Eur Arch Otorhinolaryngol
DOI 10.1007/s00405-007-0271-7

HEAD AND NECK

A combined third and fourth branchial arch anomaly: clinical and embryological implications

H. Mehrzad · C. Georgalas · C. Huins · N. S. Tolley

Received: 13 August 2006 / Accepted: 11 January 2007

Abstract Embryological abnormalities of the branchial apparatus present an interesting diagnostic and surgical challenge. Thymic cysts are a rare form of branchial apparatus anomaly, resulting from abnormal development of the third pharyngeal pouch. We present two cases of a thymic cyst coexisting with a non recurrent inferior laryngeal nerve (NRILN), two anomalies that to our knowledge have not been associated previously. A possible embryological explication for this double abnormality is discussed, while the clinical implications of this association are presented.

Keywords Thymic cyst · Third pharyngeal pouch cyst · Non recurrent inferior laryngeal nerve

Case report

A 38-year-old lady presented to our clinic with a 2-year history of a fluctuating midline neck swelling. She had recently become symptomatic with shortness of breath on exertion and a moderate degree of intermittent dysphagia affecting solids. There was no history of any hoarseness. Physical examination revealed a well-defined 5 cm × 7 cm midline swelling just above the sternal notch. A CT with IV contrast of her neck and chest showed a large non-enhancing cystic lesion displacing the thyroid and extending from the level of the thyroid cartilage to the brachiocephalic vein (see Fig. 1). After discussion with the patient a decision was made to remove the mass surgically. A horizontal skin crease incision was made halfway between the thyroid cartilage and sternal notch. The cyst was identified and dissected carefully from the carotid sheath and thyroid. It was found to be mainly midline in position. A fibrous cord was identified arising from the cyst extending behind the clavicle towards the superior mediastinum. The cyst was excised with part of the fibrous cord while the remaining part was transfixed. At the same time it was noted that the patient had a high-variant (type 2) non recurrent inferior laryngeal nerve (NRILN) on the right side. Its function was tested and confirmed with a nerve stimulator and monitor (Figs. 2, 3, 4).

The pathology report showed that the specimen macroscopically consisted of fatty tissue with a fibrotic cyst wall measuring 5 cm × 2.5 cm × 0.8 cm. Microscopically it showed a fibrous cyst wall containing remnants of parathyroid tissue and benign thymic remnants (see Fig. 5) with a single reactive lymph node. No features of malignancy were seen. The findings were consistent with a third pharyngeal pouch (thymic) cyst. More recently a second patient was found to have exactly the same double anomaly, confirming the previous findings.

H. Mehrzad · C. Georgalas · C. Huins · N. S. Tolley
Department of Otolaryngology,
St. Mary's Hospital, Paddington, London, UK

H. Mehrzad (✉)
28 Fernwood Court, 5 Pickard Close,
Southgate, London N14 6JF, UK
e-mail: h_mehrzad@hotmail.com

Discussion

Thymic cysts

Thymic cysts were first described by Lieutaud in 1832 and Dubois in 1850, who found cystic changes of the

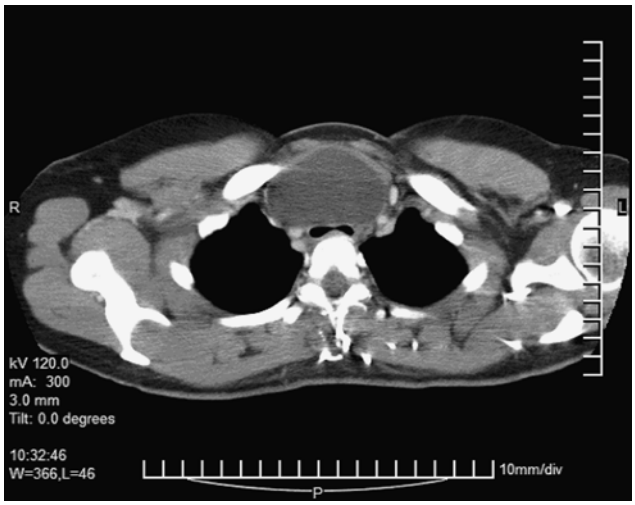

Fig. 1 Contrast CT scan of cystic lesion compressing the trachea in the chest

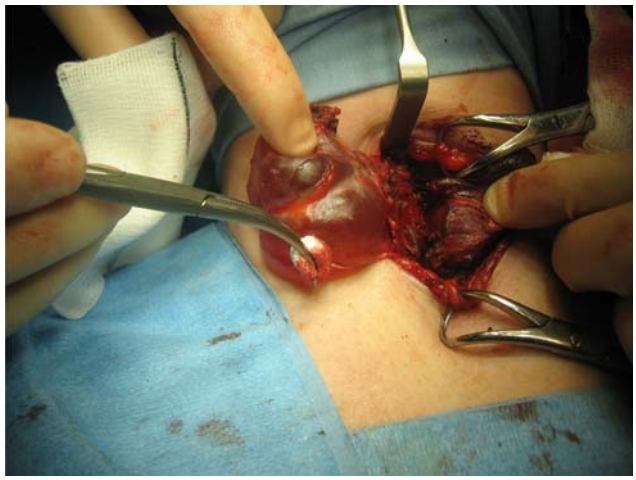

Fig. 3 Showing thymic cyst carefully dissected and retracted from wound

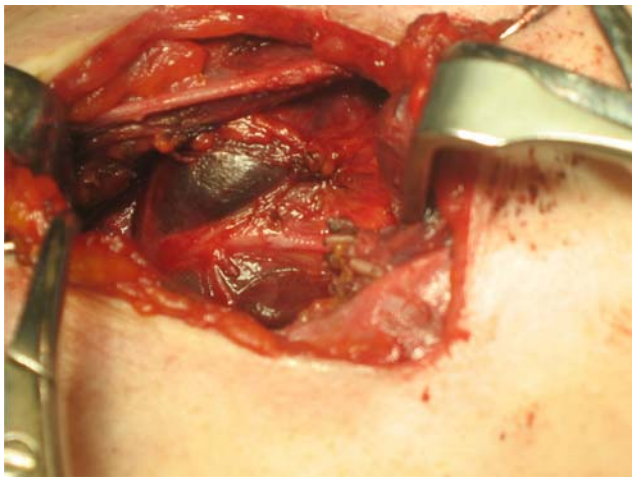

Fig. 2 Thymic cyst close to thyroid gland

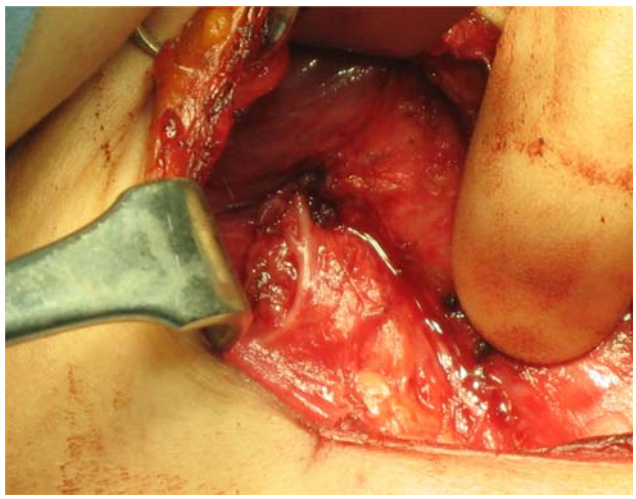

Fig. 4 Type 2 NRILN identified in the wound

thymus in patients suffering with syphilis, which lead them to link the two conditions. In 1912 however, Ribbert raised doubts concerning this theory as he described the presence of Hassall's corpuscles, filled with keratin and necrotic debris within this cysts [2].

The thymus is derived from the ventral part of the third pair of pharyngeal pouches, whereas the parathyroid gland is derived from the dorsal part. During embryonic development the thymus descends from the lateral neck to the anterior-superior mediastinum along paired thymopharyngeal tracts. During this descent remnants of the pharyngeal system may persist and lead to the formation of a third pharyngeal pouch anomaly—a congenital (true) thymic cyst. The mechanisms that could account for this anomaly could include arrest in migration, failure of involution, or sequestration of thymic tissue during descent, which will generally be asymptomatic [1, 3, 7]. This theory is further supported by the relatively frequent observation of parathyroid gland inclusions within the cyst [2]. The subsequent transition from solid to cystic thymic tissue is thought to occur as a result of cystic degeneration of Hassall corpuscles or cystic change in persistent remnants of the thymopharyngeal duct.

Thymic cysts are divided into true and false thymic cysts, on the basis of their structure of origin: True cysts originate, as discussed, from maldevelopment of the thymopharyngeal duct. False cysts are heterogenous histologically, containing elements of second branchial cleft, with incidental thymic tissue present. Another classification by Zarbo et al. [8] divided thymic lesions into seven groups, according to their location and their consistency.

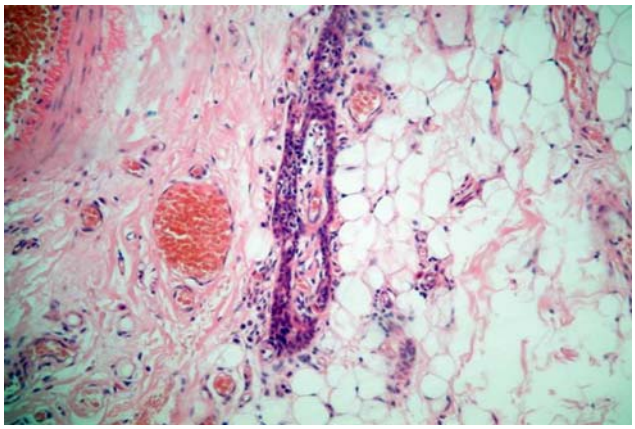

Fig. 5 Microscopic image showing a fibrous cyst containing remnants of parathyroid tissue and benign thymic remnants

Cervical thymic cysts are rare in comparison to other congenital neck masses: Nicollas et al. in their retrospective review of 191 congenital neck masses found that only 2% were thymic cyst malformations, while only around 100 cases of thymic cyst cases have been reported in the literature.

Thymic cysts may be located either in the midline or in the lateral side of the neck. When these masses span the entire length of the neck from mandibular angle to clavicle, along one of the paired tracts of descent they are termed thymopharyngeal duct cysts. It may be difficult to palpate the inferior aspect of these masses because in 50% of cases they maintain a connection with the mediastinal thymus via an atrophic fibrous cord attachment [3].

The majority of patients with thymic cysts present in the first decade of life. The reported sex distribution has been conflicting with Kaufman et al. [3] stating that males are more commonly affected and Rieker et al. [2] reporting an equal sex distribution. There is further conflict between which side these lesions presented, with some reporting a higher incidence of left sided lesions whereas others report a right sided preponderance. The most common clinical presentation is an asymptomatic painless swelling, although hoarseness, dysphagia, and stridor especially in neonates, have been reported.

Non recurrent laryngeal nerve and fourth aortic arch anomalies

A right NRILN is defined as an inferior laryngeal nerve that does not loop around the subclavian artery. Presence of this variant of the inferior laryngeal nerve is constantly associated with an aberrant right subclavian artery—an "arteria lusoria." The embryological explanation is as follows: The recurrent laryngeal nerve is the nerve of the sixth branchial arch. It arises from the vagus and follows a recurrent course under the distal part of the sixth aortic arch [5]. However, as the fifth and the distal part of the sixth aortic arch regress on the right, the inferior laryngeal nerve ends up looping under the fourth arch, which on the right becomes the subclavian artery. On the left however it loops around the sixth arch remnant the ductus arteriosus. In abnormal development a regression of the fourth right aortic arch prevents this from happening, resulting on the right inferior laryngeal nerve arising directly from the cervical part of the vagus nerve. There is an associated absence of the branchiocephalic artery, resulting in the right subclavian artery being formed from the distal part of the dorsal aorta and from the seventh segmental artery [5]. Thus, arising from the left part of the distal aortic arch, it usually reaches the right upper limb by a retroesophageal and rarely intertracheo-oesophageal or pretracheal course. Similarly, the common carotid arises directly from the aortic arch, and may follow an aberrant route anterior to the trachea.

Non recurrent inferior laryngeal nerve is a rare disorder as its incidence varies from 0.3 to 2% of right neck dissections [4–6]. This compares with 0.04% for NRILN among left dissections [4, 6]. To date more than 250 cases of right NRILN have been reported and only a handful of cases of left NRILN, found in patients with dextrocardia and situs viscerum inversus with a left retroesophageal artery. Its origin may be at various levels: the first tracheal ring, the inferior thyroid artery, and the superior pole of the thyroid lobe. Two variants of this anomaly have been described [4, 6]. In high-variant (type 1) NRILN, the nerve originates from the trunk of the vagus near the superior pole of the thyroid lobe and turns transversely to reach the larynx. This variety can be injured at the ligation of the superior thyroid vascular pedicle. In low-variant (type 2) NRILN, the nerve originates in the lower cervical region, following an upward course giving the illusion of a recurrent path, although it is in fact parallel to the inferior thyroid artery. The surgeon may damage this variant nerve during lateral dissection of the thyroid lobe.

A diagnosis of a NRILN and/or arteria lusoria differ according to whether the patient is a child or an adult. The neural anomaly is always asymptomatic while the vascular anomaly may have variable symptoms [4]. In the child arteria lusoria is usually picked up within the first 6 months when it presents with tracheoesophageal compressive symptoms. The diagnosis is usually made from the images on the barium swallow test which shows a suggestive posterior notch at the level of the second or third vertebra. Only the most severe forms

require surgical treatment. In adults the vascular anomaly is usually clinically silent and hence preoperative diagnosis is very difficult. It is most frequently encountered during thyroid or parathyroid surgery.

When the surgeon is considering surgery for a suspected thymic cyst in an adult the appropriate preoperative investigations include a contrast enhanced CT of the neck. MRI imaging has also been used to confirm an association between the cervical neck mass and the mediastinal thymus because of its ability for greater soft tissue delineation. An FNA can confirm the presence of thymic tissue and thus promote further investigation as to the presence of a mediastinal thymus prior to surgery. In most cases complete surgical excision is recommended, prognosis is excellent with minimal morbidity. There have been no reports in the literature of recurrence particularly in children [3].

The presentation of this patient was with a fluctuating swelling and the associated intermittent dysphagia. The investigations included a contrast CT scan of the neck and chest, which lead to the finding of the thymic cyst. The neural anatomy was as expected clinically silent as the aberrant subclavian did not compress the oesophagus or the trachea.

This is the first reported cases of a combined third pouch and fourth pharyngeal arch anomaly. We hypothesise that a single abnormality during the fourth to sixth weeks of embryological development has lead to these coexistent anomalies. The close proximity of the third pharyngeal pouch and fourth aortic arch make it possible that the same external or internal factor that lead to the programming of an excessively large area of cell death during the formation of the third pouch resulted also in loss of part of the fourth arch area including the arch artery. This has resulted in an aberrant subclavian artery. This embryological explanation for their co-existence makes us hypothesize that this constellation of findings may not be as rare as previously thought, although it has not been reported.

This is an important clinical association as it has significant surgical implications. The NRLN is at risk during the excision of a thymic cyst. The fact that these cysts could be associated with a NRILN could further complicate surgery and place the ILN at a higher risk. To prevent damage to the inferior laryngeal nerve, it is important for the surgeon to be aware of this double anomaly. Early identification and preservation of the inferior laryngeal nerve along its course and the use of a nerve stimulator and monitor would be very useful in this context.

Conclusion

We report two cases of patients with a double embryological anomaly, which has not been previously reported in the literature, a third pharyngeal pouch cyst and a NRILN due to a fourth aortic arch developmental abnormality. We hypothesize that due to the close proximity of these two branchial appendices during embryological development a single external or internal factor has lead to this associated anomaly. The head and neck surgeon should be alert to the possibility of this double anomaly during surgery for a suspected third pouch cyst, as a NRILN may be encountered and therefore be at increased risk of injury. It may be that this anomaly has been previously present in other patients with a third pouch cyst. However because it has not been common practise until more recently to actively identify the inferior/recurrent laryngeal nerve, a NRILN may not have been reported previously.

Acknowledgement Our thanks to Professor Firth (anatomy department, Charing Cross Hospital, London) for his kind contribution.

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