shadow, suggests cervical sequestration of thymic remnants. Also, several reports have demonstrated the coexistence of thymus and parathyroid glands in lateral cervical masses.⁶⁻⁸ Because the parathyroid glands are derived from the dorsal wing of the third pharyngeal pouch and descend with the thymus, an ectopic thymus-parathyroid complex mechanistically suggests aberrant migration. An additional cause of cervical thymic anomaly is marked hyperplasia of a normally positioned mediastinal thymus

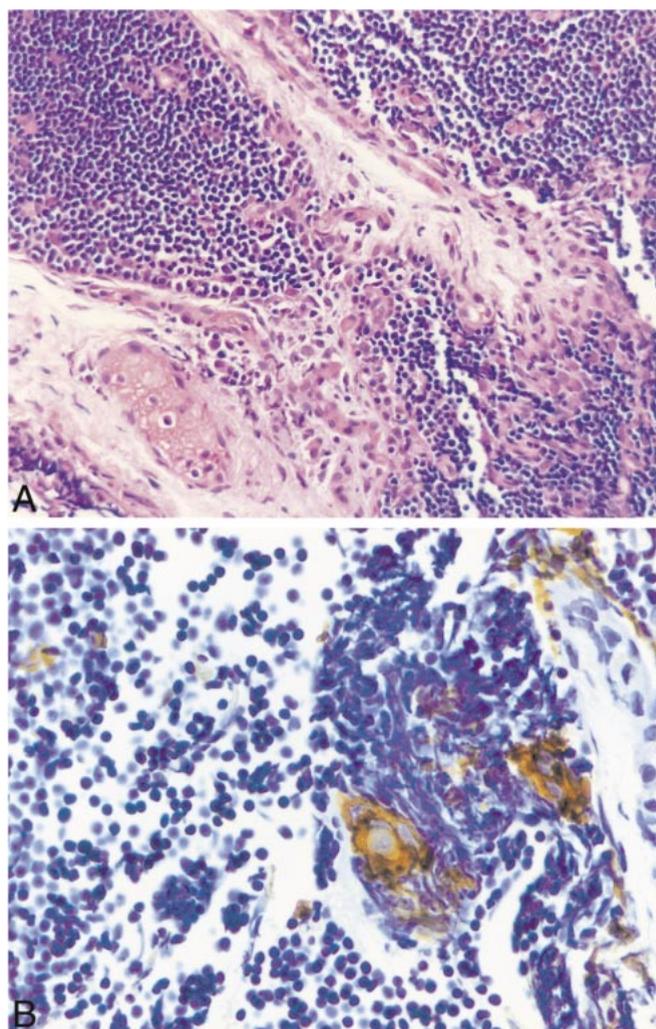


Figure 2. (A) Fine needle aspiration biopsy section prepared from cell block material showing lobules of small, round lymphocytes separated by vascularized bands of fibrosis. Although monomorphic, the cells lack malignant features (hematoxylin-eosin, original magnification $\times 40$). (B) Immunoperoxidase study demonstrating clusters of keratin-positive cells forming Hassall corpuscles (cytokeratin, original magnification $\times 60$).

in early childhood. Thymic hyperplasia may occur following vaccination or in association with an infectious process and often resolves with antibiotics or steroid therapy.⁹

Ectopic thymic masses are congenital lesions of either solid or cystic nature and usually present between 2 and 13 years of age as asymptomatic nodules or neck swellings on routine examination. Considering that the thymus reaches its greatest absolute size at puberty and its greatest relative size between 2 and 4 years of age, presentation and diagnosis during early childhood are not surprising. Occasionally, large or hyperplastic ectopic thymic tissue may compress or displace neighboring structures and cause hoarseness, stridor, or dysphagia.¹⁰ Most cervical thymic lesions are unilateral and, for unknown reasons, are more commonly reported on the left side and in male patients.^{11,12} They have been known to occur as high as the mandibular angle and as low as the thoracic inlet and superior mediastinum. Thymic masses in the trachea and

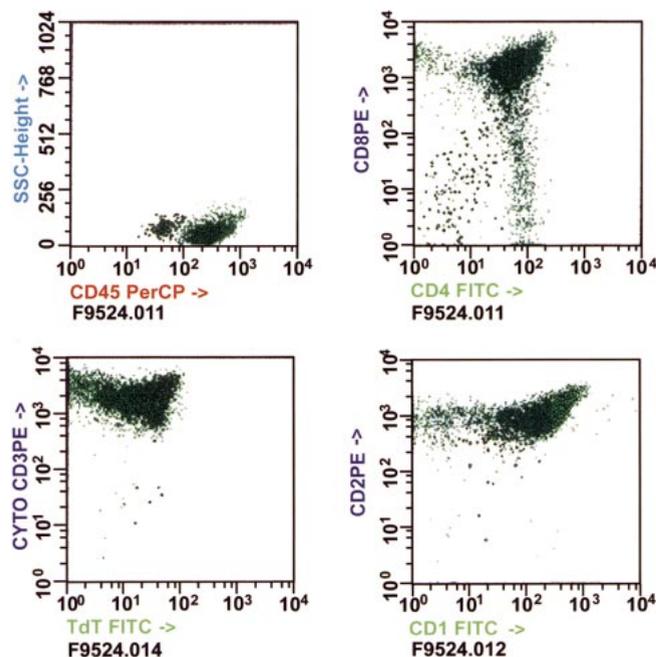


Figure 3. Flow cytometry histograms illustrating a dominant population of CD45-positive, CD3-positive T lymphocytes with an immature immunophenotype. Most T cells express the early antigens CD1 and TdT and coexpress CD4 and CD8.

pharynx and at the base of the skull have also been reported⁸ and likely result from an aberrant migration pathway in thymus embryogenesis.

Nearly all published reports of cervical thymic lesions were initially identified at autopsy or by excisional biopsy. Preoperatively, the diagnosis of ectopic thymic tissue is rarely considered and difficult to establish. Since approximately 90% of the lesions have cystic features,¹³ they are usually clinically misinterpreted as branchial cleft cysts or cystic hygromas. Other neck masses in the differential include thyroglossal duct cysts, cystic teratomas, thyroid or parathyroid lesions, lymphoproliferative disorders, reactive adenopathy, and vascular tumors. An intraoperative frozen section diagnosis may narrow the differential and guide therapeutic decisions. For symptomatic masses, a preliminary diagnosis of ectopic thymus may warrant complete or partial resection of the lesion. However, invasive procedures of the neck carry the risk of pneumothorax, hematoma formation, vagus or hypoglossal nerve damage, and wound infection. In infants and young children, a surgical approach may be particularly ill advised, since inadvertent total thymectomy may lead to impaired cell-mediated immunity and possible autoimmunity. Although a causal relationship between acquired athymia and immune dysregulation has yet to be established, thymectomies in patients younger than 3 months have been shown to result in lower numbers of circulating T cells and diminished responses to T-cell mitogens.¹⁴ Hence, preoperative imaging studies are recommended to verify the presence of mediastinal thymic tissue prior to surgical neck exploration.

Alternatively, FNA performed by an experienced pathologist, otolaryngologist, or radiologist is a safe and

minimally invasive technique of investigating neck masses in children.¹⁵ Not only does FNA provide rapid results, but it also may avoid the need for open biopsy. As we have shown, the morphologic and flow cytometric evaluation of cytologic material can reliably and accurately identify ectopic cervical thymic tissue. Papanicolaou- and Romanowsky-stained smears of the aspirated material typically demonstrate a dominant population of small, round, nonactivated lymphocytes with variable numbers of epithelial cells scattered in the background. Granted, the evaluation of a monomorphous population of lymphocytes in the absence of architectural context may make the distinction from a low-grade lymphoma difficult if not impossible. However, the lack of overt malignant features combined with an immature T-cell phenotype by flow cytometry analysis favors the interpretation of thymic tissue. Moreover, the presence of fibrous septa, Hassall corpuscles, and other characteristics of normal thymic architecture on cell block material confirms an unequivocal diagnosis of ectopic thymus.

In addition, FNA has therapeutic implications in the management of cervical thymic tissue. Standard therapy for a symptomatic thymic mass has historically been surgical decompression. If a symptomatic mass is predominantly cystic, however, the FNA procedure may reduce the mass and palliate the patient without surgery. Similarly, for asymptomatic lesions, a definitive diagnosis by FNA may warrant expectant management without additional procedures. Arguably, a relative indication for surgical excision of an asymptomatic mass is the potential for neoplastic transformation. Rare cases of cervical thymoma with secondary manifestations of myasthenia gravis and invasive thymoma with malignant histologic findings have been documented.¹⁶ Nonetheless, the risk of surgical complications far exceeds the likelihood of neoplastic transformation of asymptomatic thymic tissue, suggesting that a 'watch and wait' approach is the optimal course of management.

In summary, we report the FNA diagnosis of ectopic thymic tissue in an infant with a unilateral, asymptomatic, solid neck mass. Cervical thymic anomalies are uncommon and are rarely considered in the preoperative differential of a neck mass. The unequivocal diagnosis of ectopic thymus has nearly always relied on histopathologic evaluation, and the standard of therapy for symptomatic lesions has been surgical excision. However, invasive surgical procedures may result in variably morbid complications and, in particular, may render the patient athymic and at risk for developing immune dysregulation. We document the utility of FNA as an effective means to establish the diagnosis of ectopic thymus. An FNA is relatively inexpensive, provides rapid and reliable diagnostic results, and avoids the complications of surgery. Furthermore, definitive diagnosis by FNA will significantly affect clinical management and may have therapeutic benefit. If surgery remains necessary for optimal therapy, we recommend preoperative imaging studies to assess the presence of mediastinal thymic tissue.

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