

## A Branchiogenic Carcinoma: A Case Report on the Delivery of the Branchial Triplets and

### Literature Review

#### Brankiojenik Karsinom: Brankiyal Üç Kistin Çıkarılmasına İlişkin Bir Vaka Sunumu ve Literatür Taraması

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#### ABSTRACT

Branchiogenic carcinoma is an extremely rare condition, with its diagnosis being contentious and is of much debate till date. Due to its vexed clinicopathological entity, a meticulous histopathological examination is essential. Various criteria have been laid out to ensure that the exact diagnosis of branchiogenic carcinoma can be established. We report a 37-year-old male presented with unilateral left sided neck cystic swelling of almost one-year duration, which had gradually increased in size. Imaging showed three cysts altogether in which he underwent surgical excision of three cystic lesions. Histopathological examination showed possibility of a branchiogenic squamous cell carcinoma and the patient completed adjuvant radiotherapy. He was disease-free after 2 years under regular surveillance. Despite the history and clinical examination being strongly suggestive of a benign cervical disease, the differential of a more sinister entity such as branchiogenic carcinoma or cervical cystic metastatic squamous cell carcinoma should be considered. Exclusion of any primary elsewhere in the upper aerodigestive tract is of utmost importance.

**Key Words:** Branchiogenic carcinoma, branchial cleft cyst, squamous cell carcinoma, cystic metastatic neck disease

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#### ÖZET

Brankiojenik karsinom, teşhisi tartışmalı ve bugüne kadar çok tartışmalı olan son derece nadir bir durumdur. Sıkıntılı klinikopatolojik varlığı nedeniyle titiz bir histopatolojik inceleme gereklidir. Brankiojenik karsinomun kesin tanısının konulabilmesini sağlamak için çeşitli kriterler ortaya konmuştur. Neredeyse bir yıl süren tek taraflı sol taraflı boyun kistik şişliği ile başvuran 37 yaşında bir erkek hastayı sunuyoruz. Görüntüleme, üç kistik lezyonun cerrahi olarak eksizyonu yaptığı toplam üç kisti gösterdi. Histopatolojik incelemede branşiyojenik skuamöz hücreli karsinom olasılığı görüldü ve hasta adjuvan radyoterapiyi tamamladı. Düzenli gözetim altında 2 yıl sonra hastaliksiz kaldı. Öykü ve klinik muayene, iyi huylu bir servikal hastalığı güçlü bir şekilde düşündürse de, brankiojenik karsinom veya servikal kistik metastatik skuamöz hücreli karsinom gibi daha uğursuz bir antitenin farklılığı düşünülmelidir. Üst solunum ve sindirim yolunun başka yerlerinde herhangi bir primerin hariç tutulması son derece önemlidir.

**Anahtar Sözcükler:** Branchiyojenik karsinom, brankial yarık kisti, skuamöz hücreli karsinom, kistik metastatik boyun hastalığı

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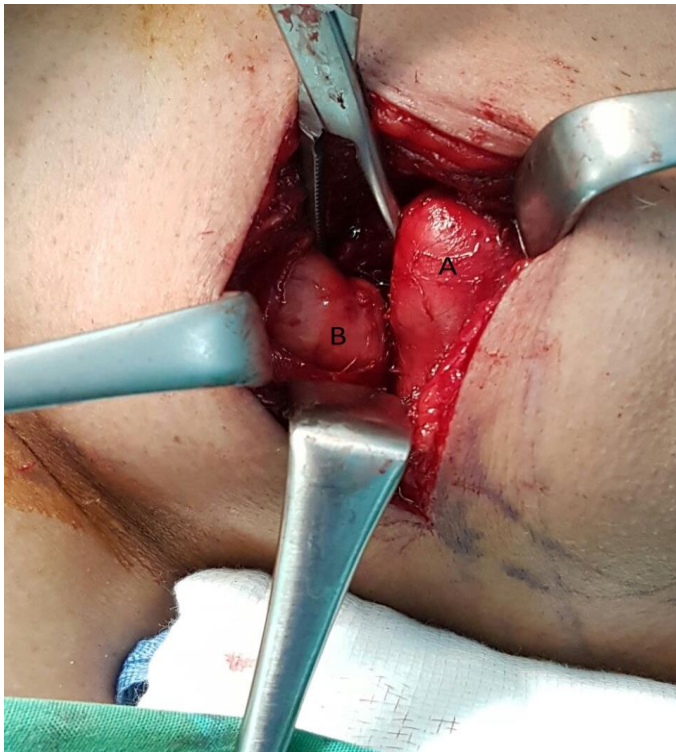
**INTRODUCTION**

The term 'branchial' is derived from the Greek word 'branchia' meaning 'gills'. The branchial apparatus develops between the 3<sup>rd</sup> to 8<sup>th</sup> weeks of embryonic life with various invaginations of clefts and pouches. A branchial cleft cyst is a relatively common congenital anomaly that occurs over the lateral aspect of the neck. It results due to incomplete obliteration of one of the branchial clefts during embryonic development. Primary branchiogenic carcinoma is carcinoma arising from a pre-existing branchial cleft cyst and is an extremely contentious clinicopathological diagnosis. Although Von Volkmann described this entity in 1882, it was not till 1950 when Martin *et al* laid out a series of confirmatory diagnostic criteria. Khafif *et al* went on to further refine these diagnostic criteria with their publication in 1989. This case report presents a patient who underwent complete excision biopsies consisting a triplet of branchial cleft cysts, which revealed squamous cell carcinoma in its lining.

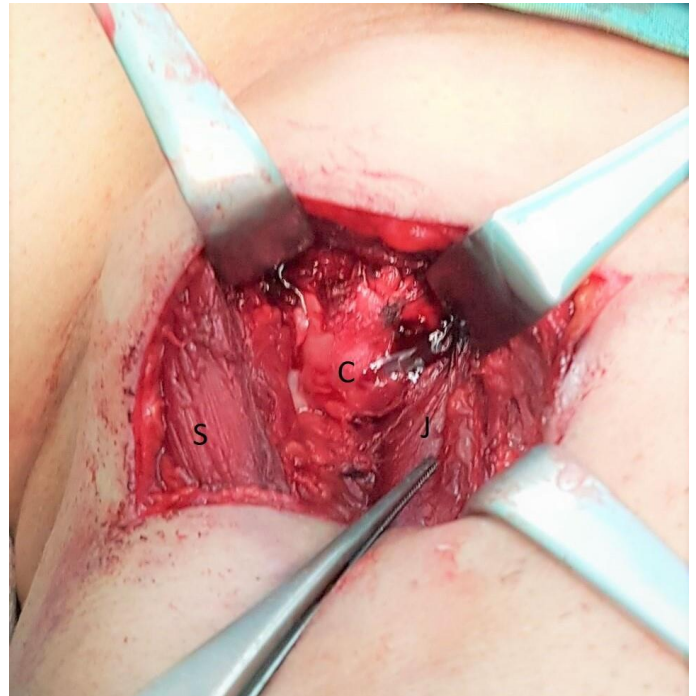
**CASE REPORT**

A 37-year-old male presented with left sided neck swelling of almost one-year duration. The swelling had an insidious onset starting approximately as the size of a marble and gradually increasing to the size of a tennis ball. The swelling was painless throughout and there was history of fever with the swelling. There was also no difficulty to swallow or noisy breathing. Clinical examination revealed a 11 cm x 6 cm cystic, painless, mobile swelling, located along the anterior border of left sternocleidomastoid. No other ipsilateral or contralateral neck swellings were present. Other ear, nose and throat (ENT) clinical examination was unremarkable.

A flexible nasopharyngolaryngoscopy revealed no anomalies in the upper aerodigestive tract. Bedside aspiration revealed 15 cc of yellow serous fluid and a final cytological impression of branchial cleft cyst was made. Subsequently, a computed tomography scan of the neck revealed three well-encapsulated cystic lesions, largest measuring 8 cm x 8 cm, over the left internal jugular vein with no focal lesions to suggest any primary. As the history, clinical examination and needle aspirate were suggestive of a benign disease, the patient underwent excision of all the three cysts under general anesthesia (Figures 1 & 2). All were removed *in toto* and sent for histopathological examination (Figure 3).



**Figure 1:** Initial steps of delivering the first 'A', and the second 'B', cysts prior to delivering the third cyst. Langenback retractor adjacent to 'B' retracting on left sternocleidomastoid.



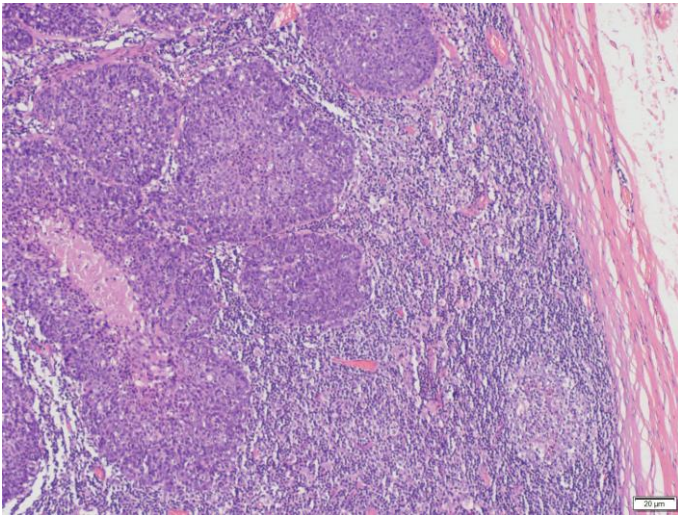
**Figure 2:** The third cyst 'C', adhered to the left internal jugular vein (J), deep to the left sternocleidomastoid (S)



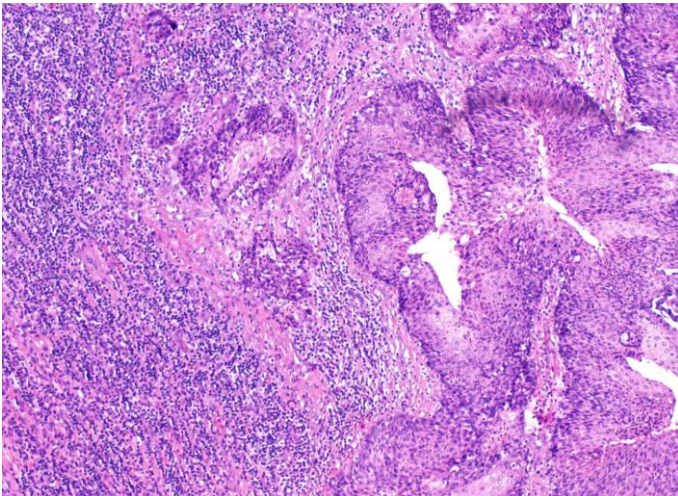
**Figure 3:** All 3 cysts removed *in toto* and sent for histopathological examination

The excised masses had a smooth outer surface with necrotic content. The first cyst 'A', had a fibrotic cyst wall. It was focally lined in areas by dysplastic squamous type epithelium which invades the lymphoid stroma (Figure 4). The second cyst 'B', showed moderately differentiated squamous cell carcinoma with residual nodal architecture in the background (Figure 5). The third cyst 'C', showed anastomosing nests of malignant squamous cells in a lymphocyte-rich and desmoplastic background (Figure 6). No intact normal squamous epithelium was seen in all three cysts that would enable demonstration of a transition from normal epithelium to dysplasia, then invasive carcinoma.

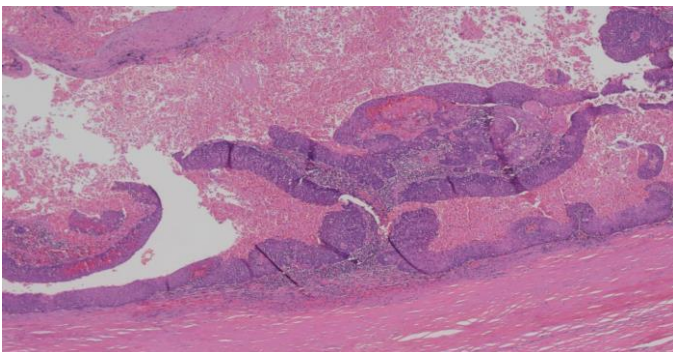
An urgent positron emission tomography (PET) scan confirmed the disease localized to the neck with no evidence of primary elsewhere (Figure 7). Adjuvant radiotherapy was instituted to clear any potential microscopic residual. After 2 years, the patient is still disease-free and will be kept under close surveillance follow ups.



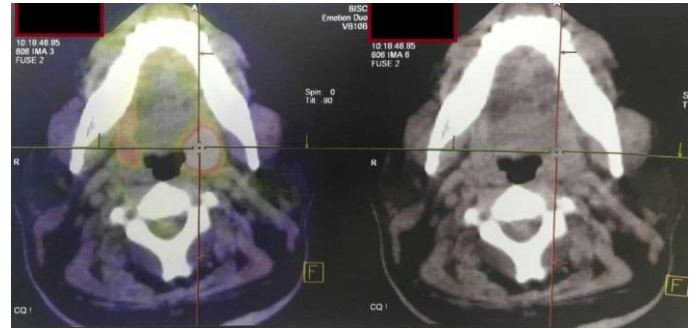
**Figure 4:** Photomicrograph of the first cyst, 'A', showing fibrotic cyst wall, lined by dysplastic squamous epithelium and invasive nests of squamous cell carcinoma within the lymphoid stroma (Hematoxylin and eosin (H&E) stain at magnification x100)



**Figure 5:** Photomicrograph of the second cyst 'B', showing moderately differentiated squamous cell carcinoma (H&E magnification x100)



**Figure 6:** Photomicrograph of the third cyst 'C', showing anastomosing nests of squamous cell carcinoma seen in a lymphocyte-rich background (H&E magnification x40)



**Figure 7:** PET scan confirming disease localized to operative site with no evidence of primary lesion

### DISCUSSION

The term branchiogenic carcinoma dates to 1882 when it was first described by Von Volkmann. Despite being identified as a distinct disease entity back then, subsequent authors like Willis and Sutton have argued that it is a misnomer and the diagnosis of branchiogenic carcinoma was not accepted widely(1,2). It was not until 1950 when Martin *et al* laid out succinct criteria to procure a diagnosis of branchiogenic carcinoma. This was known as the 'Memorial Hospital Criteria For The Tentative Diagnosis of Branchiogenic Carcinoma'(3). Almost four decades later, Khafif *et al* further refined these criteria, which has remained the gold standard in diagnosing cases of branchiogenic carcinoma(4). As this disease remains extremely rare with no clear treatment algorithm or protocol of management, various treatment options have been published(5).

Our patient presented with a slow growing, painless cystic mass of the neck, as similarly reported in previous cases. There was also no history of constitutional symptoms like weight loss or pressure symptoms. Aspiration of the cyst revealed yellow-amber fluid which was similarly reported in previous literature. The radiological images were suggestive of a benign disease, which was well-circumscribed cysts lateral to great vessels of neck with no lymphadenopathy or neck masses seen. The diagnosis of benign branchial cyst was made and patient was subjected to excision of the cyst after radiologic investigation.

A transverse cervicotomy incision was made and the cysts were sent for histopathological examination. It is now known that to diagnose branchiogenic carcinoma, both Khafif *et al* and Martin *et al* diagnostic criteria remain crucial to distinguish it from cervical metastases of unknown primary(6). Martin *et al* had 4 criteria (Table 1)(3). However, Khafif *et al* refined the criteria, as they felt the 5-year period was not important. This was because many patients will eventually die before the 5-year period has elapsed. Khafif *et al* instead had a new set of criteria (Table 2)(4).

In keeping with the above histologic findings, our patient underwent PET scan post operatively to confirm that there were no other primary lesions elsewhere. He underwent adjuvant radiotherapy and is currently keeping well 2 years post-surgery. Although no exact treatment algorithm has been identified for this vexed and debatable diagnosis, surgical excision is still the mainstay of treatment(7). The key in diagnosing branchiogenic carcinoma is to demonstrate a transition from normal epithelium to carcinoma within branchial cyst wall and ruling out any source of primary tumor(8).

Although our case did not show a clear transition zone (No.4. Table 2), we strongly believe it to be a case of branchiogenic carcinoma as it fulfils all the other 4 criteria laid out. In fact, till date, regular ENT examination during our patient's surveillance follow ups have not shown any primary tumors, especially the tonsils. The commonest area of a primary for a cervical cystic squamous cell carcinoma has been reported to arise from the tonsils(7). The probable reason that the transition zone was not seen in our patient was because the patient had kept the swelling for a long period prior to seeking medical attention, and hence the loss of normal healthy cyst wall lining completely being replaced by dysplastic epithelium.

**Table 1:** Memorial Hospital Criteria for tentative diagnosis branchiogenic carcinoma by Martin *et al*(5)

1. The cervical tumor must have occurred somewhere along a line extending from a point just anterior to the tragus of the ear, downward along the anterior border of the sternocleidomastoid muscle to the clavicle
2. The histologic appearance of the growth must be consistent with an origin from tissue known to be present in branchial vestigia
3. The patient must have survived and have been followed by periodic examinations for at least 5 years without the development of any other lesion which could possibly have been the primary tumor
4. The best criterion of all would be histologic demonstration of a cancer developing in the wall of an epithelial lined cyst situated in the lateral aspect of the neck

**Table 2:** Criteria proposed by Khafif *et al* to diagnose branchiogenic carcinoma(6)

1. The location of the tumor in the same anatomic description as previously mentioned by Martin *et al*
2. The histologic appearance of the tumor is consistent with branchial vestiges
3. Presence of carcinoma within the lining of the epithelial cyst
4. Demonstrating a transition from normal epithelium of the cyst to carcinoma
5. Absence of identifiable primary elsewhere by thorough evaluation of patient (scopes, imaging and appropriate biopsies)

## CONCLUSIONS

Primary branchiogenic carcinoma is a squamous cell carcinoma arising in a branchial cleft cyst and remains as a rare disease encountered. In our case, histopathological examination of the resected 'benign' neck mass revealed areas of dysplastic squamous epithelium along the cyst wall with stromal invasion. The exact nature of branchiogenic carcinoma remains ambivalent. This case highlights the histopathologic criteria in diagnosing branchiogenic carcinoma proposed by Martin *et al* and later revised by Khafif *et al*. Primary branchiogenic carcinoma. We successfully managed to treat this disease and our patient is under our regular surveillance.

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## Conflict of interest

No conflict of interest was declared by the authors.

## REFERENCES

- 1.Sutton, J.B. Tumors, Innocent and Malignant: Their Clinical Features and Appropriate Treatment. The American Journal of the Medical Sciences 1894, 107, 708.
- 2.Willis, R.A. The spread of tumours in the human body; J. & A. Churchill: 1934.
- 3.Martin, H.; Morfit, H.M.; Ehrlich, H. The case for branchiogenic cancer. Annals of Surgery 1950, 132, 867.
- 4.Khafif, R.A.; Prichep, R.; Minkowitz, S. Primary branchiogenic carcinoma. Head & neck 1989, 11, 153-163.
- 5.Nakano, A.; Mishima, K.; Katase, N.; Ueyama, Y. A case of squamous cell carcinoma arising from branchial cleft cyst. Journal of Oral and Maxillofacial Surgery 2015, 73, 781-785.
- 6.Al-Mufarrej, F.; Stoddard, D.; Bite, U. Branchial arch anomalies: Recurrence, malignant degeneration and operative complications. International journal of pediatric otorhinolaryngology 2017, 97, 24-29.
- 7.Bradley, P.T.; Bradley, P.J. Branchial cleft cyst carcinoma: fact or fiction? Current opinion in otolaryngology & head and neck surgery 2013, 21, 118-123.
- 8.Black, B.; Maran, A. Branchiogenic carcinoma. Clinical Otolaryngology & Allied Sciences 1978, 3, 27-36.