A case of intravascular epithelioid hemangioendothelioma occurring 14 years after coil embolization for an extracranial internal carotid artery aneurysm

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Epithelioid hemangioendothelioma (EHE) is a rare neoplasm originating from various organs. The clinical outcome mostly depends on surgical resectability. The authors report an EHE of the extracranial internal carotid artery developed in a 59-year-old male patient 14 years after the intravascular coil embolization for a carotid aneurysm at the same site. Because the lesion was initially diagnosed as regrowth of the thrombosed aneurysm, decision for radical resection was delayed, and the patient died from rapid tumor progression. Differential diagnosis of atypical vascular mass lesions should include neoplasm, because initial radical resection may be the key to achieve a better prognosis. (J Vasc Surg 2012;55:230-3.)

Blood vessel tumors are rare, and include heterogeneous group of benign and malignant tumors.1 Because of its rarity and various clinical patterns,1,2 the initial diagnosis is often difficult.

Epithelioid hemangioendothelioma (EHE) is the most aggressive and common variant of hemangioendothelioma.1 It arises rarely from intravascular origin. Three cases of EHE have been reported in the peripheral arteries.3-5 We report a case of EHE of the extracranial internal carotid artery, which arose from an aneurysmal lesion that was treated by endovascular coil embolization 14 years earlier.

CASE REPORT
A 59-year-old man complained of slowly progressing hoarseness, dysphasia, and a palpable mass in the left submandibular region. He had a history of a left extracranial internal carotid artery aneurysm, which was treated 14 years earlier. At that time, magnetic resonance imaging (MRI) demonstrated a large mass in the left cervical region (Fig 1). The lesion was diagnosed as an aneurysm of the internal carotid artery by conventional angiography (figures are not available). He was treated by endovascular parent artery occlusion with interlocking detachable coils (IDC). The aneurysm disappeared angiographically, and the symptoms recovered completely.

His medical history was uneventful for 9 years after the coil embolization. Then dysphagia, hoarseness, and localized submandibular swelling appeared, and they aggravated gradually during the next 4 years.

The left submandibular mass was elastic hard, immobile, and showed no tenderness. Left-sided lingual atrophy was evident, and endonasal laryngoscopy showed symptoms of laryngeal and hypoglossal nerve palsy. A blood examination showed only mild inflammatory findings of increased C-reactive protein, which were compatible with subclinical aspiration pneumonia.

Computed tomography (CT) and MRI demonstrated a well-circumscribed large mass (50 × 40 × 80 mm) in the left cervical region (Fig 2, A and B). The signals of the mass on CT and MRI were similar to those of the surrounding soft tissue. Marked enhancement was observed around the border and in the lower portion (just above IDC). A left common carotid angiogram revealed complete occlusion of the internal carotid artery (Fig 2, C and D). The lower part of the mass received blood flow from the common carotid artery. The mass was thought to be a thrombosed and partially recanalized aneurysm.

Total resection of aneurysm through a mandibulotomy was proposed because we considered that the thrombosed aneurysm might enlarge even after blocking blood flow from parent arteries due to residual blood channels around the wall such as vasa vasorum. The patient rejected this option due to its invasiveness, and separation of the aneurysm from the proximal artery to at least reduce blood supply to the mass was performed by cutting the origin of internal carotid artery and suturing the orifice. The mass lesion occupied the whole intraluminal space of the internal carotid artery above the level of 1 cm distal to the carotid bifurcation. The surface of arterial walls appeared normal. No histologic specimen was obtained during the initial surgery.
Fig 1. Axial (A) and coronal (B) sections of contrast-enhanced T1-weighted magnetic resonance imaging (MRI) taken 14 years ago showing a giant mass lesion in the left anterior cervical region. The lesion was $35 \times 25 \times 30$ mm in size and showed heterogeneous signal intensity compatible with a giant aneurysm (arrowheads).

Fig 2. Axial (A) and coronal (B) sections of contrast-enhanced T1-weighted magnetic resonance imaging (MRI) taken on admission showing a heterogeneous mass ($45 \times 55 \times 70$ mm), which compressed the trachea and adjacent tissue. The upper border of the mass was near to the skull base. An oblique view of the left carotid angiogram (C: arterial phase, D: capillary phase) showed the previously occluded internal carotid artery and blood flow passing between the coil and the arterial wall into the lower part of the mass (black arrows). This blood flow was compatible with the strong enhancement areas seen on MRI (white arrows in A and B).
During the 2 months after the first operation, clinical symptoms and radiological findings worsened. Therefore, a second operation was performed to remove the mass through the same skin incision, but only partial removal was performed because of excessive bleeding from the mass. The patient then returned to work because clinical symptoms temporarily improved. The histopathological study revealed an EHE. Another surgery through the same route was performed when the mass regrew to compress the trachea 2 months later. Despite the planned total removal, the surgery resulted in partial removal due to excessive bleeding. Postoperative full body CT and positron emission tomography revealed multiple metastases in cervical lymph node and bilateral lung.

The patient then presented with an even more aggressive local recurrence, so a subtotal removal through a midline mandibulectomy was finally performed 2 weeks later. Residual cervical lesion was treated by radiation; however, he died 6 months after the initial surgery.

Pathologic examination of the specimen during the second operation showed that the tumor cells demonstrated abundant eosinophilic cytoplasm and ovoid nuclei, as well as perivascular epithelioid alignment with focal papillary proliferation (Fig 3, A). The mitotic index was 1 in 10 high-power fields (HPFs). Immunohistochemical evaluation revealed that the tumor cells were positive for CD31 (Fig 3, B), CD34, vimentin, pancytokeratin (AE1/AE3), and factor VIII, and negative for S-100 and HHF-35 (muscle specific actin). The Ki-67 staining index peaked at 24%. Pathologic diagnosis was an EHE. The findings obtained in the fifth operation showed higher cellular atypia, a less differentiated epithelioid architecture, and a mild increase in the mitotic index (Fig 3, C) to a level similar to that seen in angiosarcoma.

**DISCUSSION**

Malignant tumors derived from vascular endothelial cells include EHE and angiosarcoma. Previously, EHE was defined as an intermediate grade malignant tumor, but the recent World Health Organization classification redefined EHE as a fully malignant tumor due to its clinical behavior. EHE can occur almost anywhere in the body; over 30 cases with an intravascular origin have been reported, predominantly from veins rather than arteries. In cases originating from arteries, the origin is usually the aorta. There have been three case reports of EHE originating from peripheral arteries (occipital, radial, and palmar arteries). In the carotid arteries, three angiosarcomas and no EHE cases have been reported. The present case may be the first report of intimal EHE originating from the extracranial internal carotid artery.

For malignant tumors arising in blood vessels, it is often difficult to make a correct diagnosis in the early phase. This is partly because they are extremely rare and also because their imaging characteristics are nonspecific resembling inflammatory or atherosclerotic lesions. In our case, several findings may have been clues to suggest possible malignancy; hardness, immobility, the similarity of signals on CT and MRI between the mass and soft tissue,
and adjacent nerve palsies. The first step toward a correct diagnosis is to consider this disease in cases involving atypical lesions and, if so, we should have planned a total resection or at least obtained a histologic specimen at the first surgery.

Definitive treatment involves curative resection with an adequate tumor-free margin.\textsuperscript{1,4,9,11,15-16} Previously reported cases of peripheral arterial EHE underwent successful curative resection and achieved good outcomes.\textsuperscript{3-5} The role of adjuvant chemotherapy and/or radiation therapy is ambiguous.

Although the prognosis of EHE is superior to that of angiosarcoma, it cannot be considered indolent. In a previous report, more than 3 mitoses per 50 HPF and a tumor size >3 cm were prognostic factors that implied a 5-year disease-specific survival of 59%, and no patient without either of these factors died.\textsuperscript{17} Our patient demonstrated both risk factors at the time when pathologic diagnosis was achieved.

The etiology of EHE is not well known; however, causalities for angiosarcoma have been suggested to include radiation,\textsuperscript{17} defunctionalized arteriovenous fistula,\textsuperscript{18} foreign body,\textsuperscript{16} carotid endarterectomy,\textsuperscript{10} and intravascular prosthesis (eg, Dacron intra-aortic grafts).\textsuperscript{12,15,19-20} In our case, a platinum coil (which has been reported to have few dysplastic effects) had been implanted about 9 years preceding the first symptoms. Several speculations are possible for the relationship between the treatment and the EHE, although none of them is conclusive. Albeit unlikely, existence of tumor 14 years earlier and its malignant transformation cannot be ruled out.

Nevertheless, the authors emphasize that it is important to consider vascular neoplasm in cases of atypical vascular mass lesions.

REFERENCES