Clinical Case Report

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Ectopic hamartomatous thymoma (biphenotypic branchioma)

A case report and review of the literature

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Abstract

Rationale: Ectopic hamartomatous thymoma is a very rare soft tissue neoplasm that commonly occurs in the lower neck of adult men.

Patient concerns: A 32-year-old male presented 1-year history of the tumor lying in left supraclavicular fossa.

Diagnoses: Initial consideration of ultrasound and computed tomography was lipoma. After the operation, the pathologist diagnosed it as Ectopic Hamartomatous Thymoma.

Interventions: A complete resection was performed.

Outcomes: To date, the patient had no evidence of metastasis or recurrence for 26 months after the operation.

Lessons: Ectopic hamartomatous thymoma is rare. The mastery of the clinical and pathological features of the disease will contribute to the rapid diagnosis and treatment of the disease. In addition, it can be considered to update the name to "biphenotypic branchioma" in order to avoid conceptual confusion.

Abbreviations: CT = computed tomography, EHT = ectopic hamartomatous thymoma, SETTLE = spindle cell tumor with thymus-like elements.

Keywords: biphenotypic branchioma, ectopic hamartomatous thymoma, lower neck, soft tissue tumor, spindle cells

1. Introduction

Ectopic hamartomatous thymoma (EHT), a very rare tumor, commonly occurs in the lower neck suggesting branchial origin. There are 80 cases of the disease reported in English literature up to now. In 1982, Smith and McClure[1] described the lesion as "a mixed tumor exhibiting mesenchymal, lymphangiomatous and squamous elements." Rosai et al[2] reported that it may be a spindle cell thymic anlage tumor and subsequently named it "ectopic hamartomatous thymoma" in 1984. There is no indication of thymic filiation or differentiation, although it contains the term for thymoma. In this paper, the clinical, pathological, and immunohistochemical features of EHT located in the left supraclavicular fossa are discussed, along with a discussion on new name and a review of the literature.

2. Case presentation

A 32-year-old Chinese man provided a 1-year history of a nodule in the left supraclavicular fossa. No evidence of trauma was observed on his neck. The neck mass was larger than 1 year ago, and patient recalled no fever, pain, redness, and swelling. An oval mass can be palpable in the left supraclavicular fossa, with mild tenderness upon palpation; the nodule was moderately hard and well circumscribed. No vascular murmur was found on his neck. No other abnormalities were found upon further physical examination. A 3.1 cm × 2.4 cm well-circumscribed mixed-type nodule with heterogeneous density was found in the neck through ultrasound imaging (Fig. 1A), which is based on slightly higher density. Neck computed tomography (CT) scan showed a

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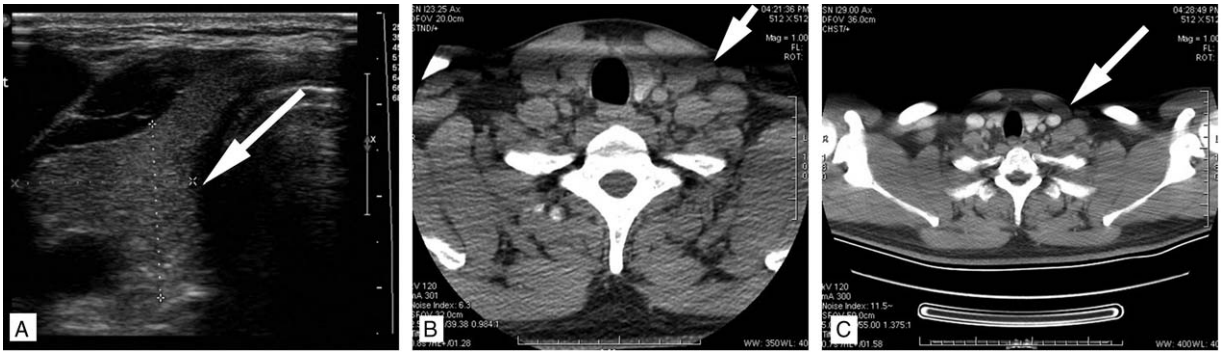

Figure 1. Imaging findings of the patient. (A) Ultrasound imaging showed a 3.1 cm × 2.4 cm well-circumscribed mixed-type nodule (arrow) with heterogeneous density. (B) Computed tomography scan revealed a lamellar abnormal density mass (arrow) in the suprasternal fossa. (C) The nodule (arrow) had not been enhanced by enhancement scan.

lamellar abnormal density mass in the suprasternal fossa (Fig. 1B). Floccular and tubercular fat density shadows were found in the mass. The maximal section area of the node was approximately 1.9 cm × 1.4 cm. An enhancement scan failed to improve the image (Fig. 1C). Slightly enlarged lymph nodes were found along the right neck and mandibular areas. Ultrasonography and CT findings suggest that the mass may be an unusual lipoma. Fine-needle aspiration showed that the tumor included small spindle cells and mature adipose cells. Initially, the mass was speculated to be a benign tumor. Subsequently, a total surgical resection of the mass was performed under general anesthesia and revealed absence of obvious residual tumor tissue. During operation, a well-demarcated and moderately hard mass, sized 3.0 cm × 2.0 cm × 1.5 cm was found lying beneath the platysma without invasion. Fat and gelatinoids were also found around the mass. No contact was found between the tumor and the surrounding tissues. Surgery went well. His postoperative course revealed no abnormalities 28 months after resection, and no sign of metastasis or recurrence was observed.

Upon gross pathology, the tumor, which is 3.0 cm × 2.0 cm × 1.5 cm in size, had moderate hardness and a clear border (Fig. 2A). Cut surface of the mass was gray-yellow and gray-white. A 1 cm vesicle was found in the surface. As the mass was cut, clear liquid flowed from the cyst (Fig. 2B). Microscopically, the tumor consisted of 3 components: spindle cells, epithelial cells, and mature adipocyte islands (Fig. 3A). Several small lymphocytes were dispersed throughout the spindle cells. The spindle cells were clearly arrayed in a fascicular (Fig. 3B) and storiform (Fig. 3C) pattern, with occasional emergences of ambiguous whorled structure. Keratinizing and nonkeratinizing squamous nests were found in other areas (Fig. 3D and E). Some irregularly shaped cysts were found in the lesion. Moreover, the luminal lining cells of cysts were multilamellar and were flattened, cuboidal, or columnar. Unusual lumen-like and tube-like structures could be seen in the tumor (Fig. 3F). It is rare for EHT to exhibit keratinizing squamous nests. A certain amount of dilated vessels and some hemorrhagic areas could be seen in the tissue.

Immunohistochemically, both plump spindle and epithelial cells showed positivity for AE1/AE3 (Fig. 4A) and p63 (Fig. 4B), and they were negative for CK20 (Fig. 4G) and the neurogenic marker S-100 (Fig. 4H). The spindle cells also showed staining for CD10 (Fig. 4C), CD34 (Fig. 4D), and Vimentin (Fig. 4F). Furthermore, spindle cells partly stained for smooth muscle actin (SMA) (Fig. 4E) but were negative for Calponin. The stromal elements, cytoplasm of vascular smooth muscle cells, spindle cells, and the cytomembrane of adipocytes tested positive for vimentin staining. All components were negative for GFAP,

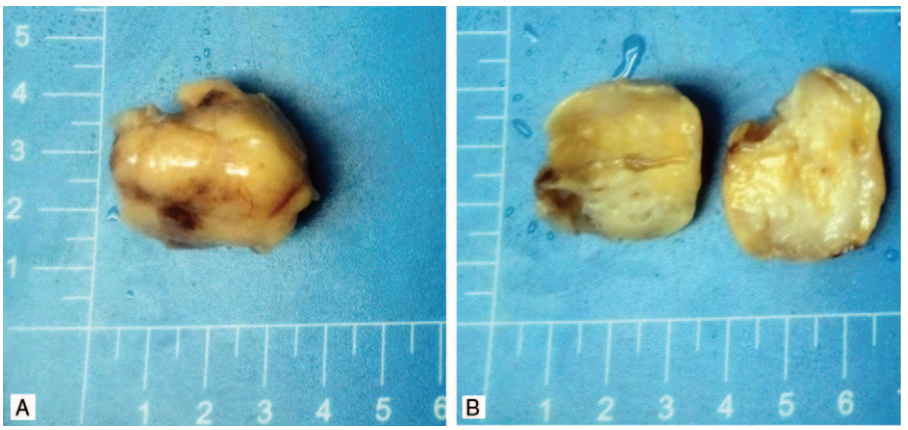

Figure 2. Gross findings of the tumor. (A) The tumor was elastic and well-circumscribed. The ruler is graduated in centimeters. (B) The cut surface of the mass was gray-yellow and gray-white.

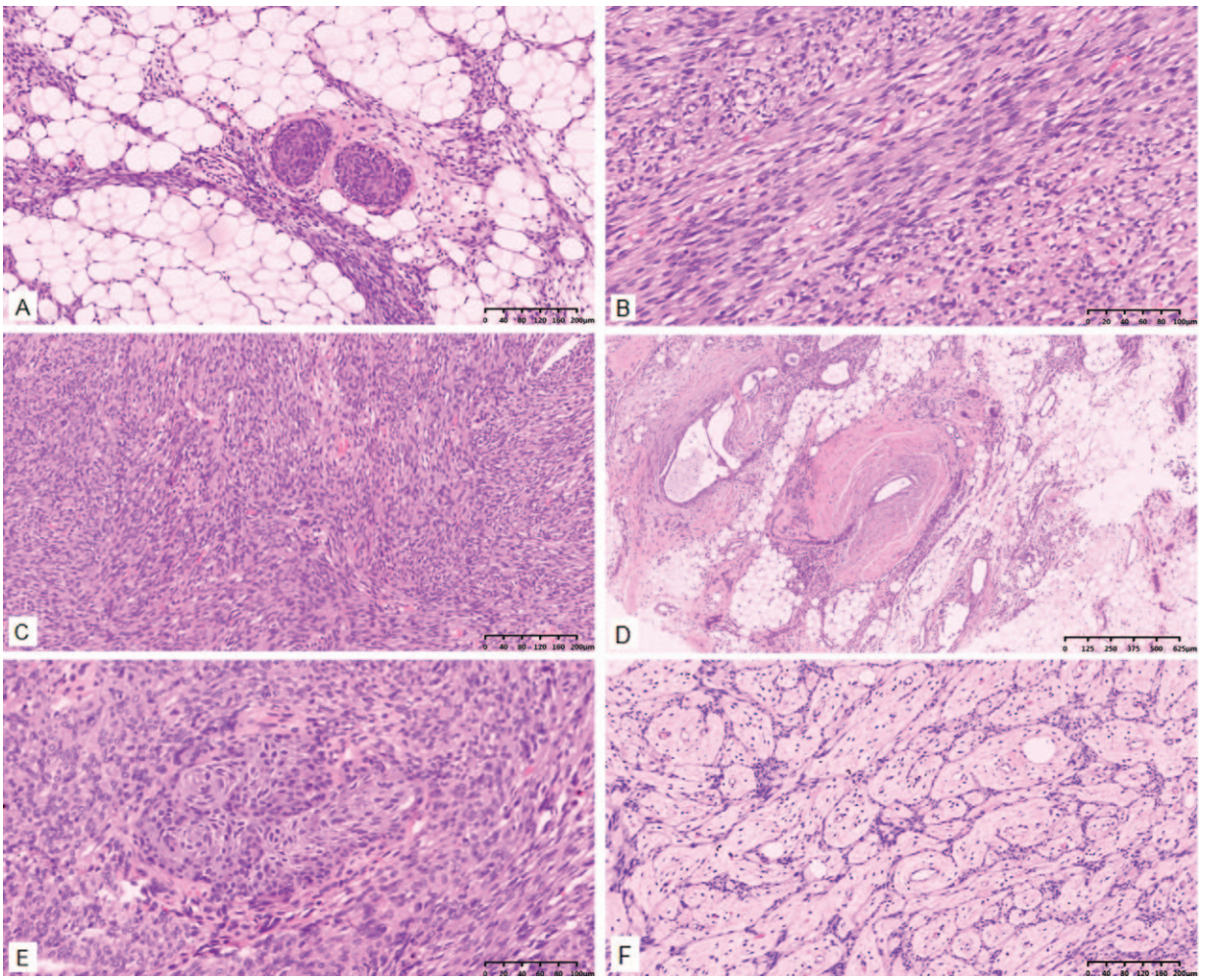

Figure 3. Microscopic features of the tumor (H&E staining). The tumor consists of spindled cells, epithelial islands, and mature adipose tissue (A ×100). The spindle cells of the tissue are clearly arranged in a fascicular manner (B ×200) and in storiform manner (C ×100). In addition, keratinizing squamous nests (D ×40), nonkeratinizing squamous nests (E ×200) and gland-like structures (F ×100) can be seen in other areas.

Calponin, and CK20. Specific analysis of immunohistochemistry is in Table 1.

3. Discussion

Ectopic hamartoma thymoma, characterized by a mixture of spindle cells, epithelial elements, and mature adipose components, is a very rare soft tissue tumor of the lower neck.[3,4] Our case presented in this paper has the typital clinical and pathological features of ectopic hamartomatous thymoma. Around 80 pathologically verified cases of EHT have been reported so far, we have made a summary and analysis above them (Table 2).[1–26] The age of EHT ranges from 19 to 89 years (mean: 45.9 years). It has an obvious male predominance with the ratio of male: female (62:18). The tumor affected mostly the lower neck of the patient with the ratio of lower neck: all (76:80). Its major histologic components include spindle cells type and mixed type. EHT is known to be a slow-growing tumor or mass. There was neither recurrence nor metastasis during follow-up of 46 cases, except for 2 patients who had recurrence because of incomplete local excision as reported by Fetsch et al.[3] Local surgical resection is the first choice of treatment because of its good clinical outcome.[3,7]

Clinically, EHT is easily misdiagnosed as lipoma. The exact diagnosis is based on histologic diagnosis. However, it is easy to confuse this lesion with other biphasic tumors, such as mixed tumor, skin/soft tissue myoepithelial adenoma, thymic lipoma, spindle cell tumor with thymus-like elements (SETTLE), malignant peripheral nerve sheath tumor, and biphasic synovial sarcoma.[8,9,25] Thus the differential diagnosis of the tumor is particularly important. The common feature of mixed tumor, skin/soft tissue myoepithelial adenoma and EHT is that they have nests and squamous elements. But, distincting from mixed tumor, EHT lacks hyalinized or chondromyxoid stroma.[3] Thymic lipoma is almost always located in the mediastinum and lacks spindle cell nests. SETTLE arises around thyroid glands, without sex predilection, and are comprised of spindle cells and a glandular cavity, which is composed of mucinous epithelium. Biphasic synovial sarcoma has apparent heteromorphism in spindle cells.[27] Generally, it does not express smooth muscle actin (SMA) and rarely has squamous differentiation in the epithelial elements of synovial sarcomas.[10] Malignant peripheral nerve sheath tumor with epithelial differentiation also has obvious heteromorphism in spindle cells and should be S-100 protein positive but cytokeratin negative.[10] Based on the characteristic morphology, immunohistochemical characteris-

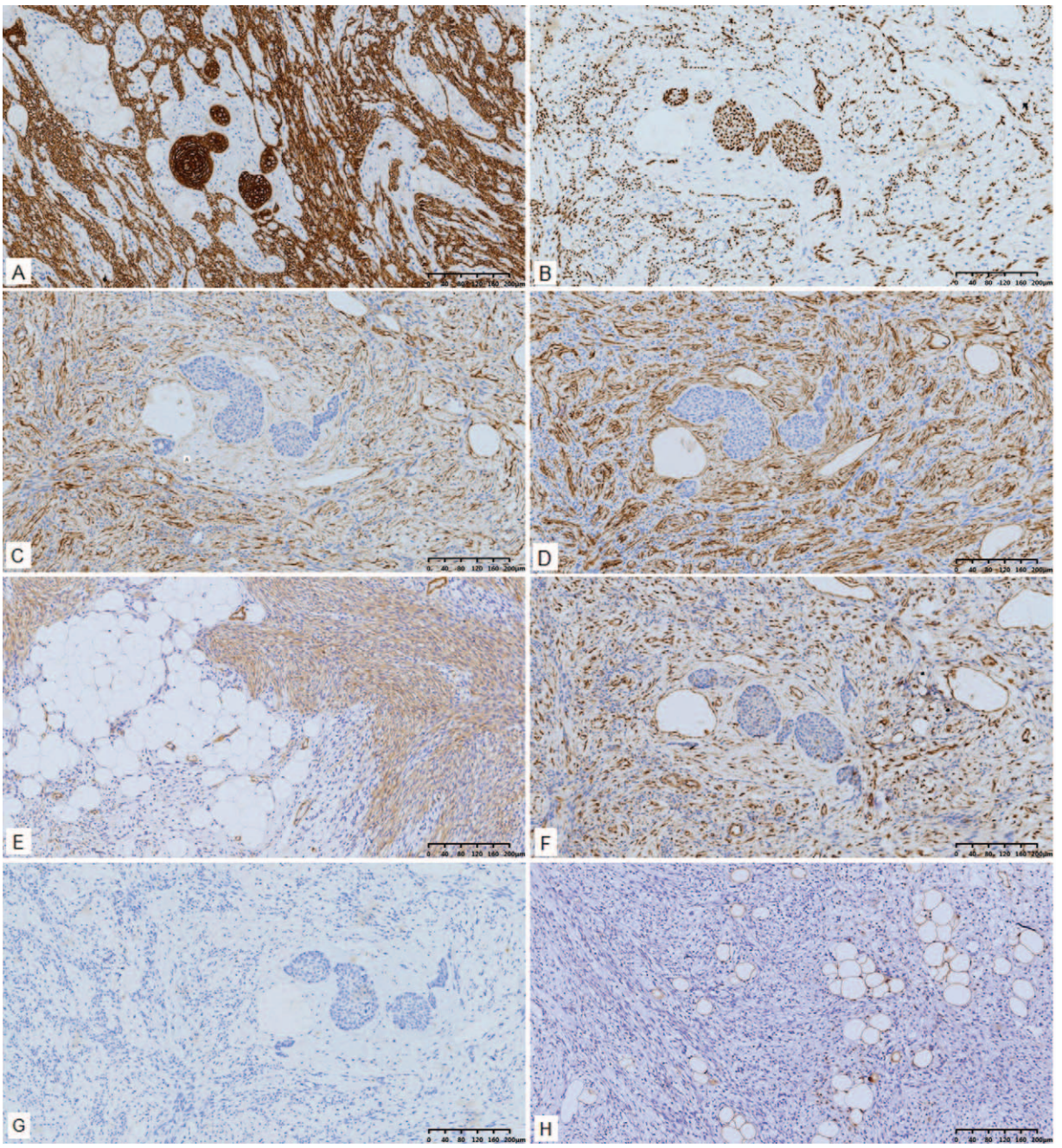

Figure 4. Immunohistochemistry findings of the tumor. (A–H: Original magnification ×100.). Spindle and epithelial islands were strongly positive for AE1/AE3 (A) and p63 (B). Spindle cells were positive for CD10 (C) and CD34 (D). Spindle cells were stained partly in SMA (E) and vimentin (F). Spindle and epithelial cells were negative for CK20 (G) and S-100 (H).

tics, and classic anatomic position of EHT, it can be easily differentiated from other diseases. Therefore, for the diagnosis of EHT, it is important that clinicians recognize the location and characteristic histological and immunohistochemical features of the tumor.

The precise origin of EHT remains indefinite.[26] Originally, researchers proposed that it may be caused by developmental abnormalities of the thymus, originating from the third branchial pouch.[2,9] However, the hypothesis of thymus origin of EHT will be highly debatable. Currently, no correlation was found between residual thymus structures and EHT in all reported cases of the latter, and no case was reported to occur in the mediastinum or thymus.[4] EHT may originate at the third and fourth branchial pouches,[6] the postbranchial body,[11] or the cervical canal of His.[5] At present, researchers generally recognize that the tumor originates from the branchial apparatus. "Branchial anlage mixed tumor" is more appropriate than ectopic hamartomatous thymoma. However, "mixed tumor" is easily confused with the salivary gland tumor in the head and neck, and there is not chondromyxoid features in EHT. In 2017, Sato et al[26] proposed that a more appropriate name for it may be "biphenotypic branchioma" owing to the origins and tissue types

Table 1

Immunohistochemical findings of our patient.

Antibodies used	Source	Clone	Spindle areas	Epithelial areas	Adipocytes
AE1/AE3	ZSGB-BIO	AE1/AE3	(+)	(+)	(−)
S-100	Gene Tech	15E2E2 + 4C4.9	(−)	(−)	(+)
SMA	ZSGB-BIO	HHF35	(+)	weakly, small areas (+)	(−)
P63	ZSGB-BIO	UMAB4	(+)	(+)	(−)
CD34	ZSGB-BIO	EP88	(+)	(−)	(−)
CD10	ZSGB-BIO	56C6	(+)	(−)	(−)
Vimentin	Gene Tech	EP21	(+)	(−)	(+)
Calponin	ZSGB-BIO	EP63	(−)	(−)	(−)
GFAP	ZSGB-BIO	EP13	(−)	(−)	(−)
Cytokeratin20	ZSGB-BIO	EP23	(−)	(−)	(−)

(−) = negative; (+) = positive; AE1/AE3, cytokeratin, mouse anti-CK (pan) monoclonal antibody; S-100, polyclonal rabbit anti S-100; SMA, mouse anti-actin (smooth muscle) monoclonal antibody; P63, mouse anti-P63 monoclonal antibody; CD34, endothelial cell marker, mouse anti-CD34 monoclonal antibody; CD10, mouse anti-CD10 monoclonal antibody; Vimentin, monoclonal mouse anti-vimentin; Calponin, rabbit anti-calponin monoclonal antibody; GFAP, monoclonal mouse anti-human glial fibrillary acidic protein; ZSGB-BIO, Golden Bridge Biotechnology CO.LPD; Gene Tech, Gene Tech (Shanghai) Company Limited.

Table 2

The summary of clinicopathological and histologic features for reported cases of EHT.

Clinical and histologic characteristics	Information	Mean
Age, years	19–89	45.9
Sex	Male: Female = 62:18	
Site	Neck	76
	Chest wall	3
	Interface of the posterior axillary region and back	1
Size, cm	1.4–19	4.8
Predominant histologic Pattern	Spindle cells type	26
	Mixed type	21
Follow-up, years	0.5–16	2.9
Recurrence	2 patients (incomplete local excision)	

EHT = ectopic hamartomatous thymoma, Total patients: 80.

of the tumor, which derives from the mesoderm and endoderm. Maybe the term biphenotypic branchioma more appropriately generalizes the origins and tissue types of this tumor.

4. Conclusion

In conclusion, EHT is a benign tumor. Mastery of its differential diagnosis is helpful to the diagnosis and treatment of the disease, and more accurate naming helps to recognize the disease. We hope that our case will contribute to the diagnosis and treatment of EHT in the future.

Author contributions

Data curation: Yuwen Pang, Liang Zhang.
Funding acquisition: Chunxia Liu.
Methodology: Dongliang Li, Yuwen Pang.
Resources: Dongliang Li.
Software: Wenwen Cui, Yang Liu, Liang Zhang.
Visualization: Yang Liu.
Writing – original draft: Wenwen Cui.
Writing – review & editing: Chunxia Liu, Feng Li.

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