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Branchial cleft cyst: An unusual site for the cervical metastasis of nasopharyngeal carcinoma

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ABSTRACT

Objective: Cancers found in the resected branchial cleft cyst are rare clinically but usually impose substantive diagnostic and treatment challenges for clinicians.
Methods: A 31-year-old man presented with a lateral neck mass that was suspected to be an inflammatory branchial cleft cyst. After excision, the pathologic specimen revealed a benign cystic appearance with a focus of undifferentiated carcinoma. Serologic tests for Epstein–Barr virus were negative. A positron emission tomography scan and upper aerodigestive tract endoscopies were negative for any other suspicious lesion.
Results: The patient underwent random biopsies of the nasopharynx, tongue base, and hypopharynx and bil tonsillectomy. Pathologic examination of the nasopharyngeal biopsies showed the presence of undifferentiated carcinoma. The cancerous part of the branchial cleft cyst and this nasopharyngeal specimen were positive for the latent membrane protein-1 and EBV-encoded RNAs of Epstein–Barr virus (EBV) and confirmed our diagnosis.
Conclusion: This is the first report of a NPC metastasizing to a branchial cleft cyst. Molecular diagnostic techniques facilitate the definite diagnosis that enabled us to refine treatment plans and offered the patient a favorable outcome.

1. Introduction

Second arch branchial cleft cysts related to the second pouch represent the most common branchial pouch anomaly. The typical cyst presents as a blind cyst just anterior to the sternocleidomastoid muscle and may have an open tract communicating with the pharynx. The lining of these cysts is usually squamous epithelium and sometimes columnar ciliated epithelium. Although the masses are congenital, they are usually identified only in the second to fourth decades of life [1]. Although it is unusual for a carcinoma to arise in a branchial cleft cyst, a primary cancer originating from the branchial cleft cyst or other primary cancers that metastasize into the branchial cyst should be carefully differentiated [1]. Differentiating between a primary malignancy derived from a branchial cleft cyst or the metastasis of another primary cancer into the branchial cleft cyst is frequently a difficult challenge for clinicians. Here we report our experience making a definite diagnosis using our established molecular methods for a case with occult nasopharyngeal carcinoma (NPC) that metastasized to a resected second arch branchial cleft cyst.

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2. Case presentation

A 31-year-old man presented with a two-week history of a movable, painless, cystic mass above the right upper sternocleidomastoid muscle. No other symptoms presented, and there was no palpable lymphadenopathy. The patient denied smoking or regular alcohol consumption. A high-resolution ultrasound scan of the mass showed a well-defined hypoechoic cystic mass with an echogenic rim and some internal echoes in the right upper neck. An ultrasound-guided aspiration biopsy was performed. The cytology showed some benign squamous cells, some macrophages, many neutrophils, and few lymphocytes. A computed tomography scan of the head and neck showed a circumscribed unilocular thick-walled cystic lesion in the right upper neck, lateral to the carotid sheath and anteromedial to the sternocleidomastoid muscle (Fig. 1). Neither an obvious focal soft-tissue mass nor enlarged cervical lymph nodes were noted near the mass or elsewhere in the head and neck region.

Under the impression of an inflammatory branchial cleft cyst, we performed a transcervical excision. Pathohistology demonstrated a branchial cleft cyst lined by benign squamous and columnar epithelia. However, an area of undifferentiated carcinoma was identified in the wall of the cyst. Further work-up was then conducted. Circulating Epstein–Barr virus (EBV) DNA by real-time polymerase chain reaction (PCR) and anti-EBV antibodies against EBV viral capsid antigen, early antigen, and nuclear antigen-1 immunoglobulin A tests were all negative. The positron emission tomography scan from the skull base to the midthigh showed only an inflammatory reaction in the left neck. To exclude the possibility of tumor metastasis into the resected branchial cleft cyst rather than primary malignancy in the cyst, we arranged for endoscopic evaluation and biopsies for the upper aerodigestive tract. Nasopharyngoscopy, laryngoscopy, and esophagoscopy were conducted, but no specific findings were noted during the examinations. Random biopsies of the nasopharynx, hypopharynx, and tongue base were taken, and a bilateral tonsillectomy was simultaneously performed. The pathological description of the nonkeratinizing undifferentiated carcinoma was revealed only in the nasopharyngeal specimens. To prove that both tumors in the nasopharynx and metastatic site in the cyst arose from the same origin, we detected the presence of EBV infection by the EBV-encoded RNAs (EBERs) in-situ hybridization (Fig. 2) and the EBV-derived latent membrane protein-1 (LMP-1) (Supplementary materials) by the PCR protocol as we described previously [2]. The results from both the branchial cleft cyst and nasopharyngeal specimens were positive for EBV EBERs and LMP-1 expression.

After the confirmatory diagnosis of NPC, the patient was treated with concurrent chemoradiotherapy. The regimen consisted of cisplatin, uracil/tegafur, and leucovorin biweekly for 2 cycles, followed by weekly cisplatin for 6 cycles. A total radiation dose of 70 Gy in 35 fractions was given. The patient showed no signs of tumor relapse during the 6-year clinical and imaging follow-ups.

3. Discussion

Second arch branchial cleft cyst is a common congenital cyst in the anterior triangle of the neck. Considering its benign nature, primary malignant tumors that originate from the cyst are very rare and have been reported in fewer than 40 cases that fulfill the strict criteria initially described by Martin et al. [1,3]. The usual histopathology finding is squamous cell carcinoma, and the treatment of choice is resection with adjuvant radiotherapy or chemoradiotherapy [1,3]. On the other hand, some reports have found cancer metastasis to the

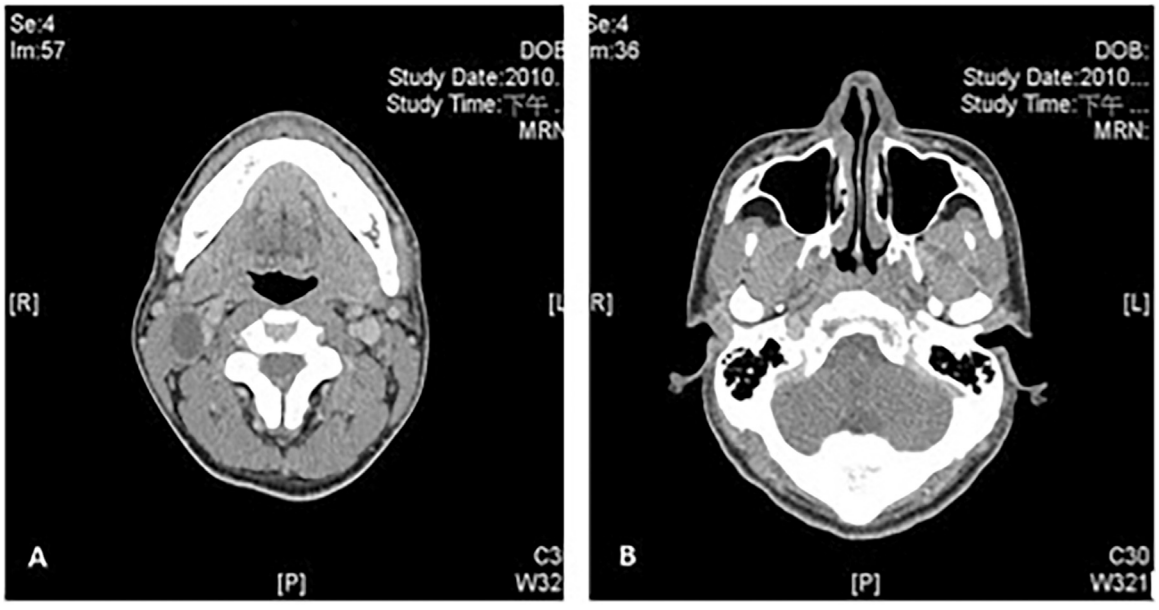

Fig. 1. (A) Axial CT of head and neck region shows a well-circumscribed cystic swelling in the upper part of the left neck, anteromedial to sternocledomastoid muscle. The cyst measures 1.8 × 2.5 cm. No other apparent pathologies or enlarged lymph nodes. (B) The nasopharynx shows normal lining appearance. Neither soft tissue masses nor ulcerations could be detected.

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