Case Report

Angiosarcoma initially presented as repeated shedding tonsil neoplasm: a case report and literature review

Jisheng Li1*, Minghao Li2*, Xiaofang Zhang3, Yuekai Li4, Hua Geng5, Xiaolan Cai6, Xiangling Wang1, Ming Li1, Limei Sun1, Fengping Qin1, Xuejun Yu1

1Department of Medical Oncology, Cancer Center, Qilu Hospital of Shandong University, Jinan, PR China; 2School of Medicine, Shandong University, Jinan, PR China; 3Department of Pathology, Qilu Hospital of Shandong University, Jinan, PR China; 4Department of Nuclear Medicine, Qilu Hospital of Shandong University, Jinan, PR China; 5Research Center of Basic Medical Sciences, Tianjin Medical University, Tianjin, PR China; 6Department of Otorhinolaryngology, Qilu Hospital of Shandong University, Jinan, PR China. *Equal contributors.

Received December 3, 2015; Accepted February 13, 2016; Epub April 1, 2016; Published April 15, 2016

Abstract: Background: Angiosarcomas are rare malignant vascular tumors composed of several clinical subtypes and collectively have a poor prognosis especially with metastases. They can involve any soft-tissue structures or visera and commonly present in the head and neck anatomical region. However, both primary and metastatic angiosarcomas in tonsil are extremely rare. Herein we reported a peculiar case of diffused metastatic angiosarcoma initially presented as a repeated shedding tonsil neoplasm. Case presentation: A 45-year-old Chinese man without history of cancers or radiation in the head and neck region presented with a left tonsil neoplasm which enlarged progressively. And shortly pieces of necrotic tissues began repeatedly shedding from the tonsil neoplasm. About 2 months later he gradually presented with systematic symptoms including fever and dyspnea. Twice tissue biopsy for the tonsil neoplasms in local hospital failed to prove malignant disease with preliminary pathological diagnosis of necrosis and chronic inflammation. In our hospital, functional imaging with PEC-CT supported a diffused metastatic disease status involving left tonsil, right atrium, mediastinum, and multiple bones. Further deep tissue biopsy and histopathology analysis revealed tonsil angiosarcoma with strong positive immunohistochemical staining for CD31 and CD34. Then the patient received two cycles of chemotherapy with paclitaxel plus cisplatin regimen and following efficacy evaluation revealed stable disease (SD). However, the patient gave up subsequent anti-cancer treatment due to personal choice and died 6 months after diagnosis due to progression of metastatic angiosarcoma. Conclusion: We described a unique case of diffused metastatic angiosarcoma involving tonsil in which diagnosis was not achieved until the third biopsy. Although we can’t fully exclude the possibility that the tonsil angiosarcoma could be metastasized from a potential heart or bone primary site, this case was still extraordinarily peculiar because of both its rarity and unique initial presentation as a repeated shedding tonsil neoplasm. We have also presented a review of published reports concerning its rare incidence.

Keywords: Angiosarcoma, head and neck, metastasis, pathology, tonsil

Introduction

Angiosarcomas are a rare subtype of soft tissue sarcoma of vascular or lymphatic endothelial cell origin with aggressive behavior [1]. It’s estimated that about 2% of soft tissue sarcomas and 5.4% of cutaneous soft tissue sarcomas are angiosarcomas [2, 3]. The term heman-gioendothelioma indicates vascular tumors of intermediate malignancy while angiosarcoma indicates high-grade neoplasm. Most angiosarcomas arise spontaneously while some cases are associated with radiation and chronic lymphedema [1]. Treatment is challenging in many angiosarcoma cases and prognosis is relatively poor, however, antiangiogenic therapies could offer some hope for an effective angiosarcoma specific treatment in future [1].

Based on its clinical behavior, angiosarcoma could be classified into following subtypes: cutaneous angiosarcoma, lymphedema-associated angiosarcoma, radiation-induced angiosarcoma, primary-breast angiosarcoma, and soft-tissue angiosarcoma [4]. It develops from vascular or lymphatic endothelial cells and can
involve any soft-tissue structure or viscera such as head and neck, breast, liver, heart, spleen and bone [5-9]. Although angiosarcomas originated in head and neck region represent about 27% of all angiosarcomas, they only account less than 0.1% of all head and neck malignancies [10]. Angiosarcomas in tonsil, either primary or metastatic, are ever rarer and only occasionally seen in case reports.

In the present report, we described a unique case of diffused metastatic angiosarcoma involving tonsil, heart, mediastinum and bones. Diagnosis for this case was challenging and not achieved until the third biopsy. Although we could not fully exclude the possibility that the tonsil angiosarcoma could be metastasized from a potential heart or bone primary site, this case was still extraordinary peculiar and interesting because of both its rarity and unique initial presentation as a repeated shedding tonsil neoplasm. We have also presented a review of published reports concerning its rare incidence.

Figure 1. The left tonsil angiosarcoma presented as a dark red neoplasm of about 3 cm×3 cm×2 cm in its primary focus with small spots of caseous necrosis scattered in its surface (A). Using positron emission tomography-computed tomography (PET-CT), this malignant disease were detected by elevated standard uptake values (SUVs) in left tonsil (B), mediastinum masses (C, D), right atrium masses (maximum 4.6, average 2.4; C and E), and multiple bones (sternum and lumbar vertebra as examples, C, F).

**Case presentation**

A 45-year-old Chinese man without any history of cancers or radiation in the head and neck area presented with a swollen left tonsil after a cold. The tonsil swelling enlarged progressively and shortly pieces of dark red tissues began to repeatedly shedding from his left tonsil, which caused bloody sputum and even obvious tonsil bleeding occasionally. About two months later after the presence of tonsil neoplasm, the patient gradually presented with other systematic symptoms including fever, cough, dyspnea and weight loss of about 3 kilograms. Contrast-enhanced computerized tomography (CT) for neck, chest and abdomen in local hospital revealed a left tonsil neoplasm accompanied with pericardium, mediastinum and liver mass as well as pericardial effusion, which suggested a malignant disease with extensive metastases. Biopsy for the tonsil neoplasm was performed twice in local hospital but pathological analyses failed to reveal malignant disease in this case with preliminary pathological diagno-
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sis of necrosis and chronic inflammation in tonsil. The patient was then referred to our hospital for further diagnosis and treatment.

In our hospital, physical examination revealed a left tonsil mass of about 3 cm×2 cm with the color of dark red and small areas of caseous necrosis scattered in the surface of the tonsil neoplasm (Figure 1A). No enlarged lymph nodes were found in the head and neck region or the supraclavicular region. A preliminary diagnosis of metastatic malignant disease was made based on the medical history and disease presentation. Then positron emission tomography-computed tomography (PET-CT) was arranged for the patient and detected elevated standard uptake values (SUVs) in the left tonsil (maximum 3.7, average 2.2; Figure 1B), right atrium mass (maximum 4.6, average 2.4; Figure 1C and 1E), mediastinum masses (maximum 3.6-5.7, average 2.2-3.6; Figure 1C and 1D), and multiple bones (maximum 1.3-4.4, average 0.6-2.5; Figure 1C and 1F) in addition to mild pericardial effusion. Cardiac ultrasound revealed a 4 cm×3 cm mass in the lateral wall of right atrium and mild pericardial effusion with a left ventricular ejection fraction of 0.75.

Multiple discipline teams (MDT) discussion involving otorhinolaryngology surgeon was arranged for this case and consensus was made that a metastatic malignant disease was preferentially considered and further tonsil biopsy was strongly recommended. The fact that pieces of tissues frequently shed from the neoplasm suggested that the tonsil malignancy grew very fast and the surface tissue might be necrotic and had lost typical malignant pathological characteristics. Previous two biopsies in local hospital might be too superficial to collect

Figure 2. Histopathology and immunohistochemical staining results confirmed the diagnosis of angiosarcoma. Haematoxylin and eosin staining of section of the angiosarcoma showed pleomorphic spindle endothelial cells with large hyperchromatic nuclei and the distinct vasoformative areas filled with red blood cells (A, HE 200×). Immunostaining showed strong staining for CD31 (B, 200×) and CD34 (C, 200×), moderate staining for FLI1 (D, 200×) and Vimentin (E, 200×), but negative for S-100 (F, 200×), DOG1 (G, 200×), CR (H, 200×) and MC (I, 200×).
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Typical cancerous tissues probably for fear of causing severe bleeding, thus a deep tissue biopsy by an experienced otorhinolaryngology surgeon was arranged for this case. Deep tonsillar tissue biopsy was performed and histopathology analysis revealed angiosarcoma. Microscopically, multiple sections showed a malignancy comprising tumor cells arranged in a vasoformative growth pattern with complex anastomosing channels, which was consistent with typical angiosarcoma histological findings. The immunohistochemical results showed that tumor cells were stained positive for CD31, CD34, FLI-1, Vimentin and Ki67 (approximately 10%) but negative for S-100, DOG1, MC and CR (Figure 2), supporting the diagnosis of angiosarcoma.

Based on the fact that this patient initially presented with an enlarging tonsil neoplasm with repeated tissue shedding and didn’t present with systematic symptoms until two months later, we tent to consider this case as a metastatic angiosarcoma with tonsil primary. However, based on the limited previous medical history, accessible imaging study results and biopsy pathology, we cannot exclude the possibility that the tonsil angiosarcoma could be metastatic from a potential heart or bone primary site. But it’s quite important to notice the unique initial disease presentation as repeated shedding tonsil neoplasm for this case in addition to its rarity.

Due to the diverse metastatic disease status, systematic chemotherapy was recommended as the initial treatment modality for this patient after a MDT discussion. The patient received two cycles of chemotherapy with paclitaxel plus cisplatin regimen accompanied with diphosphonate which he tolerated well. Following efficacy evaluation after two cycles of chemotherapy suggested stable disease (SD). The patient gave up subsequent anti-cancer treatment due to personal choice and died 6 months after diagnosis due to progression of metastatic angiosarcoma.

Discussion

Angiosarcoma is also known as malignant hemangioendothelioma, angioblastoma, hemangiosarcoma and intravascular endothelioma. As histologic high-grade tumors arising from vessels, angiosarcomas are no longer subgrouped into lymphangiosarcomas and hemangiosarcomas [11]. According to the latest WHO classification of soft tissue tumors, malignant vascular tumors include epithelioid haemangioendotheliomas and angiosarcomas of soft tissue [12]. A study of the distribution of angiosarcoma with pooled data from 534 patients suggests that commonly affected anatomical sites include head and neck (27.0%), breast (19.7%), extremities (15.3%), trunk (9.5%), liver (6.0%), heart (4.7%), bone (3.6%), spleen (2.6%) and other (or unknown) (11.6%) [1]. About thirty percent angiosarcomas patients present with metastases and common metastases involve lung (28.8%), bone (21.2%), liver (9.2%) and lymph node (18.1%) [5, 13, 14]. Prognosis for this rare disease of high malignancy is relatively poor. Soft-tissue sarcomas are associated with a 5-year survival rate of 50-60% [15], but angiosarcomas only have a 5-year survival rate of about 40% [6, 7, 16].

Sarcomas are rare in the head and neck region and most malignancy in this anatomical region are squamous cell carcinomas [17]. Although about 60% of cutaneous angiosarcomas arise in the skin of head and neck region, non cutaneous sarcomas of the head and neck are exceptionally rare, accounting for approximately 4% to 10% of all sarcomas and less than 1% of all head and neck malignancies [17]. Within head and neck region, angiosarcomas originated in the oral cavity area are much rarer. In 2014, M. Nagata et al. reported three cases of intraoral angiosarcoma and summarized reports of primary oral angiosarcomas since 1998 [18]. Among the 15 cases of oral angiosarcoma, the common locations involved gingiva, hard palate, buccal mucosa and tongue. Clinically, they were usually presented as painful, spontaneously bleeding, round or ovoid nodules with rapid onset and invasion of adjacent tissues [18]. The oral region is not easy for metastatic tumor to colonize [19]. The oral cavity metastases of angiosarcoma have been reported for limited times with about half of them in gingiva [20-26]. Compared to oral cavity, the reports of angiosarcoma in tonsil are even scarcer.

Tonsil sarcomas constitute a rare entity in tonsillar neoplasms and are only described in some case reports. The common primary tonsillar neoplasms include lymphomas and squa-
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Table 1. Summary of six reported angiosarcoma cases involving tonsil

<table>
<thead>
<tr>
<th>Publication year</th>
<th>Diagnosis</th>
<th>Age (year)</th>
<th>Gender</th>
<th>Primary site</th>
<th>Metastases</th>
<th>Survival time</th>
<th>Treatment</th>
<th>IHC Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present case</td>
<td>Metastatic angiosarcoma</td>
<td>51</td>
<td>Male</td>
<td>Unknown</td>
<td>Tonsil, right atrium, mediastinum, bones</td>
<td>6 months</td>
<td>Chemotherapy (paclitaxel plus cisplatin)</td>
<td>Positive: CD31, CD34; Negative: DOG1, MC and CR</td>
</tr>
<tr>
<td>2013 [54]</td>
<td>Cardiac angiosarcoma</td>
<td>37</td>
<td>Male</td>
<td>Heart</td>
<td>Both lungs, tonsil, duodenum</td>
<td>About 3 weeks</td>
<td>No treatment</td>
<td>N.A.</td>
</tr>
<tr>
<td>2012 [51]</td>
<td>Epithelioid tonsil angiosarcoma</td>
<td>71</td>
<td>Female</td>
<td>Tonsil</td>
<td>Buccal mucosa, duodenum, small bowel, uvula</td>
<td>&gt;9 months</td>
<td>Surgery, radiation therapy (70 Gy), chemotherapy (taxol)</td>
<td>Positive: KL-1, Lu5, cytokeratin (8, 18, 19), vimentin, CD31, ERG, FLI-1; Negative: CK5, 34βE12, cytokeratin 7, 13, 20</td>
</tr>
<tr>
<td>2012 [55]</td>
<td>Multifocal laryngeal angiosarcoma</td>
<td>83</td>
<td>Female</td>
<td>Epiglottis and base of tongue</td>
<td>Tonsil, pharynx</td>
<td>About 18 months</td>
<td>Surgery, adjuvant chemotherapy (taxotere)</td>
<td>Positive: CD31, CD34; Negative: P63, CAM5.2, FVIII-RAg, cytokeratin AE1/AE3, CK903</td>
</tr>
<tr>
<td>2011 [53]</td>
<td>Primary breast hemangiosarcoma</td>
<td>54</td>
<td>Female</td>
<td>Breast</td>
<td>Tonsil, chest wall, submandibular lymph node, supraclavicular lymph node, foramen magnum</td>
<td>&gt;7 months</td>
<td>Tonsillectomy, therapeutic embolization</td>
<td>Positive: CD31, CD34; Negative: HMG 45 and S-100</td>
</tr>
<tr>
<td>1952 [74]</td>
<td>Lymphangiosarcoma</td>
<td>54</td>
<td>Female</td>
<td>Arm</td>
<td>Both tonsils, lungs, bones</td>
<td>&gt;8 months</td>
<td>Amputation</td>
<td>Not performed</td>
</tr>
</tbody>
</table>

IHC: Immunohistochemistry; FLI-1: Freudeukemia integration site 1; FVIII-RAg: factor VIII-related antigen; HMG: High-molecular weight cytokeratins; N.A.: not available.
Angiosarcoma presented as repeated shedding tonsil neoplasm

Malignant cell carcinomas. Meanwhile, tonsil is neither a commonly affected anatomical site for metastatic neoplasms. Reported primary malignancy include rectal adenocarcinoma [27-29], melanoma [30-33], renal cell carcinoma [34, 35], breast malignant phylloides tumor [36], endometrial adenocarcinoma [37], seminoma [38], small cell lung cancer [39-41], and small cell neuroendocrine carcinoma [42]. In 2014, Rokkjaer et al. reviewed the prevalence of malignant tumors detected in routine tonsillectomy specimens and found that only 11 out of 72,322 (0.015%) patients had malignancy [43]. Reported sarcoma subtypes detected in tonsil include follicular dendritic cell sarcoma [44, 45], primary monophasic synovial sarcoma [46], interdigitating dendritic cell sarcoma [47] and Kaposi’s sarcoma [48-50], in addition to limited case of angiosarcoma.

Thorough literature searches were performed in MEDLINE, Web of Science and Google Scholar using keywords of “tonsil” and “angiosarcoma” with proper search strategy and to the best of our knowledge, totally five cases of tonsil angiosarcoma has been detailedly reported in English literatures. The related literature and clinical information including the present case have been summarized in Table 1. Actually only one of the five cases is primary tonsil angiosarcoma while the other four cases are all metastatic tonsil angiosarcoma. The case reported by Agaimy et al. in 2012 might be the first reported primary angiosarcoma of tonsil [51]. The patient was a 71-year-old woman without history of malignancy or radiation to the head and neck. She was treated with tonsillectomy for the refractory tonsil symptom of diffuse painful swelling and the histologic and immunohistochemical findings proved angiosarcoma. Except its rarity, another diagnostic challenge lied on the strong expression of cytokeratin in this case. This kind of pitfall has also been reported in other epithelioid angiosarcomas [52]. Ronen et al. demonstrated the difficulty in the diagnosis of angiosarcoma which initially presented as tonsillar hemorrhage in their case report [53]. In this case, the 54-year old female patient showed abrupt and massive tonsillar hemorrhage and the true diagnosis was made until obtaining the immunohistochemical results after bilateral tonsillectomy. Subsequent PET-CT demonstrated disseminated metastases in the chest wall, left submandibular lymph node, supraclavicular lymph node, and right lobe of the liver. Compared to our cases, the patient has a history of high-grade breast angiosarcoma and this episode was proved to be the recurrence of her primary breast angiosarcoma. The earliest report we found, which was diagnosed as lymphangiosarcoma in arm, dated to 1952 and nowadays we no longer subdivide angiosarcomas into lymphangiosarcomas and hemangiosarcomas in diagnosis [11].

In this case, a female patient with post-mastectomy lymphedema presented with an ulcerating lesion of the dorsum of left arm which was proven to be lymphangiosarcoma and presented with metastasis in both tonsils, lungs and bones 8 months later. In addition to above 3 cases, a case of cardiac angiosarcoma metastasized to lung, tonsil and duodenum as well as another case of laryngeal angiosarcoma metastasized to tonsil and pharynx were also described in previous literature [54, 55].

In the present report, we described a unique case of diffused metastatic angiosarcoma involving tonsil, heart, mediastinum and bones. In addition to its rarity, the most particular feature is its initial presentation as an enlarging and repeated shedding tonsil neoplasm. At the time point of pathological diagnosis, the disease has already diversely metastasized and we cannot elucidate which anatomical site is the primary one because head and neck region, heart or bone are all common primary site for angiosarcoma. Neither could further pathological analysis help to clarify the primary site. But based on its unique initial presentation and the fact that the patient didn’t present with systematic symptoms until two month later after the presence of tonsil neoplasm, we tent to consider this case as a metastatic angiosarcoma with tonsil as primary site, though neither could we fully exclude the possibility that the tonsil angiosarcoma might be metastasized from a potential heart or bone primary site.

Diagnosis for this case was also challenging and not achieved until the third biopsy. Based on the disease presentation and imaging study, a metastatic malignant disease was preferentially considered once the patient was referred to our hospital. However, previous two biopsies in local hospital failed to detect malignancy with only a preliminary pathological diagnosis.
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of necrosis and chronic inflammation. A quick enlarging and repeated shedding tonsil neoplasm suggested that the malignancy grew very fast and the surface tissue might be necrotic and have lost typical cancerous pathological characteristics. Further deep tissue biopsy by experienced otolaryngology surgeon and histopathology analysis did successfully collect enough typical cancerous tissue which was proved to be angiosarcoma. MDT discussion and the involvement of experienced otolaryngology surgeon played important role in the diagnosing process for this patient.

As mentioned earlier, neoplasms in tonsil are mostly lymphoma and squamous cell sarcoma with much fewer sarcoma especially angiosarcoma, which could be misdiagnosed because of their rarity. In histopathology, the pleomorphic malignant endothelial cells in angiosarcoma might appear polygonal or spindle shape with large hyperchromatic nuclei. In well or moderately differentiated area, distinct vascular channels or sinusoids with or without filled blood cells, often irregular in size and shape and surrounded by chronic inflammatory cells, are typical character for vascular neoplasms. In poorly differentiated angiosarcomas, the vascular architecture became more various and the cells more pleomorphic and mitotically active. The high grade epithelioid angiosarcomas might be histologically similar to anaplastic carcinoma or melanoma [1, 12, 56]. Given its various clinical characteristics and histologic features, immunohistochemistry is preferred to make a definite diagnosis by detecting the expressions of vascular molecule makers. The endothelial markers including CD31 (Platelet Endothelial Cell Adhesion Molecule-1), CD34 (Human Hematopoietic Progenitor Cell Antigen), Factor VIII-related antigen (FVIIIRA), FLI1 (Friend leukemia integration 1 transcription factor) and Ulex europaeus lectin type 1 (UEA-1) are commonly used to verify the vascular origin of the neoplasm [57]. The membrane and cytoplasmic staining of CD31 is evidenced more sensitive and specific than CD34, though it dose express in macrophages and platelets [58]. Another highly specific maker is nuclear staining ERG (erythroblast transformation specific related gene), which could be independently more sensitive than conventional markers in some angiosarcomas [59, 60]. It is notable that in some cases, especially oral angiosarcomas, the reactions for some non-specific markers, such as vimentin and pancytokeratins, might be misleading for diagnosis [18, 51, 52]. For the present case, multiple sections showed a malignancy with tumor cells in a vasoformative growth pattern with complex anastomosing channels, which were typical angiosarcoma histological findings. And tumor cells were stained positively for CD31, CD34, FLI1 and Vimentin but negative for S-100, DOG1, MC and CR, supporting the diagnosis of angiosarcoma.

For treatments and outcomes, angiosarcomas are often analyzed together, though they involve several different clinical subtypes. Owing to its high malignancy by definition, angiosarcomas have poor prognosis comparing to other vascular tumors or soft tissue sarcomas [6-8, 15]. The five years survival rate of angiosarcomas varied around 40% and the overall median survival time ranged from 7.3 to 42 months among different studies [5, 6, 8, 61]. The prognosis was moderated by clinical factors such as age, tumor size, anatomic site, and metastatic status instead of histologic features, partly for the reason of the difficulty for conventionally histologic grading [4, 14, 56, 61, 62]. In a recent retrospective study of 434 cutaneous angiosarcoma cases, patients younger than 50 years had a 10-year relative survival rate of 71.7%, while in older patients the rate dropped to 36.8%. And angiosarcoma of scalp and neck might have a lower 10-year relative survival rate compared to other sites [63]. But patients with primary or secondary angiosarcoma of oral and salivary gland might have a better prognosis than with other primary cutaneous or deep soft tissue angiosarcoma [64]. In addition to age, the extent of primary tumors, resection status and the pattern of tumor growth, indicated by whether the solid areas greater than 80%, were also prognostic factors for angiosarcoma of head and neck [65].

There are no specific treatment guidelines for subtypes of angiosarcoma up to now. Treatment of angiosarcomas has been included in management guidelines for other soft-tissue sarcomas, such as guidelines from European Society for Medical Oncology (ESMO) and the National Comprehensive Cancer Network (NCCN) [16, 66]. Most published reports of angiosarcoma treatment are retrospective case series instead of randomized trials and prospective studies.
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For localized disease, radical surgery with complete resection is the primary treatment modality. Adjuvant radiotherapy with high dose and wide treatment field is recommended after surgery due to the high risk of local recurrence [7, 67]. Considering the risk of metastasis there is a rationale for the use of adjuvant chemotherapy, however, by now there still lacks sound evidence supporting neoadjuvant or adjuvant chemotherapy after radical surgery and radiotherapy for angiosarcoma [8, 16]. For metastatic angiosarcoma, cytotoxic chemotherapy is the primary treatment of choice, though evidence supporting this modality is also limited. The commonly used cytotoxic drugs include anthracyclines, taxanes and ifosfamide. A large meta-analysis of anthracycline-based chemotherapy demonstrated an overall response rate of 26% and median survival of 51 weeks in soft-tissue sarcomas [68]. Similar response rates but worse survival time were reported in angiosarcoma [69]. Over the past decade there has been growing interest using taxane agent to treat angiosarcoma. The ANGIOTAX study, the only prospective phase II study of chemotherapy in angiosarcoma, investigated the efficacy of paclitaxel in the treatment of locally-advanced and metastatic angiosarcoma [70]. Based on this trial, paclitaxel is listed as the cytotoxic agent of first choice for systemic treatment of angiosarcoma in the NCCN Guidelines. However, there are no available trials comparing the efficacy of anthracycline and taxane in angiosarcoma yet. Retrospective comparisons suggest similar response rates and survival for both cytotoxic agents [6]. Most recently, the role of several antiangiogenic molecules including bevacizumab, sorafenib and sunitinib in the treatment of angiosarcomas has been explored with great interest by several groups. Evidence in three phase II trials supports the use of sunitinib and sorafenib (broad-spectrum tyrosine-kinase targeting VEGFRs) as well as bevacizumab (VEGF-A monoclonal antibody) in the use of targeted treatment for locally-advanced and metastatic angiosarcoma [71-73].

Conclusion

We described a unique case of diffused metastatic angiosarcoma involving tonsil and which diagnosis was not achieved until the third biopsy. This case was still extraordinarily peculiar because of both its rarity and unique initial presentation as a repeated shedding tonsil neoplasm. The disease quickly deteriorated and the patient died of progressed metastatic angiosarcoma 6 months after diagnosis. For metastatic angiosarcoma, palliative chemotherapy is hampered by poor response rates and toxicities, while biological therapies especially antiangiogenic therapies offer hope for an angiosarcoma specific treatment in future.

Acknowledgements

This study was supported by National Natural Science Foundation of China (81201934, 81202100), and Tianjin Research Program of Application Foundation and Advanced Technology (12JCYBJC15600). Written informed consent was obtained from the legal guardians of the patient for publication of this case report and any accompanying images.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Xuejun Yu, Department of Medical Oncology, Cancer Center, Qilu Hospital of Shandong University, 107 Wenhuai Xi Road, Jinan 250012, PR China. Tel: 86-531-82169851; E-mail: yuxuejun99@163.com

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