

Branchial cleft anomalies – a literature review followed by a case report

Anomalie szczeliny skrzelowej – przegląd literatury wraz z opisem przypadku

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SUMMARY

Branchial cleft anomalies are congenital masses of the head and neck that arise from the incomplete involution of the branchial apparatus during embryogenesis. Most commonly observed anomalies originate from the 2nd branchial cleft and usually manifest as sinuses, fistulas or cysts. They are said to be benign lesions and may be either asymptomatic or associated with recurring local infections. Typically, they are isolate lesions, but may be an element of a congenital genetic disorder. The diagnosis is based on clinical examination, supported by radiological imaging, sometimes also fiberoscopy/rigid laryngoscopy, final diagnosis is always proved by histopathological examination. According to the literature review, a surgical excision remains a ‘gold standard’ in the treatment of branchial cleft anomalies.

We would like to present a case of a 6-year-old male patient diagnosed with branchio-oto-renal syndrome (BOR syndrome), who was admitted to our university clinic for the removal of bilateral cervical fistulas. He also presented with bilateral preauricular fistulas, right-sided microtia, right-sided sensorineural hearing loss and slight renal insufficiency.

It is important to emphasize that patients with multiple branchial cleft anomalies require multidisciplinary assessment and supervision, to exclude, monitor and treat (if needed) any associated comorbidities, like hearing loss, renal dysfunction.

SŁOWA KLUCZOWE:

zmiany szyjne, guzy szyjne, anomalie rozszczepu skrzelowego, zespół BOR, przetoka szyjna, torbiel szyjna, zatoka szyjna, embriologia, rozszczepy skrzelowe, kieszonki skrzelowe, łuki skrzelowe

STRESZCZENIE

Anomalie szczeliny skrzelowej to wrodzone masy głowy i szyi, które powstają w wyniku niepełnej inwolucji aparatu skrzelowego podczas embriogenezy. Najczęściej obserwowane anomalie pochodzą z drugiej szczeliny skrzelowej i zazwyczaj manifestują się jako zatoki, przetoki lub torbiele. Są to zmiany łagodne i mogą być bezobjawowe lub związane z nawracającymi zakażeniami miejscowymi. Zazwyczaj są to zmiany izolowane, ale mogą być elementem wrodzonego zaburzenia genetycznego. Rozpoznanie ustala się na podstawie badania klinicznego, uzupełnionego badaniami radiologicznymi, czasami również fiberoskopia/sztywną laryngoskopia, a ostateczne rozpoznanie zawsze potwierdza badanie histopatologiczne. Zgodnie z przeglądem literatury wycięcie chirurgiczne pozostaje „złotym standardem” w leczeniu anomalii szczeliny skrzelowej.

Przedstawiamy przypadek 6-letniego pacjenta płci męskiej z rozpoznaniem zespołu skrzelowo-otrzewnowo-nerkowego (zespół BOR), który został przyjęty do naszej Kliniki Uniwersyteckiej w celu usunięcia obustronnych przetok szyjnych. U pacjenta stwierdzono również obustronne przetoki przeduszne, mikrocję prawostronną, prawostronny niedosłuch odbiorczy oraz niewielką niewydolność nerek.

Należy podkreślić, że pacjenci z wieloma anomaliami rozszczepu skrzelowego wymagają wielodyscyplinarnej oceny i nadzoru, aby wykluczyć, monitorować i leczyć (w razie potrzeby) wszelkie współistniejące schorzenia, takie jak niedosłuch czy dysfunkcja nerek.

INTRODUCTION

Branchial cleft anomalies are congenital lesions of the head and neck developing from the 1st through 4th pharyngeal clefts, however, almost 95% of cases derive from the 2nd cleft.

Physiologically, during embryological development around 4th week of gestation, when neural crest cells migrate into the future head and neck region, a branchial (or pharyngeal) apparatus is shaped. It is responsible for the development of head and neck structures. There are 6 pairs of branchial arches formed by mesoderm, with depressions separating arches, known as clefts on the external, ectodermal surface and corresponding pouches on the internal, endodermal side. As a result, although originally there are 5 pharyngeal clefts, in humans the 5th cleft is residual and disappears quickly, clinical significance is attributed to 4 clefts. Normally they should involute by the 7th week of gestation, but if it doesn't happen or happens incompletely branchial cleft anomalies are formed. Due to their embryological origin, these congenital anomalies are always present at birth, but unless in a form of an external sinus/fistula, they usually become more apparent later in life, in childhood, adolescence or young adults, manifested as a painless lump on the neck (1, 2). Those anomalies can occur in many localizations, laterally due to their origin from a specific type of the branchial cleft.

Normally, they are benign lesions and when treated properly, they do not pose a threat to the general development of a child, but sometimes they can be associated with multiple complications, usually infections or recurrences (if resected incompletely) (3). The development of branchial cleft anomalies is said to be the result of incomplete obliteration of branchial clefts and pouches during embryogenesis (4).

DISCUSSION

Epidemiology

Branchial cleft anomalies are among the most common congenital malformations of the head and neck in pediatric population, placing at 2nd place in terms of frequency, just after thyroglossal duct cysts (accounting for 20% of congenital neck lesions) (2). Exact prevalence in the population is not known, but no predisposition in sex or race was stated. Approximately 10% of branchial cleft anomalies are bilateral (1). Most cases are sporadic, but they can also be a part of genetic disorders/syndromes, like Branchio-oto-renal syndrome (BORS, BOR syndrome). It is a rare autosomal dominant genetic disorder consisting of ear malformations, kidney's defects, together with branchial cleft anomalies. The major and minor criteria were proposed for the diagnosis of this syndrome. The major criteria are preauricular pits, hearing loss, renal anomaly, and 2nd branchial cleft anomaly. The minor criteria include ear anomaly, preauricular tags, platelet abnormality, and facial asymmetry. Patients have to meet at least three major

criteria or two major and two minor criteria to be diagnosed with BORS. Hearing loss can be both conductive and/or sensorineural, and in some cases, it can be quite severe, what poses a need for an early hearing screening and support, if needed. It is also advised to avoid ototoxic drugs to preserve any remaining hearing function. This syndrome is highly heterogeneous, with significant familial prevalence. Many gene dysfunctions have been proposed as a potential cause of this anomaly. However, to date, there is no conclusive and evident data for those assumptions (5). Lesser prevalent syndrome is Branchio-oculo-facial syndrome (BOFS) that, apart from branchial cleft anomalies, manifests in vision impairment, lip or palate cleft, and abnormalities of the external or middle ear (1, 6).

Clinical manifestation

Branchial cleft anomalies may have the form of sinuses (internal or external), fistulas or cysts. Cysts are closed masses with epithelial lining and need to be differentiated from abscesses, enlarged lymph nodes, lymphomas and other neck anomalies. In contrast, sinuses have an opening (incomplete fistula) on the skin (external sinuses) or pharynx/larynx (internal sinuses), while fistulae represent a direct junction between skin and pharynx or larynx (1). Cysts usually become symptomatic in adolescence, while due to the obvious opening external sinuses/fistulas are mostly diagnosed in infancy (2). Branchial cleft anomalies become symptomatic typically as a result of an upper respiratory tract infection. Characteristic symptoms include painful swelling of the neck, redness, and fever, additionally, in case of sinuses/fistulas, there can be a purulent exudate. An unfavorable, hopefully rare, scenario is an enlarged mass of a branchial cleft anomaly, which causes compression-related symptoms, like dysphagia, dyspnea, and stridor. It can require immediate surgical and anesthesiological attention when life-threatening (1).

1st branchial cleft anomalies

This anomaly is rare, consisting of less than 1% of cases. Usually, it is located in the preauricular area, between the external auditory canal and the mandibular angle. The most common form is a smooth, soft, painless mass, sometimes with an external opening of the fistula on the skin surface, through which there may be oozing a fluid discharge (serous, mucous or purulent). In some cases, otorrhea can be presented as a result of a cyst draining into the external auditory canal (1), sometimes this anomaly is named as "duplication of the external auditory canal". It is also important to remember that there may be a connection between the anomaly and middle ear space, what affects the diagnostic and therapeutic approach.

First branchial cleft anomalies can result in facial nerve paresis, as they can often be located near the parotid gland – location in the postauricular region (a cyst in the postauricular region – 2nd type of the anomaly). Due to their location, they can be mistaken for a parotid gland tumor (7).

2nd branchial cleft anomalies

2nd branchial cleft anomalies are most common and account for almost 95% of cases. They are usually located along the lower part of the sternocleidomastoid muscle, close to the carotid arteries and nerves: glossopharyngeal and hypoglossal. The natural embryological course of this anomaly leads towards the palatine tonsil, usually finishing before it reaches its final destination, but in rare cases there may be a continuance and, in those cases, satisfactory treatment requires tonsillectomy (true fistula). The most common form of second branchial cleft anomalies is an external sinus or fistula, rarely a cyst. In this type of anomaly, unilateral presence on the right side is more prevalent. Potential association with BORS implies a need for auditory and renal screening (1, 8).

3rd and 4th branchial cleft anomalies

Anomalies of the 3rd and 4th branchial cleft comprise less than 5% of all cases. They are typically located on the left side, in the lower part of the neck, near the supraclavicular fossa or lateral part of the chest (8). Nowadays, they are usually described together due to their similar anatomical location, with slight differences in their course on the neck. Almost always they appear as sinuses with an internal opening into the piriform recess. Clinically, they appear as recurring abscesses of the deep spaces of the neck or abscesses in the thyroid region. Due to its atypical localization, it can often be misdiagnosed and treated by repetitive surgical drainage (1).

Diagnosis

The pre-operative diagnosis of branchial cleft anomalies is based on characteristic clinical symptoms, supported by radiological imaging. Obviously, final diagnosis is stated after surgical excision and pathomorphological examination.

During medical examination, there may be found an external opening of a fistula or a mass in the head and neck region, with localization dependent on the type of the branchial arch.

Imaging tests are useful in evaluating the type (sinus/fistula/cyst) and character (cystic, solid) of the lesion, its size, anatomical location (also the course of a fistula), and relation with surrounding structures, vascularization etc., as well as potentially ongoing inflammation. They also allow to differentiate those lesions from others typically encountered in the head and neck region. Usually, the first step, and in many cases sufficient, in the assessment of branchial cleft anomalies is ultrasound examination (USG) of the head and neck. If a fistula is present, it is advised to perform a fistulography by injecting contrast into its aperture, what helps in the visualizations of its course (9). In not obvious cases or deeply located masses a computed tomography (CT) or magnetic resonance imaging (MRI) should be performed. At CT, the cyst is typically well-circumscribed, homogeneously hypoattenuating mass surrounded by a uniformly thin

wall. The extension of the cyst wall between the internal and external carotid arteries just above the carotid bifurcation (features sometimes referred to as the notch sign, tail sign or beak sign), is highly suggestive of the diagnosis but not pathognomonic (8, 10). MRI reveals variable signal dependent on protein content in T1 sequence (high protein content is connected with high signal), usually high signal in T2 sequence and no enhancement in uncomplicated lesions in T1 C+ (Gd) sequence (10).

The assumption of the 3rd and 4th branchial cleft anomalies requires fiberoscopy or rigid laryngoscopy to assess piriform recesses, where their internal opening is located (11).

Histologically, lesions are typically characterized by an epithelial lining. Stratified squamous epithelium lining is identified in anomalies deriving from a pharyngeal groove (made up of ectoderm), while ciliated columnar epithelium lining is found in the pharyngeal pouch (made up of endoderm) anomalies (11). In some lesions the character of the epithelial lining is mixed. In the surrounding tissue lymphoid tissue, inflammatory signs or fibrosis may be found.

When multiple branchial cleft anomalies are found screening for BOR syndrome is advised (audiological tests, abdomen USG, renal function assessment) (1).

Treatment

Surgical methods

The 'gold standard' treatment in cases of branchial cleft anomalies is a complete surgical resection, which is crucial in recurrence prevention and leads to a satisfactory clinical outcome (12). It should be performed as a 'planned' procedure at the optimal time for anesthesia and definitely not at the peak point of an infection. Surgical treatment is advised upon identification (or in external sinuses identified at birth - when optimal criteria for anesthesia are fulfilled), even in asymptomatic patients, because there is always an elevated risk of infection and the lesser inflammatory processes one's experienced the completeness of the procedure is easier to achieved (1, 11). The risk of malignant transformation is minimal.

In case of an acute infection, a conservative approach is recommended with antibiotic therapy (oral or intravenous), and if needed, an aspiration. Incision and drainage should be avoided due to the risk of scarring, what may complicate the operation later (dissemination of the pathologic cells and destructed/changed anatomical borders leading to harder tissue differentiation).

The operation technique is dependent on the branchial cleft anomaly, its localization and character of the lesion (fistula, sinus, cyst). Generally, it is important to determine and excise the entire extent of the lesion. In some cases, methylene blue injection into the canal of the fistula or sinus may be helpful in the identification process. In simple cases instrumental cannulation is sufficient. When there is an assumption or confirmed 3rd/4th branchial cleft anomaly rigid laryngoscopy is required in order to identify and close

(chemically or with coagulation) its internal opening in the piriform recess. Otherwise, there is a high risk of recurrence due to the incomplete removal. On the other hand, the relapse of a cyst in the same location as preoperatively should arouse a suspicion of a 3rd/4th branchial cleft anomaly. In rare cases, there may be a necessity for partial thyroidectomy or parotidectomy (1).

Some trials of cysts' sclerotherapy by ethanol injection into their interior were conducted, but cases were limited, and it was not recognized as a standard procedure (13).

There have also been some trials investigating less invasive operative techniques, like the endoscopically assisted dissection technique or transoral robot-assisted surgery in 2nd branchial cleft anomalies, what can potentially help with tissue identification reduce the number of scars on the neck (14).

Conservative treatment

Conservative methods have a limited role in the treatment of branchial cleft anomalies, and serve mainly as a preparation for a surgery to control the infection (1). Introduced antibiotics should always cover aerobic and anaerobic bacteria.

Complications

Untreated branchial cleft anomalies can potentially lead to many complications. Most common, as stated before, are recurring infections that can cause abscesses, fistula formation, excessive scarring and resultant cosmetic defects. Recurring abscesses can spread into the other parts of the head and neck, leading to deep neck infections (e.g. parapharyngeal space infection or cervical phlegmon). In most extreme cases, sepsis, significant airway obstruction, thrombotic complications and mediastinal spread were reported.

An untreated fistula can grow bigger and generate abnormal ducts. Every case of an infection requires antibiotic therapy, but as mentioned before, surgical excision is mandatory (15).

There is also a potential risk of malignant transformation called primary branchiogenic carcinoma (PBC), however, it is extremely rare and poorly documented (1).

Potential complications can also occur due to the surgical treatment. The most commonly observed is recurrence of the anomaly due to the insufficient excision. The relapse rate described in the literature usually does not exceed a few percent (12). However, unsatisfactory outcomes have a less probability to be published, so the exact number may be difficult to estimate. What's more, the relapse rate in fact also depends on the type of branchial cleft anomaly. As mentioned before, there may be a relatively high proportion of 3rd/4th branchial cleft anomaly cases due to misdiagnosis and/or not radical excision.

There may also be observed intraoperative/direct postoperative complications, dependent on the anatomical

localization of the lesion. In the 1st branchial cleft anomalies, there is a risk of the facial nerve damage and parotid gland damage due to its anatomical course and required operation extent (1). That is why, there is a risk of a transient or persistent facial nerve palsy, salivary fistula, or parotitis. In the anomalies involving the lower part of the neck, the surgery can lead to injury to the recurrent laryngeal nerve or thyroid structures. Fortunately, nowadays the use of proper surgical planning, modern intraoperative imaging techniques, facial nerve monitoring, good quality microscopes, endoscopes and magnifying glasses have resulted in significantly reduced risk of severe complications (12).

Prognosis

Long-term prognosis for children with congenital branchial cleft anomalies is promising under the condition of proper surgical treatment. The isolated incidence of a branchial cleft anomaly does not usually significantly impact one's growth. Satisfactory recovery, also from the esthetic point of view, is often obtained, provided that a radical surgical resection is achieved (14). In those cases, recurrences are fairly rare (14). In published literature, there have been described many cases of effective treatment with the relapse rate of only 4%. Postoperative scar is usually located in the skin crease, which makes it barely noticeable (12), especially in children with good healing potential.

Typically, post-operative recurrence of the branchial cleft anomaly happens shortly after the surgery, and it can be quite easily spotted and treated, but definitely requires repeated excision.

In cases with multiple or familial branchial cleft anomalies screening for other signs and symptoms of genetic syndromes is advised. If branchial cleft anomaly is a part of BOR syndrome, there is a need for multidisciplinary care, for example, periodic hearing assessments and renal function monitoring, in accordance with the syndrome-specific care profile (14).

CASE REPORT

A 6-year-old male patient with branchio-oto-renal syndrome (BORS) was admitted to the university clinic of pediatric otorhinolaryngology in April 2024 for an elective surgery. The reason for this admission was a planned surgical excision of bilateral cervical fistulas/sinuses. Patient's main complaint was periodic discharge of serous-mucoid nature, usually more pronounced on the right side. In December 2023, there was a significant purulent discharge from the right fistula, requiring systemic antibiotic therapy. Microbiological examination revealed *Streptococcus pyogenes*, and he was specifically treated. To the time of admission, no surgical interventions (like abscess drainage) have been undertaken.

Among the spectrum of BOR syndrome he also presented with right-sided microtia (figs. 1, 2a) with ear canal stenosis, bilateral preauricular sinuses (figs. 2a, b), right-sided



Fig. 1. Patient with BOR syndrome, right-sided microtia



Fig. 2a, b. Patient with BOR syndrome, right-sided microtia, right-sided scar after cervical fistula removal (a), left-sided preauricular fistula, right-sided scar after cervical fistula removal (b) 6 weeks postoperatively; bilaterally satisfactory cosmetic results, the scar on the right side looks slightly worse than on the left side due to previous history of recurrent discharges and a significant inflammation on the right side

sensorineural hearing loss managed with a hearing aid, and clinically insignificant renal dysfunction. His left auricle was excessively flexible and only slightly deformed. Preauricular sinuses are planned to be managed together with right-sided otoplasty. Due to his genetic disorder, he stays under constant specialist care with neurological and audiological surveillance. In his past medical history, he undergone adenoidectomy with bilateral tympanocentesis and left-sided ventilation tube insertion in July 2023.

On admission, our patient was positively qualified for the surgery on the following day. During operation both fistulas were identified as sinuses, running towards palatine tonsils, not penetrating parapharyngeal space, ending blindly within the neck tissues. They were excised radically, without complications. He was discharged home on the

2nd day post-operatively. He was advised to stay home, avoid physical exercise for 1 month, avoid excessive soaking and sun exposure for better esthetic results; parents were instructed how to clean the wound and change the dressings. One week post-operatively the 1st follow-up visit with stitches removal was scheduled – healing was assessed as satisfactory. Next visit in our outpatient clinic was planned 6 weeks post-operatively – satisfactory cosmetic results were achieved (figs. 2a, b). Histopathological examination revealed typical changes observed in branchial cleft anomalies, what finally confirmed the diagnosis.

CONCLUSIONS

Branchial cleft anomalies are congenital anomalies that can be found at birth (sinuses, fistulas), as well as in children and young adults (cysts, sinuses with internal opening). The most common branchial cleft anomaly originates from the 2nd branchial cleft and is usually located in the lower part of the neck, above the sternocleidomastoid muscle. They may present as cysts, sinuses (with internal or external opening), or fistulas – the frequency of their incidence depends on their origin. 2nd branchial cleft anomalies usually form a sinus with external opening or fistula (1, 8). The diagnosis is based on clinical examination, supported by radiological imaging (USG, CT, MRI) and/or fiberoscopy, and eventually finally confirmed in histopathological examination.

The 'gold standard' therapeutic approach is a complete surgical excision. The radicalness of the excision is extremely important to minimize the potential risk of recurrence. Conservative measures are limited to the management of an active infection by administering antibiotics, in preparation for surgery (1) or peri-/post-operatively in some cases. In extreme cases, local infection can spread to other parts of the neck, leading to a deep neck infections, thrombotic complications and sepsis (15). Deep masses of the neck can be associated with a higher risk of damaging important nerves and vessels during surgery, and in unfavorable events, they may be life-threatening through airway obstruction.

Unfortunately, branchial cleft anomalies can sometimes be misdiagnosed and treated by repeated abscess drainage, localizing repetitively in the same site. It is also frequent in the 3rd/4th branchial cleft anomaly cases, as they require closure of their internal opening through rigid laryngoscopy.

Branchial cleft anomalies can be associated with genetic syndromes like BOR syndrome or BOF syndrome. When such assumption is aroused (e.g. with multiple bilateral branchial cleft anomalies) the screening should be expanded to audiological screening, oculist consultation with vision assessment, abdomen ultrasound, genetic consultation (1, 6).

CONFLICT OF INTEREST
KONFLIKT INTERESÓW

None
Brak konfliktu interesów

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