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REVIEW

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Current approach to branchial remnants in the neck

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Abstract

Congenital branchial fistulas and cysts are an interesting subject in cervical pathology. There are congenital malformations with late expression in young adults that require correct diagnosis and appropriate treatment. We review essential notions of cervical embryology to understand the mechanism of occurrence of these malformations and their clinical expression. The most common cases present vestiges from the second branchial arch, with the appearance of a cystic tumor or a fistulous orifice on the anterior edge of the sternocleidomastoid muscle, at the level of the hyoid bone. Performant imagery is mandatory for appropriate diagnosis, so we recommend a cervical computed tomography (CT) scan or cervical magnetic resonance imaging (MRI) to evaluate the relations with great vessels of the neck or other lesions. The treatment implies complete surgical excision because otherwise there is a high risk of recurrence of the lesion. The differential diagnosis includes cystic lymphangioma, dermoid cyst, tuberculous adenopathy, cystic hygroma, lateral cervical cystic metastases. Histological examination is mandatory for a definite diagnosis. Also, there is a small percentage of malignancy of these malformations, but it is very important to check that all the histological diagnostic criteria for a primary branchiogenic carcinoma are accomplished. Therefore, although it is a benign cystic cervical pathology, the diagnosis and treatment must be made very accurately for a complete cure, and this review aims to summarize the current approach to branchial remnants of the neck.

Keywords: branchial, remnants, neck, diagnosis, surgery.

Introduction

During weeks 3 and 4 of embryo development, on the lateral aspects of the primary pharyngeal tube appear five endodermal pharyngeal pouches, with four corresponding ectodermal ridges on the external aspect of the embryo. Between these ectodermic and endodermic grooves develop five branchial arches of the mesoderm layer, each presenting one artery, nerve, and a corresponding muscle group [1].

During the 6th week of embryo development, the 2nd arch envelopes the 3rd and 4th and unites with the inferior precardiac mass leading to the appearance of the cervical sinus instead of the 2nd to 4th grooves. At the same time, from the 3rd to 5th pouches derive the parathyroid glands and thymus. Normally, the cervical sinus is completely resorbed at birth. The branchial fistula is in fact persistence of the exterior opening of the cervical sinus. Branchial cysts appear from the persistence of the cervical sinus, but with the closure of the external opening [2].

The histology of each congenital cervical mass differs due to the embryo origin. Dermoid cysts are derived from the ectoderm and present simple stratified epithelium with hair follicles and sebaceous glands, sweat glands, and yellowish granular content. Amygdaloid cysts are derived from the endodermis and their wall structure is like the pharyngeal mucosa and present lymphoid tissue. Branchial cysts have squamous stratified epithelium and germinal centers inside the lymphoid content of the wall. Mucoid cysts present a respiratory type of epithelium. Cysts derived from the thyroglossal duct present also thyroid tissue. Cystic lymphangiomas are derived from dilated lymphatic vessels invading surrounding tissue [3].

Aim

This review aims to summarize the current approach in branchial remnants of the neck. For this purpose, we considered useful a brief reminder of the notions of embryology on branchial vestiges.

Classification of the branchial cysts and fistula

These are congenital lateral cervical cysts and fistulas classified according to the originating branchial arch and location. These details are important for the clinical and imaging characterization of branchial cysts.

Work Classification (1972) taking into consideration the arch of origin [4]:

- 1st branchial arch cyst – type 1 positioned in pretragian area (*coloboma auris*) and type 2 posterior and inferior to angle of the mandible;
- 2nd branchial arch cyst – frequently on the anterior margin of the sternocleidomastoid (SCM) muscle, at the level of the hyoid bone (Figure 1);

▪ 3rd and 4th branchial arch cyst – very rare, deep to the SCM muscle, with mass effect on the great vessels in the neck below the level of the hyoid bone;

▪ 5th branchial arch cyst – extremely rare at a pleural or mediastinal level.

Classification of branchial cysts according to topography (Bailey, 1929) [5]:

▪ Type I – situated in the superficial neck fascia on the anterior margin of SCM;

▪ Type II – in the deep neck fascia on the anterior margin of SCM;

▪ Type III – developed around the great vessels of the neck;

▪ Type IV – smaller in dimensions and in contact with the pharynx and sometimes towards the skull base.

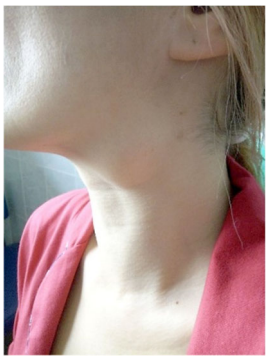

Figure 1 – ***Clinical aspect of a branchial cyst derived from the 2nd arch.***

Diagnostic and therapeutic approach to branchial fistulas

They have a genetic origin augmented during the pregnancy by various factors: hypoxemia, smoking, alcohol, Aspirin, Thalidomide, lead, mercury, metabolic dysfunction, ionizing radiations, which inhibit closure of the branchial grooves leading to persistence of the exterior opening of the cervical sinus [6].

Clinical exam reveals an external skin opening of the fistula possibly inflamed situated either on the anterior edge of the SCM muscle, in the carotid triangle for pathology derived from the 2nd arch, or at the level of the cricoid cartilage for fistulas from 3rd arch and neighboring the suprasternal notch for 4th arch fistula, with the outflow of a whitish secretion. In 5% of the cases, the fistula is on both sides of the neck [7]. The trajectory of the fistulas derived from the 2nd arch passes through the carotid bifurcation. Also, it may be encountered an opening in the palatine tonsil. The inferior brachial fistula passes behind the common carotid artery, with an internal opening in the piriform sinus [8]. Palpation of the neck presents a subcutaneous duct with a vertical trajectory, and under pressure, the conduit will express more fluid content at the opening (Figure 2). Insertion of contrast media, such as Methylene Blue, through the orifice permits visualizing the fistula trajectory and in the case of communication with the pharynx, the patient can feel the taste of the substance. We do not use this method of contrast injection, considering that it can modify the subsequent imaging, and at a high injection pressure it can break the fistulous path with the impregnation of the surrounding tissues, thus making surgery difficult. We consider much more useful the intraoperative instrumental catheterization of the fistulous trajectory [9]. This pathology can be associated with a series of syndromes, such as Franceschetti–Treacher–Collins [10].

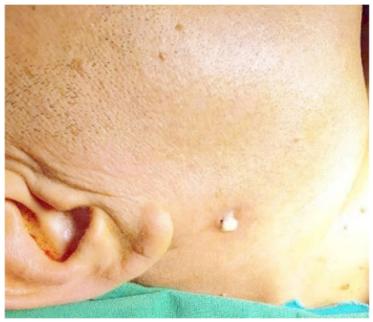

Figure 2 – ***Clinical aspect clinic of a branchial fistula derived from the 2nd arch.***

High-definition imaging computed tomography (CT) and magnetic resonance imaging (MRI) with contrast media bring further details about the trajectory of the fistula or internal orifice patency (Figure 3).

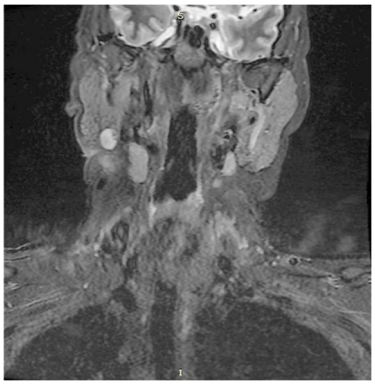

Figure 3 – ***MRI imaging of branchial fistula presenting a reservoir under the tail of the right parotid gland. MRI: Magnetic resonance imaging.***

Treatment comprises complete removal of the fistula as the only method to prevent recurrence from epithelial relics. The dissection process is laborious due to the long-term presence of chronic inflammation. Injection of contrast media should use a higher dilution to prevent tissue vital coloring [11]. During surgery try to insert a guide in the fistula for better guidance of the ablation (Figure 4, A–C).

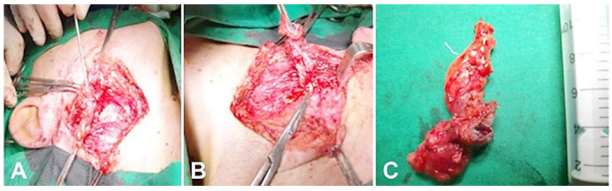

Figure 4 – ***(A–C) Radical ablation of the right branchial fistula, using instrumental catheterization of the fistulous trajectory.***

Diagnostic and therapeutic approach to branchial cysts

They have similar etiology with fistulas as an embryological remnant. Although congenital, the clinical signs appear usually in young adults during the 2nd and 3rd

decades correlated with acute inflammation of the upper airways [12].

Clinical exam presents a mass on the anterior edge of the SCM muscle, frequently on the left side or in the carotid triangle for cysts originating in the 2nd arch (Figure 5, A and B). The cyst presents a fluid content with a progressive increase in volume if neglected (Figure 6). Also, there can be associated infection of the content leads to pain and modified adjacent skin [13]. Rarely do the cysts derived from the 5th arch develop into the mediastinum [14]. Extremely rare this condition can occur bilaterally [15].

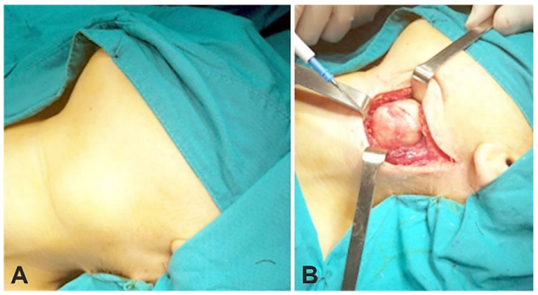

Figure 5 – ***Clinical and surgical aspect of a left branchial cyst in a patient aged 31.***

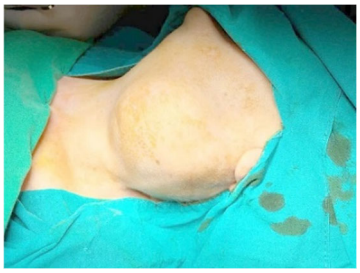

Figure 6 – ***Huge left branchial cyst in a female patient aged 55.***

Imaging studies describe the dimensions and bordering structures. Also, helps to differential diagnosis of the pathology and presurgical planning [16].

Sonography describes a well-defined mass, with posterior acoustic enhancement in 70% of the cases with a very thin wall in 82% of the cases. The content is transonic or presents cellular floating isles in a quarter of the cases or even pseudo-polyps in almost one in 10 cases [17, 18].

CT scan presents a round mass with fluid content and a thin wall, passing between the carotid arteries in a highly suggestive manner (Figure 7, A and B).

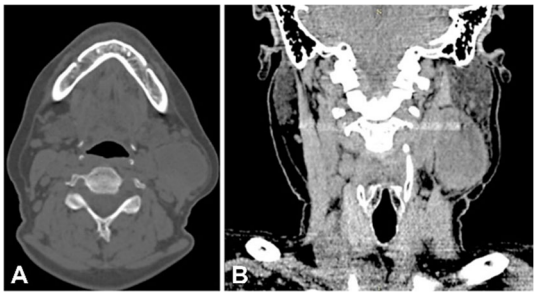

Figure 7 – ***CT scan showing a giant branchial cyst in contact with internal jugular vein and carotid bifurcation. CT: Computed tomography.***

MRI records hypersignal in T1 given the protein content of the fluid cyst, hypersignal in T2 sequences, and no contrast uptake in lesions without inflammation (Figure 8) [19].

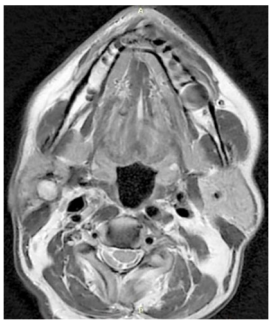

Figure 8 – ***Cervical MRI showing the reservoir of the branchial remnants inside the tail of the right parotid gland with hypersignal in T1 and T2 sequences because of high content in proteins. MRI: Magnetic resonance imaging.***

A clear diagnosis is based on the history, clinical exam, and location of the cyst confirmed on a CT scan with contrast. The imagery is essential for highlighting the cystic nature of a cervical mass, but especially for specifying the relationships with the large vessels of the neck or with the parotid gland for surgery [20].

In unclear cases, fine-needle aspiration biopsy (FNAB) will remove a yellow content of the cyst [21].

Surgical treatment is based on radical ablation of the cyst with all its fibrous adjacent tracts for prevention of recurrence. Sometimes, when the evolution of the cyst is long, stretched over many decades, surgery can be extended into the parotid gland, with the need to dissect the marginal branch of the mandible from the facial nerve, and the mass can take strange shapes (Figure 9, A–C).

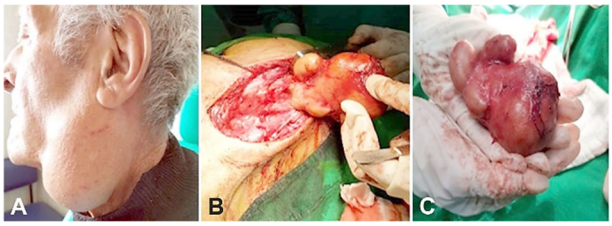

Figure 9 – ***(A–C) Huge left branchial cyst with six decades of evolution in an 84-year-old patient with a curious shape of the resection piece.***

A pathology exam is compulsory given the differential diagnosis and the reported cases of malignancy inside such cysts with long evolution, especially after 40 years. Histology describes squamous multilayered epithelium, with a wall rich in lymphoid tissue with germinal centers or respiratory epithelium with columnar cells and fibrous wall, and the inside content may present keratosis (Figures 10–12).

Differential diagnosis

The differential diagnosis will exclude cystic lymph-angiomas, dermoid cysts, thyroid cysts, aneurysms, lipomas, tuberculous lymph nodes, or cervical lymph nodes metastasis [22].

Lymphangiomas are congenital malformations of lymphatic vessels present at birth. Three-quarters of cases occur in the skin and subcutaneous tissues of the head and neck region. The submandibular region and parotid region are the most common sites. Most lymphangiomas are benign, soft, slow-growing masses, with mass effects rarely on vital structures. The adult presentation may occur because of

trauma, infection, neoplasms, or iatrogenic injuries. Their slow evolution sometimes may involve the mediastinum [23].

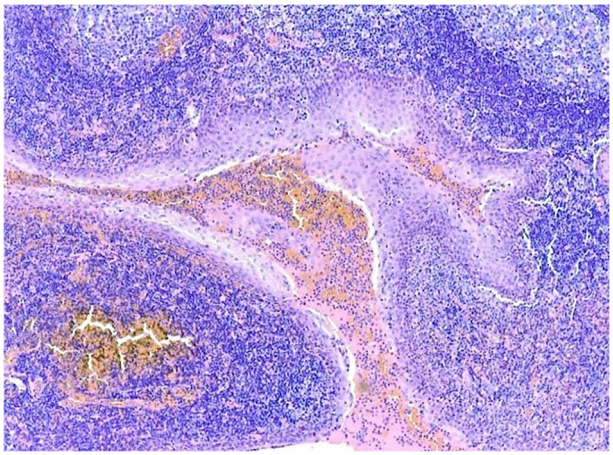

Figure 10 – ***Wall of the branchial cyst with multilayered squamous epithelium and hemorrhage, rich in lymphoid tissue with germinal centers (HE staining, ×100).***

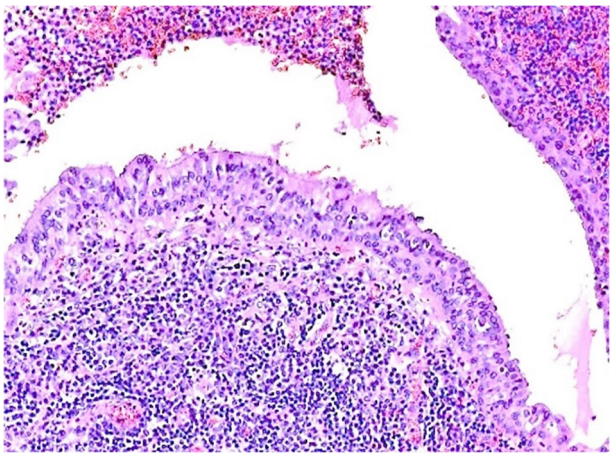

Figure 11 – ***Cystic wall with respiratory epithelium with columnar cells, at the level of the stroma lymphoid tissue, is identified (HE staining, ×200).***

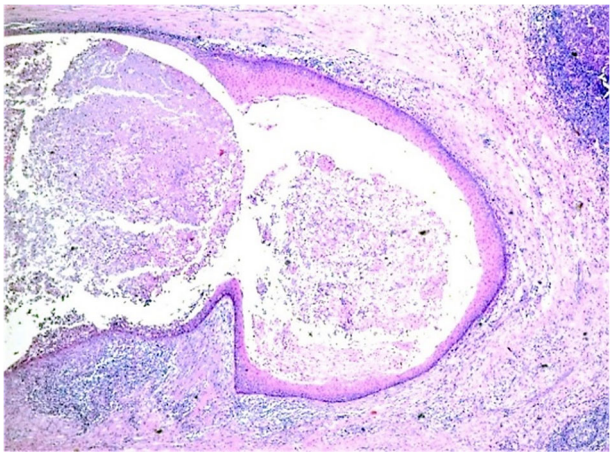

Figure 12 – ***Fibrous wall with inflammatory infiltrate, with stratified epithelium and keratosis, and necrosis content (HE staining, ×40).***

Theories for lymphangioma development [24] include blockage of normal growth of lymph channels during embryogenesis, an inappropriate connection of primitive lymphatic ducts to the venous drainage system, and induction of dormant rests of embryonic lymphatic tissue.

Another important aspect is regarding the existence of true branchiogenic carcinoma, which is still controversial and remains a diagnosis of exclusions unless detecting the primary site [25].

Moreover, the differential diagnosis should include extremely rare circumstances, such as associating xantho-granulomatous inflammation [26].

Vazquez Salas *et al*. recently published one of the most comprehensive reviews of FNAB cytology diagnosis of uncommon cystic lesions in the head and neck region [27].

Nonetheless, there should also be a certain focus on genetic conditions, such as branchio-oto syndrome (BOS)/ branchio-oto-renal syndrome (BORS), which is an autosomal dominant heterogeneous disorder uniting hearing impairment and abnormal phenotype of ears, accompanied by renal malformation and branchial cleft anomalies including cyst or fistula [28].

Sometimes, the coexistence of different pathology makes the diagnosis challenging, such being the recent case of a thymic lesion containing also parathyroid tissue [29].

Treatment options

Clinical exam is performed frequently on young patients, with late hospital admission only when the mass produces esthetic complaints. There are also multilobed masses situated superior at the angle of the mandible or inferior behind SCM muscle in the supraclavicular fossa. CT scan shows cystic tumor with septate aspect, the extension, and the mass effect on cervical structures (Figure 13).

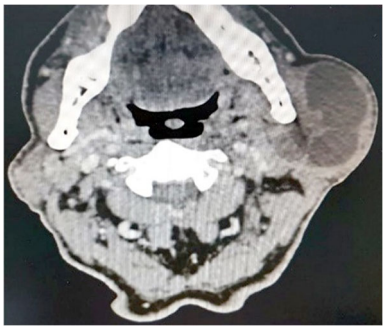

Figure 13 – ***CT scan presenting a cystic lymphangioma in the left parotid region. CT: Computed tomography.***

Surgical treatment should be applied to patients older than one year unless the mass threatens the life of the child. The dissection should be extremely cautious due to the very thin wall of the mass. Rupture of the mass during surgery is associated with almost certainty of recurrence and a second surgery is hindered by the development of conjunctive adhesions [30].

Dermoid cysts are also found in cervical embryos, which reveal a yellowish content during surgery (Figure 14). Sometimes preoperatively it is difficult to differentiate them from a gill cyst. Tuberculous lymphadenopathy is characterized by a tendency to fistulize and the purple color of the overlying skin. Pulmonary determination of tuberculosis is also not required, so FNAB with culture or sometimes an excisional biopsy is required to make a definite diagnosis. Midline cysts, especially thyroglossal tract cysts can be considered for the differential diagnosis of gill cysts especially when they are paramedian and especially in the infrahyoid variant [31, 32].

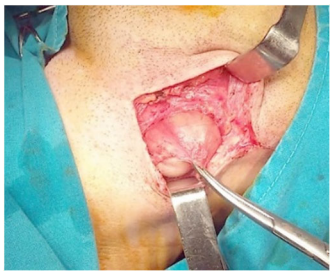

Figure 14 – ***Left cervical dermoid cyst with yellow sebaceous content.***

With a prolonged neglected evolution, the branchial cysts may develop a malignant transformation. The malignancy of branchial cysts is another controversial topic. Between 3–24% of cystic tumor masses are malignant, especially in adults over 40 years. In 1988, Khaffif reformulated the diagnostic criteria for primary branchiogenic carcinoma (PBC) and all criteria must be met to confirm the diagnosis: (*i*) the tumor is located in the anatomical region of the gill cysts; (*ii*) the histology of the tumor must be in concordance with the origin in the branchial vestiges, so it has to be squamous cell carcinoma; (*iii*) the presence of carcinoma at the level of the shell of an identifiable epithelial cyst; (*iv*) to be able to identify the transition from normal squamous epithelium to enveloped carcinoma; (*v*) comprehensive evaluation of the patient should not reveal another primary malignant tumor [33].

There were situations in which the diagnosis of malignant branchial cyst delayed the true diagnosis of a primary occult palatine tonsil carcinoma with associated cystic lymph node metastasis [34]. Therefore, in an occult cervical cystic metastasis, the palatine tonsil is the most likely site of origin. Given this possible scenario, recent guidelines recommend after surgical removal of the malignant cystic mass the use of radiation therapy extended to the ipsilateral palatine tonsil. This could help in preventing the evolution of the primary tumor with increased overall survival [35].

Conclusions

Branchial cysts and fistulas are remnants of embryo structures of the neck with later onset in adulthood. Clinical exam is straightforward but needs additional information through imaging studies. Cervical ultrasonography, CT, and MRI enable visualizing structure details, local extension, and neighboring vascular axes. A pathology exam needs to confirm the lack of malignancy. This scenario is extremely rare and should pay attention to the possibility of a cystic primitive metastatic lymph node from an occult tonsillar primary carcinoma. Current management focuses on complete surgical removal to prevent a recurrence.

Conflict of interests

The authors declare that they have no conflict of interests.

Availability of data and material

All information presented in this review is documented by relevant references.

Patient consent for publication

Patient informed consent for publication of the data/images associated with the review was obtained. The authors followed the international regulations in accordance with the Declaration of Helsinki and all identifying information was removed.

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