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Ectopic cervical thymus associated with infant death: 2 case reports and literature review

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Abstract

An ectopic cervical thymus is a rare congenital anomaly that can be located anywhere along the developmental pathway of thymic descent. Most lesions manifest as a cystic mass and have an indolent course. Two fatal cases associated with ectopic cervical thymus in the form of a solid mass are presented in conjunction with a review of the clinicopathological characteristics of the solid form. This report emphasizes the importance of considering a diagnosis of ectopic cervical thymus in infants with neck masses, with or without obstructive symptoms, to prevent possibly fatal outcomes.

Key Words: ectopic cervical thymus, mechanical asphyxia, sudden and unexpected infant death

1. Introduction

Ectopic cervical thymus (ECT) is a rare congenital anomaly found in 1% of pediatric autopsies [1]. Most cases follow an indolent course, but several cases have shown life-threatening symptoms such as respiratory distress due to tracheal compression [2-5]. Only 1 fatal case, caused by mechanical asphyxia, has been previously reported [6]. We report 2 sudden, unexpected deaths of infants with ECT and review 95 cases of solid ECT to clarify the clinicopathological features of these lesions.

2. Case Reports

2-1. Case 1

A 4-month-old boy was found dead in a prone position, approximately 5 hours after falling asleep in a supine position. His mother, who had previously borne 3 other children, did not have a significant family medical history; the pregnancy was unremarkable and the baby, who was bottle-fed, was in good health until death. The mother stated that the infant had recently started rolling over, but was not yet proficient. He had received a second combination vaccine against diphtheria, pertussis, and tetanus 2 days before his death.

Microbiological tests for rotavirus, respiratory syncytial virus, and influenza virus were negative. Tandem mass spectrometry screening showed no metabolic disorders. Horizontal sections of a computed tomography (CT) scan, performed 1-hour postmortem, showed 2 isodense nodules immediately inferior to the thyroid gland (Fig. 1).

A complete postmortem examination, performed 13 hours after death, revealed a well-developed and well-nourished boy (height, 66.0 cm; weight, 8.5 kg). External examination showed no apparent anomalies or injuries. An examination of his cervical organs revealed 2 solid nodules (maximum diameters, 1.5 and 1.9 cm), with intact capsules, lying anterolateral to the cervical trachea and immediately inferior to the thyroid gland (Fig. 2A). Histological examination of the nodules showed normal thymic structure, indicating a diagnosis of ECT (Fig. 2B-D). An intrathoracic examination confirmed a normally positioned thymus weighing 50 g (expected weight, 38.1 g [7]). The other findings were characteristic of a rapidly fatal course caused by mechanical asphyxia. Other remarkable physical or toxicological findings were not found.

The postmortem findings led to the conclusion that the cause of death was mechanical asphyxia, likely due to compression of the cervical trachea by the 2 ECTs while the infant was prone. The ECTs were considered to play a crucial role in the mechanical asphyxia because they were located such that they could easily compress the cervical trachea and were large enough to significantly compress it.

2-2. Case 2

A 2-month-old boy was found dead in a supine position, 6 hours after falling asleep. He was his mother's third child, was breast-fed, and did not have a significant family history or any birth or growth abnormalities.

A complete postmortem examination, performed 30 hours after death, revealed a well-developed and well-nourished boy (height, 58.0 cm; weight, 5.6 kg). External examination failed to reveal any apparent anomalies or injuries. An internal examination, followed by a histological examination, revealed a right-sided ECT (diameter, 1.2 cm),

anterior to the cervical trachea and immediately inferior to the thyroid gland (Fig. 3). A normally positioned thymus weighing 37 g (expected weight, 30.4 g [7]) was also found. No other remarkable physical, toxicological, or microbiological findings were found. Vitreous chemistry was not performed.

The cause of death was diagnosed as Category IB sudden infant death syndrome (SIDS), according to the San Diego definition [8]. The ECT was not considered to have been involved in the death because it could not compress the trachea while the boy was in a supine position.

3. Discussion

ECTs show 2 different macroscopic forms—cystic and solid. The cystic form is more frequently reported and accounts for 76–92% of ECTs [9-12]. This form includes 2 different entities: a thymic cyst, arising from a persistent thymopharyngeal duct, and a solid ECT, with cystic changes [11-13]. The pathogenesis of solid ECTs involves the failure of the thymus gland to descend or its sequestration and failure to involute [11-14]. All previous reviews included both forms in their analyses and documented their combined features [9-12]. Consequently, the previous reviews reflect mainly the features of cystic ECTs.

Thus far, a review focused on solid ECTs has not been reported. We searched the literature for solid ECT cases, confirmed by histological examination, and reviewed the cases to clarify their clinicopathological features. Overall, 93 cases of solid ECTs were found in 30 reports. The clinical and anatomical characteristics of the 95 solid ECT cases, including the present 2, are summarized in Tables 1 and 2, respectively

[1,3-5,11,12,14-38].

Solid ECTs are most frequently seen in males, with patient age ranging from birth to 30 years (median age, 3 months). Most cases (70%) have been diagnosed at a patient age of <6 months. Approximately 36% of patients had a concomitant congenital anomaly/disorder, but none were strongly associated with ECTs. In most patients, surgical resection or autopsy was required for a correct diagnosis [14], except for a recent case diagnosed by fine needle aspiration (FNA) [14]. The majority of symptoms associated with solid ECTs are neck masses, as previously reported (Table 1) [9-12]. Respiratory symptoms and/or dysphasia are seen in approximately 12% of solid form cases, but the overall prevalence of these symptoms in ECT patients is approximately 5% [9-12], indicating that respiratory symptoms occur more frequently in cases involving solid ECTs. Therefore, this anomaly should be added to the list of differential diagnoses of such symptoms in infants.

The respiratory symptoms are induced by the lesion's compression of the cervical trachea [3,26,29]. Severe respiratory distress had developed in some serious cases [2-5,21], and mechanical asphyxia leading to death was reported in an additional instance [6]. Shackelford et al. also reported a case, similar to our first case, presenting with tracheal compression and obstructive airway symptoms when the baby was placed in a prone position [39]. The reason for the absence of respiratory symptoms before death in the first boy in the present report is unclear. However, his recent ability to roll over may have been contributory, or there may have been some swelling of the ECTs. The latter consideration is supported by the fact that his mediastinal thymus was heavier than expected for a child of his age [7]. The relationship between the vaccination 2 days before death and the swelling of ECTs is controversial. Further evaluation is required to

clarify this association, although several reports have described vaccination-related ECT enlargement [5,13,18,20,23,29,39,40]. These observations provide evidence that solid ECTs may cause respiratory distress and mechanical asphyxia, especially in an infant in the prone position.

Table 2 shows the anatomical features of solid ECTs. Cases showing multiple lesions, such as case 1, are rare. Solid ECTs tend to localize at the level of the thyroid gland or above, with sizes ranging from 0.1 to 30 cm (mean size, 3.1 cm; median size, 3.0 cm). Most ECTs <2.0 cm in diameter are asymptomatic, except for 3 cases that demonstrated cervical masses. As the ECT in case 2 was single, had a diameter of 1.2 cm, and the infant had died in the supine position, the presence of ECT was considered to have been incidental to his death. In a review of 34 autopsy cases associated with ECTs [1], the authors also considered the ECTs to be incidental findings, including in 3 SIDS cases. Thus, most ECTs found in autopsy cases have not been the cause of death; ECTs contributing to death, as in case 1, are very rare.

Despite limited data, approximately 50% of patients with solid ECTs lack mediastinal thymuses (Table 2). Presurgical confirmation of the existence of a normal mediastinal thymus may be essential to avoid subsequent immunodeficiency, considering the role that the ECT may play in the development of cell-mediated immunity, in place of the normal mediastinal thymus [10,14,17]. Thus, accurate diagnosis of ECTs and detection of the mediastinal thymus are important for the determination of a therapeutic strategy [28]. As recent studies have reported accurate diagnoses of ECTs by imaging and FNA [16,17,28,41], these detection techniques may lead to appropriate therapy.

4. Conclusion

Two autopsy cases of infants with ECTs were presented in conjunction with the clinicopathological features of solid ECTs. Solid ECTs may occasionally play a role in causing respiratory distress and mechanical asphyxia. This report emphasizes the importance of considering a diagnosis of ECT in infants with neck masses, with or without obstructive symptoms, to prevent possibly fatal outcomes.

Conflict of interest

None.

Funding

None.

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Figure Legends

Fig. 1

Postmortem computed tomography image of the neck.

A horizontal image shows bilateral, solid nodules (surrounded by white arrowheads) anterolateral to the cervical trachea and immediately inferior to the thyroid gland.

Fig. 2

Gross appearance of the resected specimens showing 2 solid nodules beneath the thyroid gland (A). Histological examination (hematoxylin and eosin stain) of the nodules revealing normal architecture (B) and microscopic components of the thymus tissue (C and D). c, cortex; e, ECT; h, Hassall's corpuscles; m, medulla; t, thyroid gland

Fig. 3

Gross appearance of the resected neck organs showing a whitish nodule (white arrow) located anterior to the cervical trachea and immediately inferior to the thyroid gland. t, thyroid gland; ll, left lung; rl, right lung

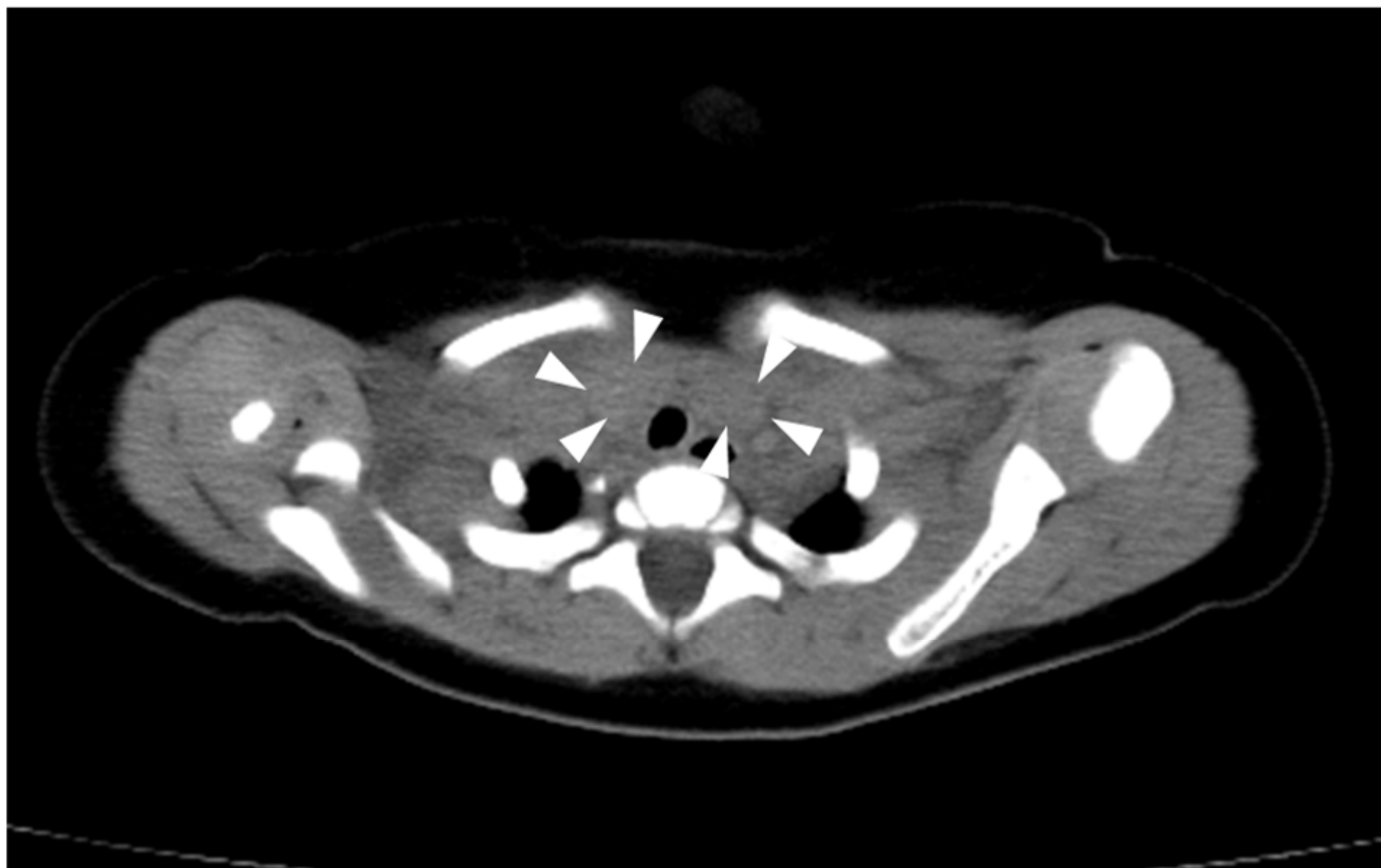


Fig. 1

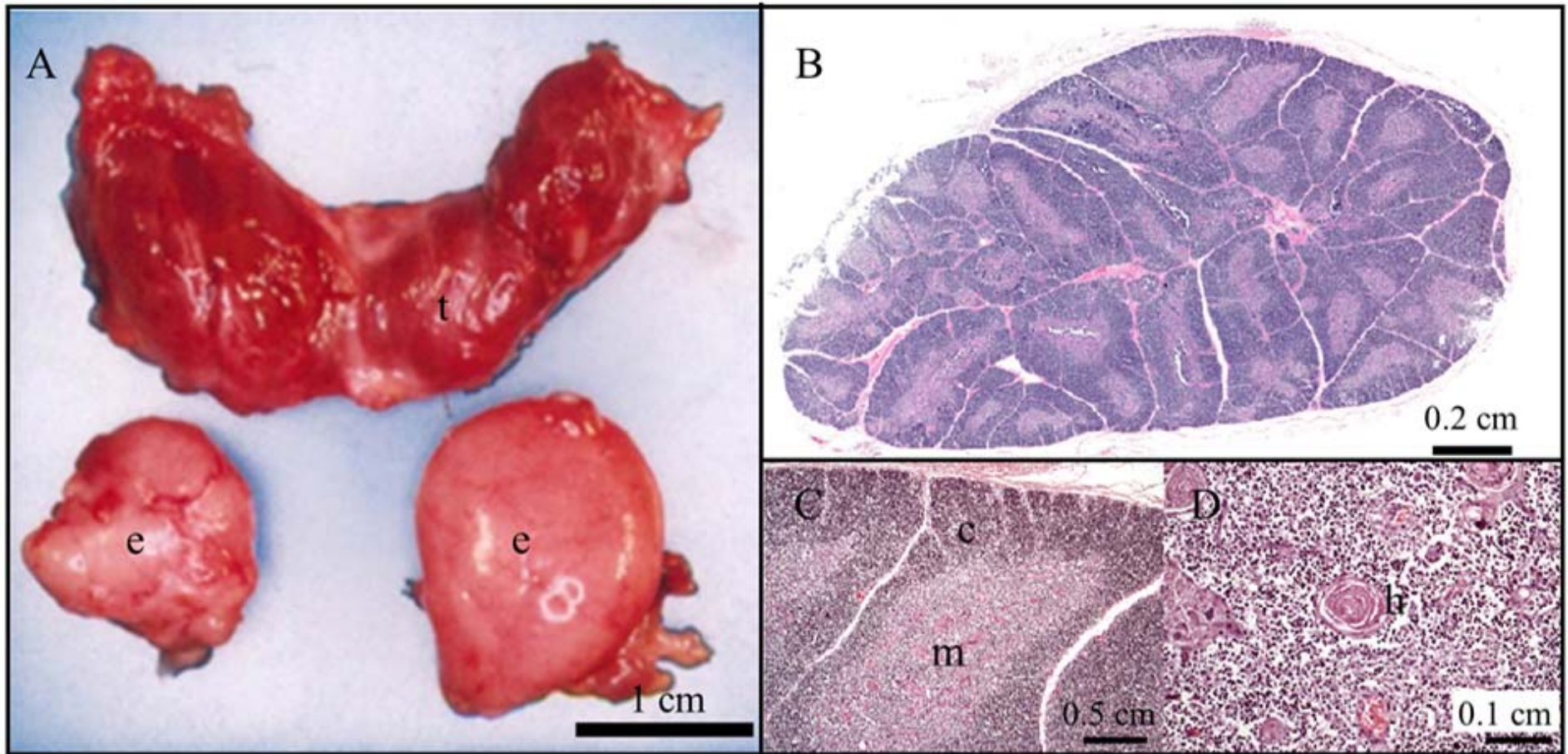


Fig. 2

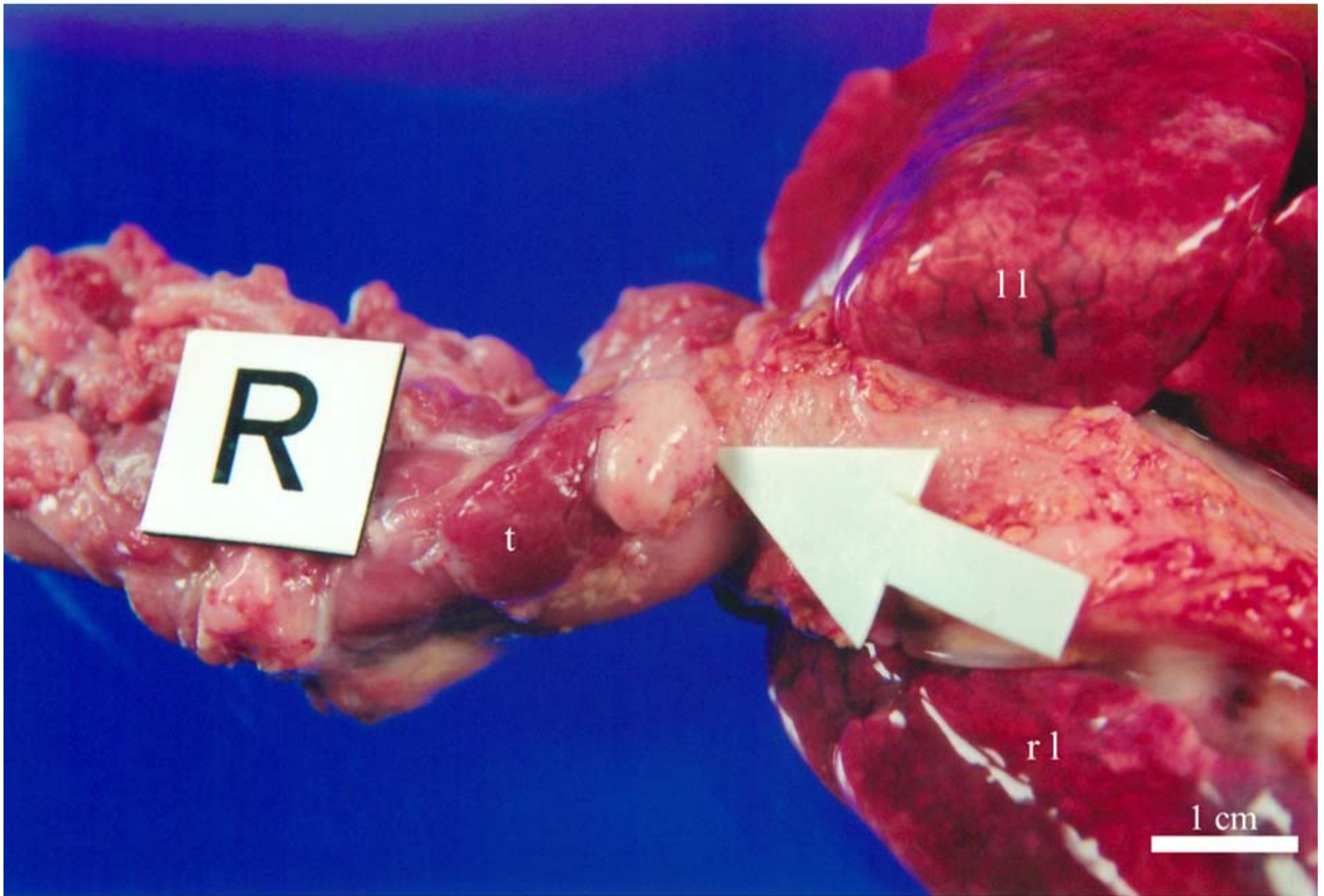


Fig. 3

Table 1. Clinical characteristics of solid ectopic cervical thymus cases

Total cases	95
Gender	
Male	63
Female	29
Not described	3
Age	
<1 month	24
1–5 months	42
6–11 months	12
1–4 years	10
5–9 years	1
≥10 years	6
Concomitant congenital disorders	
Cardiovascular ^a	24
Head and neck ^b	10
Others ^c	12
None	61
Diagnostic process	
Fine needle aspiration	1
Surgery	58
Autopsy	36
Symptoms	
Mass	45
Respiratory symptoms ^d	10
Dysphagia	3
Others ^e	3
Asymptomatic ^f	4
Not described	37

^aanomalous atrium septal defect, interrupted arch, subclavian artery, truncus arteriosus communis, and ventricular septal defect,

^babsent corpus callosum, absent pituitary, branchial remnants, cebocephaly, cleft lip, and palate, cleft soft palate, cyclopia, Goldenhar syndrome, iniencephaly, and microphthalmos

^canorectal agenesis, bicornuate uterus, duodenal atresia, hyaline membrane disease, oligohydramnios sequence, osteogenesis imperfecta, pancreatic acinar atrophy, polysplenia, renal dysplasia, syndactyly, talipes, torticollis, tracheomalacia, ureteral atresia, and VATER anomalad

^dcough dyspnea, and, snoring

^eskin defect and ulceration

^ffound at operation or autopsy

Table 2. Anatomical characteristics of solid ectopic cervical thymuses

Number	
Single	78
Multiple	5
Not described	12
Location of lesion(s) (n = 113)	
Base of skull to mandible	6
Submandibular	11
Superior region of the thyroid	16
Level of the thyroid	28
Inferior region of the thyroid	10
Thoracic inlet	4
Not described	38
Size ^a of all lesions (n = 113)	
0–2 cm	34
2–4 cm	23
4–6 cm	24
≥6 cm	5
Not described	27
Thymus in the mediastinum	
Present	28
Absent	28
Not described	39

^aEach range includes the lower bounds, and the upper bounds are not included.