Iodine-125 Interstitial Brachytherapy for Pediatric Desmoid-Type Fibromatosis of the Head and Neck: A Case Report

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Desmoid-type fibromatosis (DF) is a locally aggressive benign soft tissue tumor. It is rarely observed in the head and neck region and is particularly uncommon in the parotid gland. This report describes the case of a 32-month-old girl with DF of the head and neck. The tumor was resected with gross residual tumors. Recurrence occurred 3 months later and then the patient was treated with iodine-125 interstitial brachytherapy. The tumor was completely absent 6 months after brachytherapy. No recurrence was found 60 months after brachytherapy during follow-up. No severe toxicities or growth abnormalities were observed. Very-low-dose rate brachytherapy as the sole modality could be a reasonable alternative for the treatment of inoperable DF of the head and neck, which avoids the risk of cosmetic deformity caused by surgery, especially in pediatric patients. In addition, long-term follow-up is recommended.

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Desmoid-type fibromatosis (DF), an aggressive fibromatosis or desmoid tumor,[1] was recognized in 1954 by Stout.[2] DF is a rare benign tumor that arises from fascial and musculoaponeurotic tissues, with origins in the head and neck region accounting for 10 to 15% of cases.[3] DF usually is not capsulated, with slow-growing and locally aggressive growth patterns. However, DF has not been observed with distant metastasis.[4,5] The etiology of DF is unknown. Familial adenomatous polyposis, trauma, and endocrine factors have been associated with DF.[5,6] Treatment options include surgery, radiotherapy, chemotherapy, and hormonal therapy. The incidence of local recurrence is high after initial treatment. Local recurrence can occur even after a wide resection, with local recurrence rates after surgical treatment ranging from 10 to 80%.[7] Nevertheless, there is no ideal method for the treatment of inoperable DF. This case report describes the use of iodine-125 (^{125}I) interstitial brachytherapy for pediatric DF of the head and neck.

Report of Case

A 32-month-old girl was referred to the Department of Oral and Maxillofacial Surgery at the Peking University School and Hospital of Stomatology (Beijing, China) in June 2010. She presented with a left facial tumor of 1 month without a history of trauma or familial adenomatous polyposis. The tumor grew gradually, without complaint about pain, facial paralysis, hoarseness, or dyspnea. Physical examination showed that the mass was behind the left mandibular ramus and was approximately 4.0 × 3.0 cm^2 with an unclear

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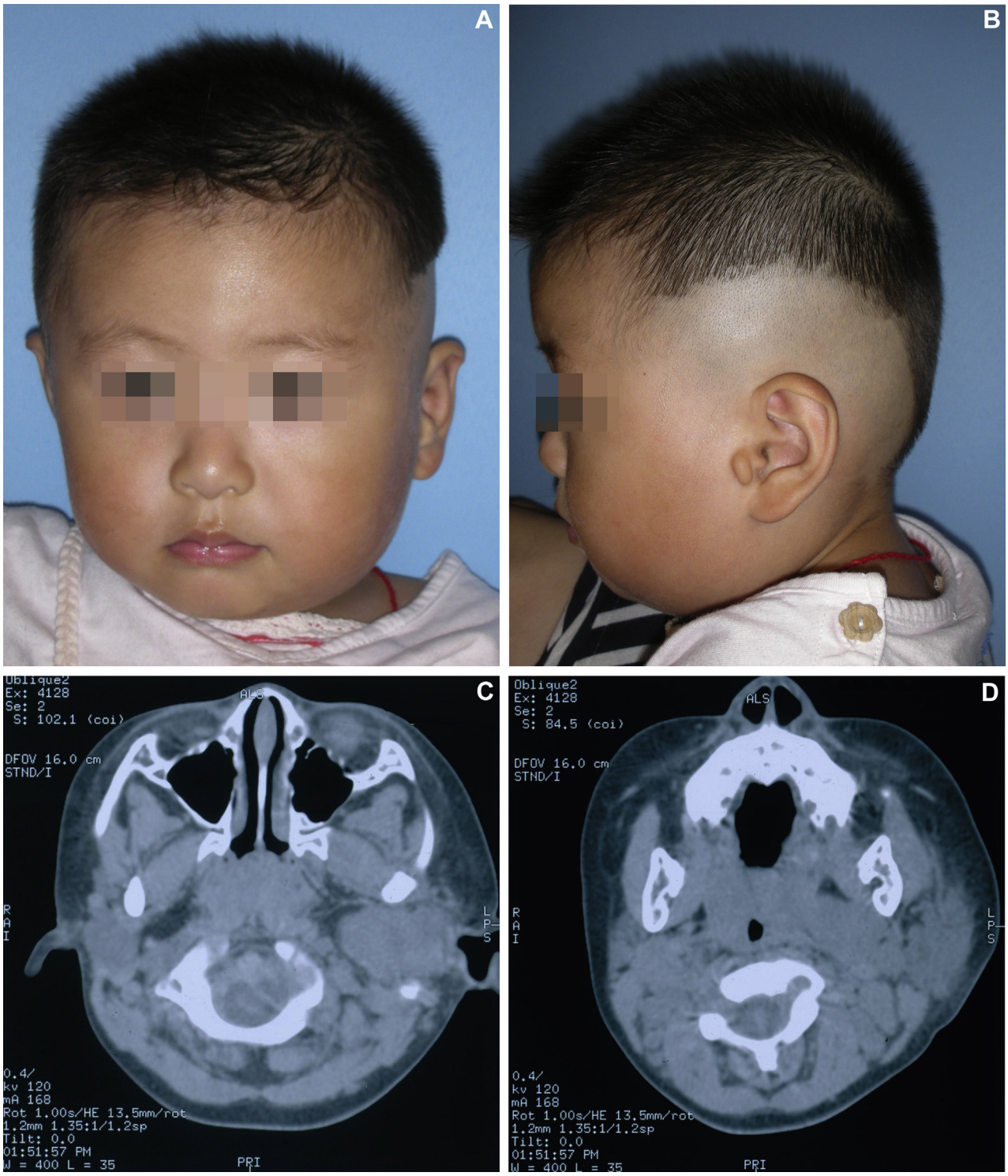

FIGURE 1. *A, B,* Photographs of the left parotid gland tumor before surgical treatment. *C, D,* Computed tomograms show the left parotid gland tumor before surgical treatment.

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border and poor mobility (Fig 1A, B). Movements of her facial muscles were normal and symmetrical and movements of her tongue, head, and shoulders were normal. A computerized tomographic (CT) scan showed that the left infratemporal fossa and the left parotid gland were filled by a lobulated and ill-defined soft tissue mass (4.0 × 4.0 × 2.3 cm; CT value, approximately 30 to 40 HU; Fig 1C, D). The upper boundary of the tumor was below the bone and chondral external auditory canal. Moreover, the tumor

occupied almost all the parotid gland and had expanded to the pharyngeal space, thus decreasing the pharyngeal space. The surrounding tissues were compressed, with the left sternocleidomastoid moving to the posterolateral side and the posterior belly of the digastric muscle moving to the inferior side. The left carotid artery and internal jugular vein also were compressed.

The patient was initially diagnosed with a left parotid gland tumor based on the previous evidence. Surgical treatment was performed. The incision started just before the left tragus, coursed vertically, and then extended to the submandibular region. Then, the tumor was exposed and was found to occupy the superficial and deep lobes of the parotid gland (Fig 2A). During the operation, the surgeons separated and protected the facial nerves from the tumor adhering to the nerves. The tumor was resected with gross residual tumors to avoid further damage to the normal tissue (Fig 2B). The final diagnosis based on the paraffin section was DF and the immunohistochemical staining showed negativity for S-100 and positivity for CD68 (Fig 2C, D).

The patient was followed carefully. However, 3 months after the operation, a recurrent tumor was found in the left face and left oropharynx. CT scan showed that the recurrent tumor was ill-defined and reoccupied the left parotid gland and the left parapharyngeal space (3.5 × 3 × 2 cm; CT value, 30 to 40 HU; Fig 3A, B). The recurrent tumor had expanded to the pharyngeal cavity, resulting in a narrowed oropharyngeal cavity. Magnetic resonance imaging (MRI) showed that the tumor exhibited low signal intensity on T1-weighted images and high signal intensity on T2-weighted images (Fig 3C, D). MRI also depicted the tumor adhering

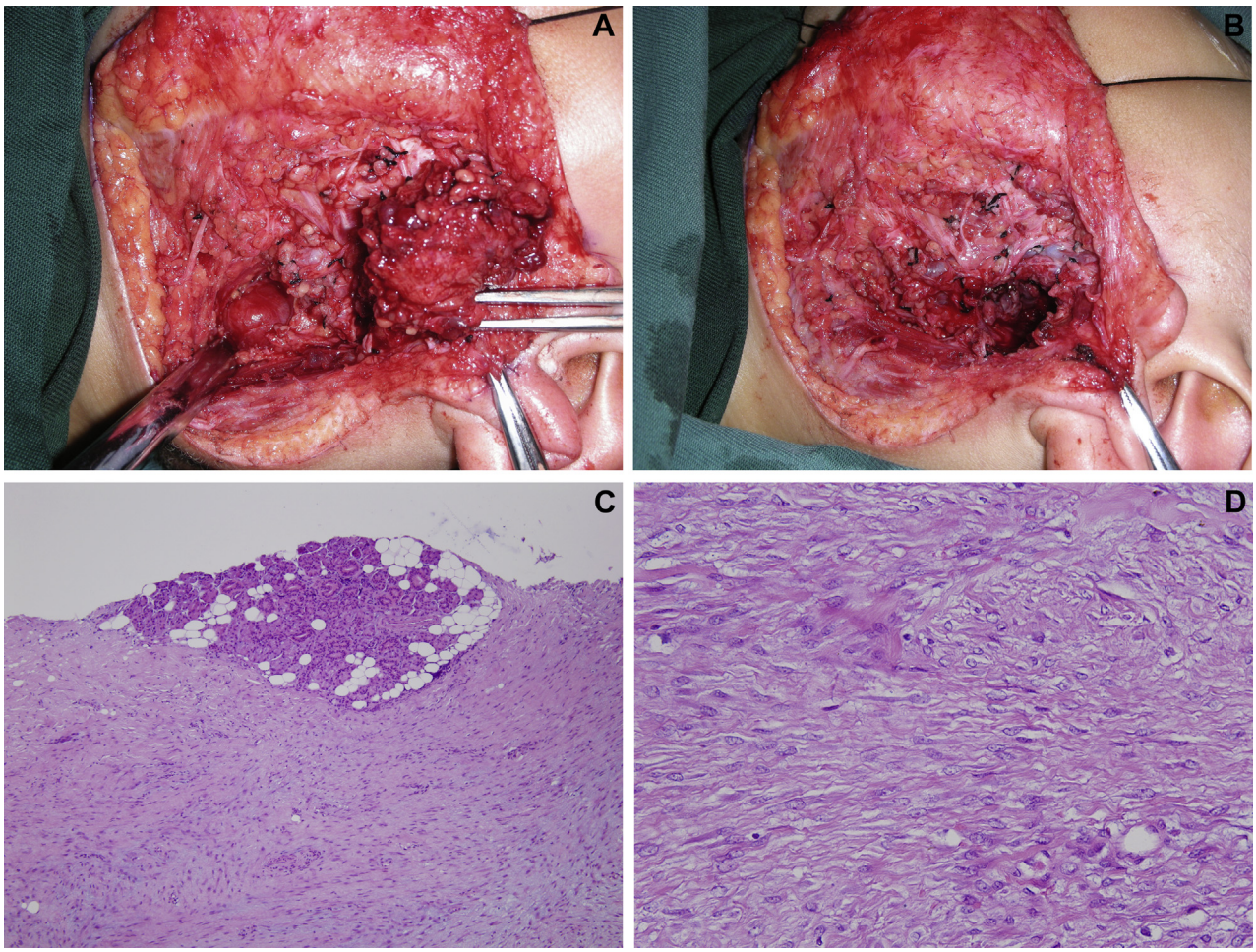

FIGURE 2. *A*, Exposure of tumor. *B*, Tumor resection and gross residual tumors during surgery. The pathologic diagnosis was desmoid-type fibromatosis based on the paraffin section, which showed that the tumor and surrounding glandular or muscular tissues had no clear margins. *C*, A high-resolution version of this slide for use with the virtual microscope is available (eSlide VM03102; hematoxylin and eosin stain; original magnification, ×100). *D*, A high-resolution version of this slide for use with the virtual microscope is available (eSlide VM03095; hematoxylin and eosin stain; original magnification, ×400).

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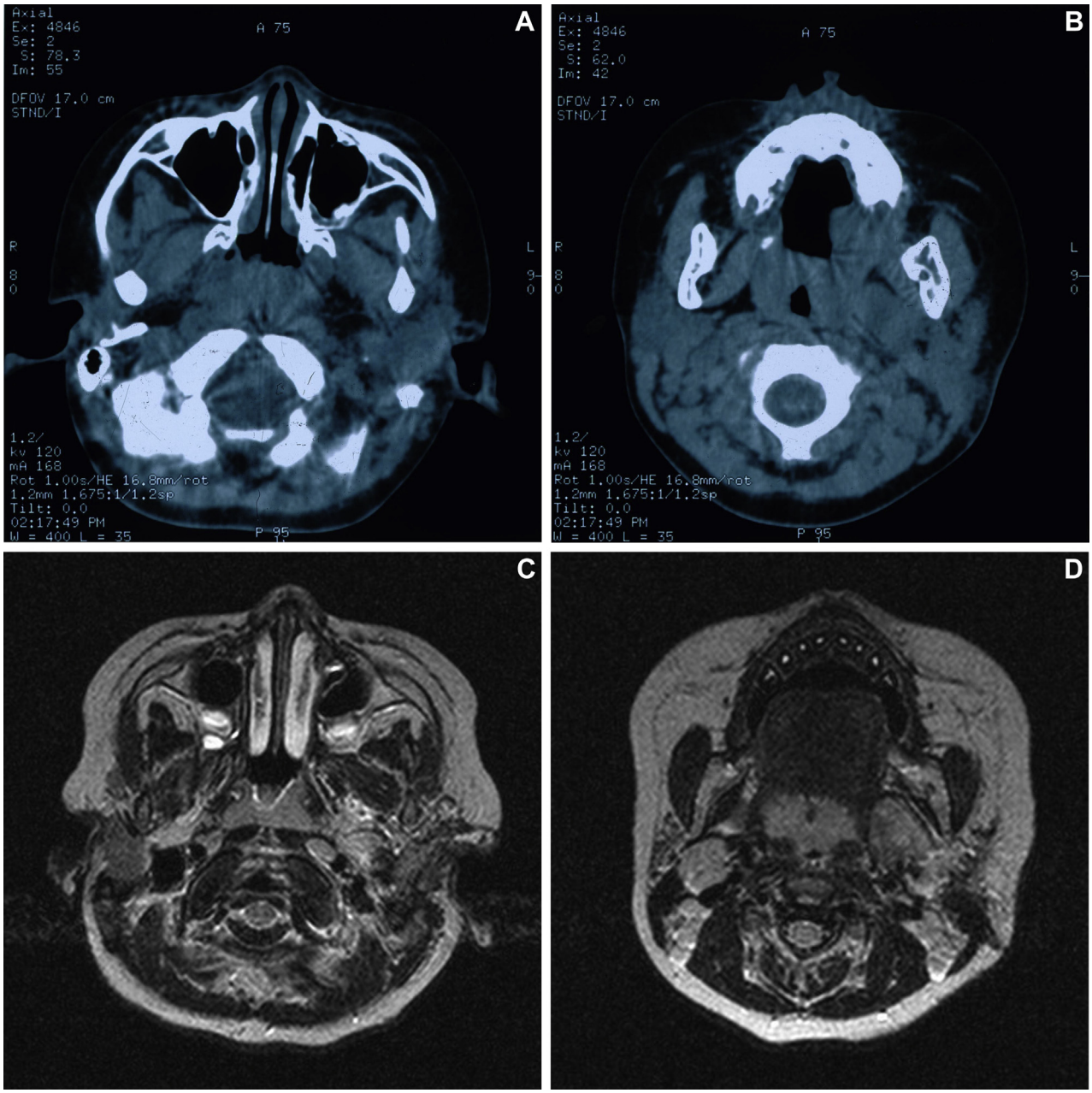

FIGURE 3. *A*, *B*, Computed tomograms show recurrent tumor 3 months after surgery. *C*, *D*, Magnetic resonance images show recurrent tumor 3 months after surgery.

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to the left internal jugular vein. In other words, the recurrent tumor was deeply located and close to important structures of the head and neck. Because of the complicated relation with the surrounding organs and deep location, complete resection with negative margins of the recurrent tumor was almost impossible, which could result in cosmetic deformity and possible recurrence. Moreover, because of the contraindication of external beam radiotherapy in younger pediatric patients, brachytherapy was planned.

Brachytherapy was performed with ^{125}I radioactive seeds (type 6711) that had a half-life of 59.4 days and a radioactivity of 22.2 MBq per seed. The preoperative plan and postoperative quality verification were performed using the Brachytherapy Treatment Planning System (BTPS; Beijing Atom and High Technique Industries, Inc, Beijing, China). The clinical target volume (CTV) was defined as the gross tumor volume and its surrounding area of potential subclinical disease or microscopic residual tumor, which was 0.5 to 1 cm beyond the margins of

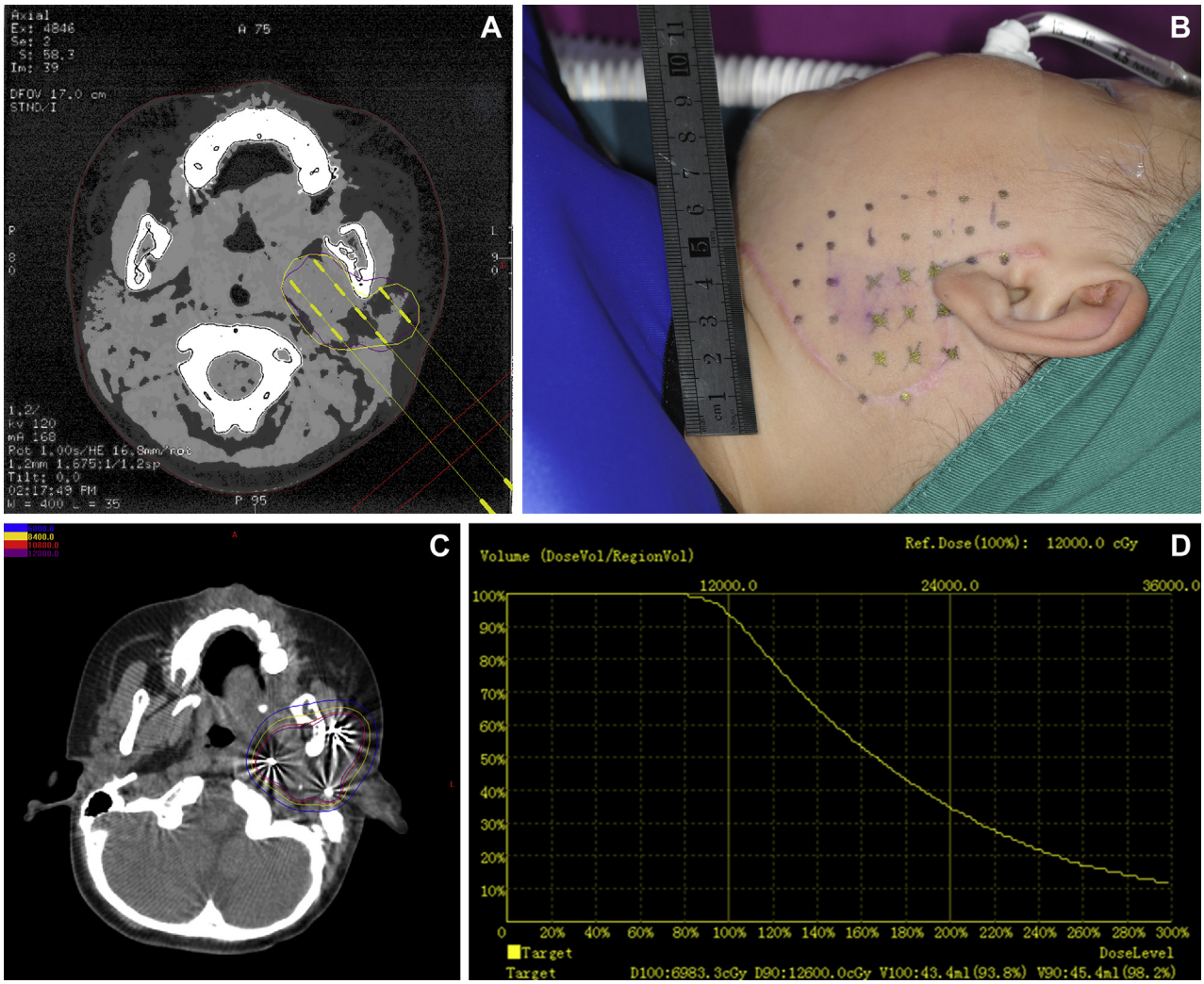

FIGURE 4. *A*, Preoperative plan using the Brachytherapy Treatment Planning System. *B*, Permanent implantation under general anesthesia was guided by computed tomography according to the plan. *C*, Postoperative quality verification using the Brachytherapy Treatment Planning System. *D*, Dose and volume histogram of quality verification.

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the tumor depending on the location (Fig 4A). A radiation dose of 120 Gy was prescribed for the CTV and calculated using the BTPS. During the operation, 54 ^{125}I seeds were implanted permanently 1 to 1.5 cm apart into the target area with CT guidance to avoid vital structures, including the carotid artery and the internal jugular vein (Fig 4B). The dose to 90% of the CTV for quality verification was 12,600 cGy and the percentage of the CTV that received the 100% isodose was 93.8% based on the BTPS (Fig 4C, D).

After brachytherapy, the patient was seen at 1, 2, 4, 6, 10, 12, 15, 18, 24, 30, 36, 48, and 60 months (Figs 5, 6). Toxicities associated with radiation were recorded and graded according to the grading system of the Radiation Therapy Oncology Group during follow-up. Two months after brachytherapy, physical examination and CT scan showed the tumor had regressed and that the pharyngeal cavity was wider than previously (Fig 7A, B). Six months after brachytherapy, physical examination and CT scan showed the tumor was completely absent and the oropharyngeal cavity was almost normal (Fig 7C, D). The patient developed an acute skin reaction of grade 1 and nonpurulent exudates of the left external auditory canal 1 month after brachytherapy. An acute skin reaction of grade 2 developed 2 months after brachytherapy, with less nonpurulent exudates of the external auditory canal. During follow-up, these signs gradually disappeared. Up to 10 months after brachytherapy, the skin reaction recovered to grade 0 and there was almost no exudate in the external auditory canal. No sign of tumor was observed during the 60 months of

FIGURE 5. Images show facial symmetry at *A*, 1, *B*, 6, *C*, 10, and *D*, 60 months after brachytherapy.

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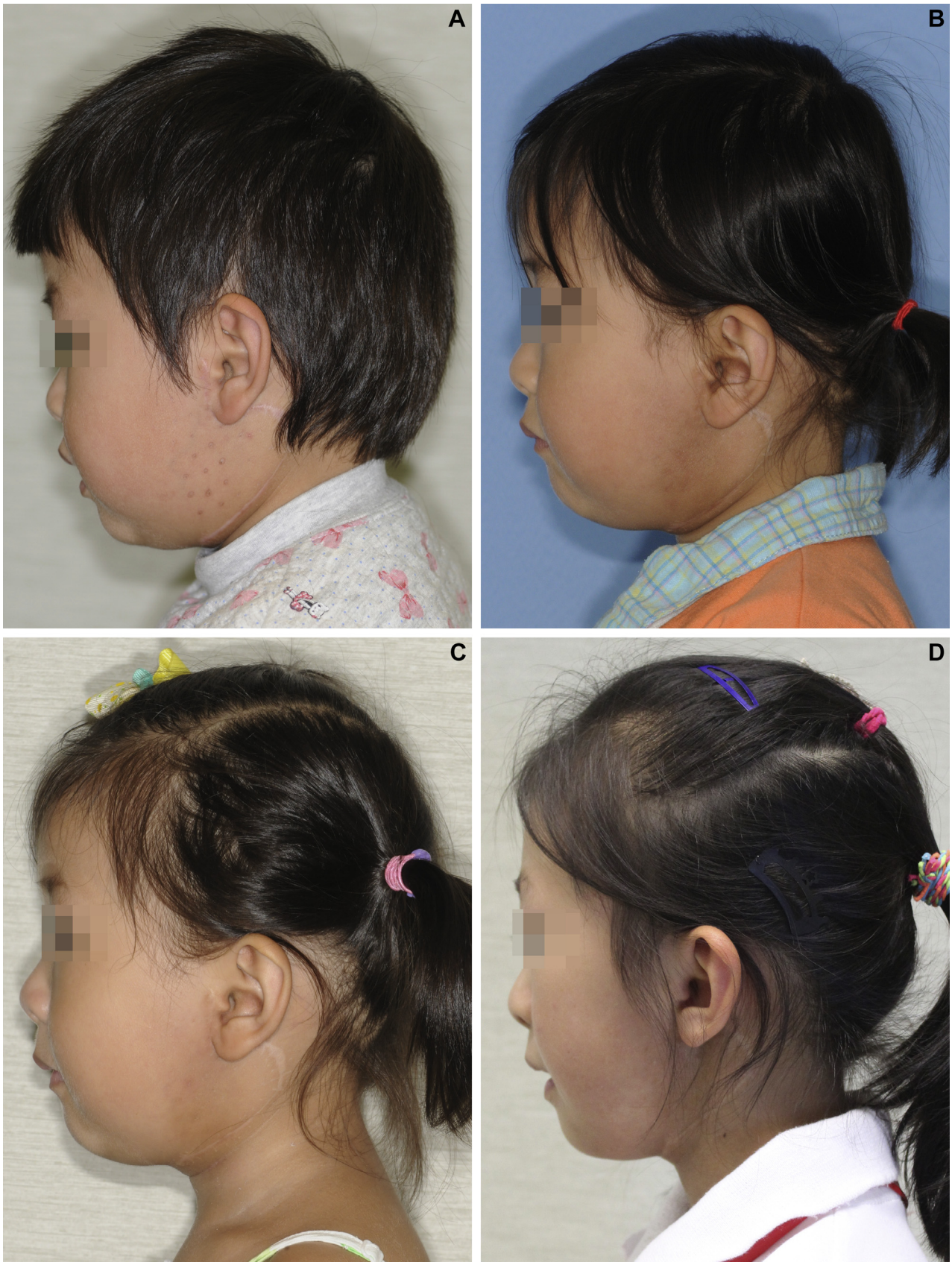

FIGURE 6. Images show facial profiles without severe side effects at *A*, 1, *B*, 6, *C*, 10, and *D*, 60 months after brachytherapy.

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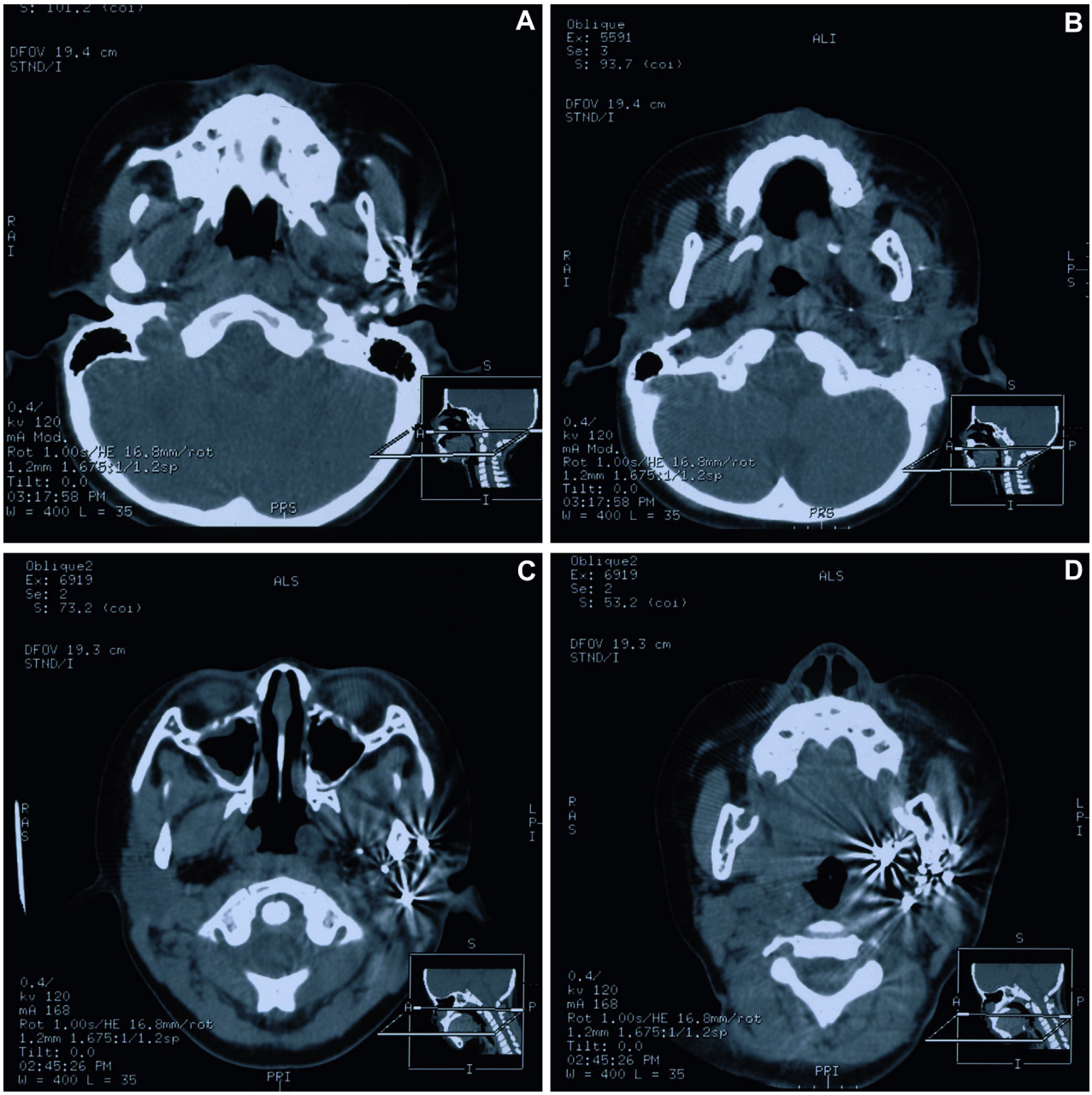

FIGURE 7. *A, B,* Two months after brachytherapy, computed tomograms show tumor regression and a wider pharyngeal cavity. *C, D,* Six months after brachytherapy, computed tomograms show no tumor and an almost normal oropharyngeal cavity.

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follow-up (Fig 8). There also were no symptoms or signs of facial paralysis.

Discussion

DF is a locally aggressive benign tumor that tends to involve the surrounding muscles, blood vessels, and nerve tissue. In addition, the clinical course of DF in pediatric patients can resemble that in adults.[7] Pediatric DF in the head and neck region is rare, whereas the overwhelming majority of tumors involve the mandible and then the neck.[3,8] Treatment remains a challenge in pediatric patients, especially in the head and neck region. The recurrence rate could be 19% after initial surgical treatment.[3] Different modalities have been adopted, such as surgery, radiotherapy, chemotherapy, and hormonal therapy. Surgery with negative margins is the mainstay of treatment for cases that can be completely resected, whereas radiotherapy is considered an adjuvant treatment for cases with positive margins or residual tumors.[3,9,10] Moreover, more

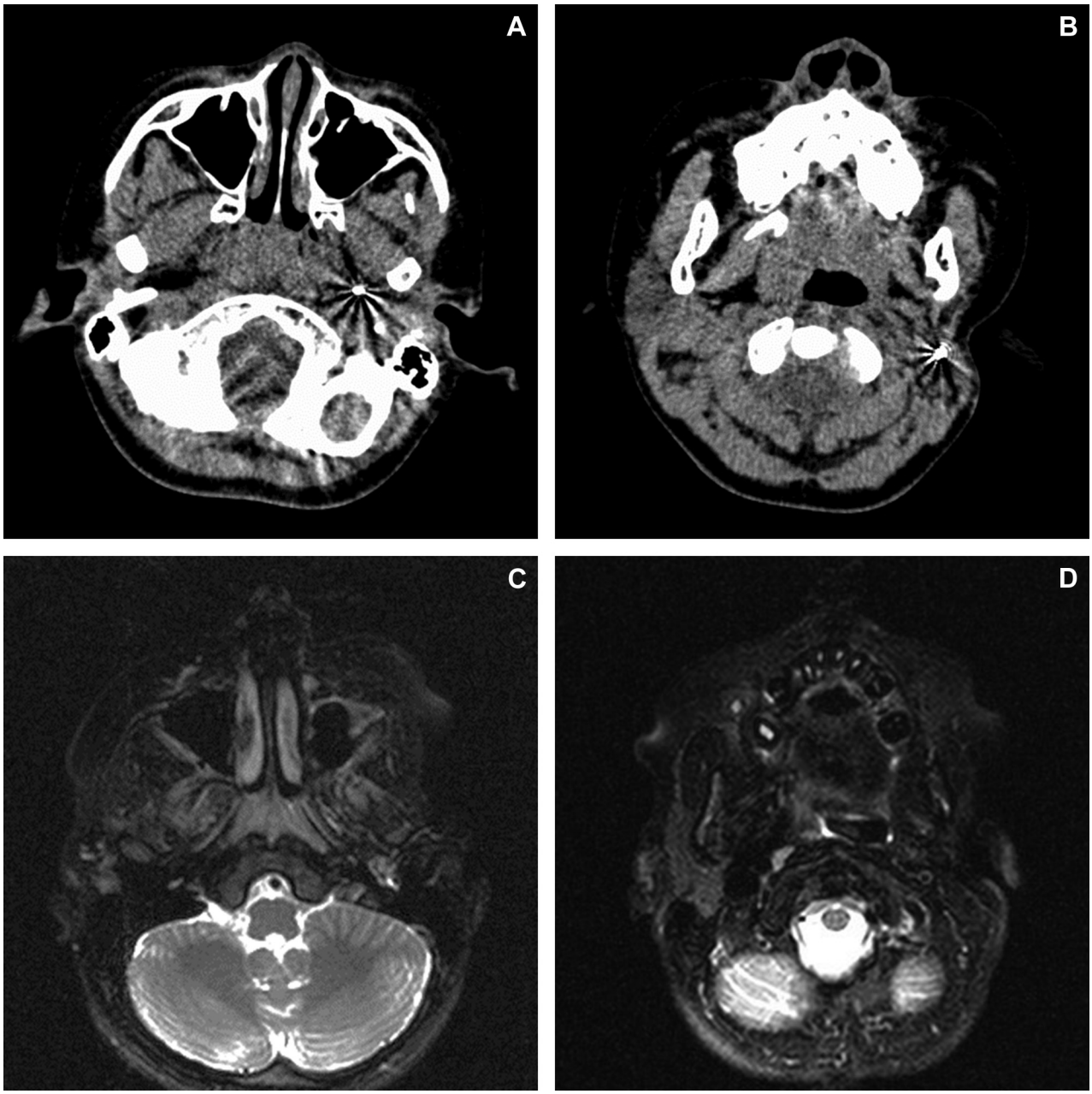

FIGURE 8. *A, B,* Computed tomograms show no sign of tumor 60 months after brachytherapy. *C, D,* Magnetic resonance images show no sign of tumor 60 months after brachytherapy.

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cases of failed local treatment have been reported when using chemotherapy and hormonal therapy. In contrast, certain asymptomatic patients with stable or regressed tumor can be carefully followed without active treatment.[11,12] The wait-and-see approach could be possible for certain patients.

Radiotherapy also is applicable as a sole modality for inoperable cases in which surgery would result in high morbidity. A comparative review of 22 articles by Nuyttens et al[13] concluded that local control rates were higher for surgery combined with radiotherapy and radiotherapy alone than for surgery alone. For cases treated with radiotherapy alone, the local control rate was 78%. A multicenter phase II trial reported that radiotherapy was an effective treatment of patients with DF of the trunk and extremities.[14] With a median follow-up of 4.8 years, the trial reported a 3-year local control rate of 81.5% for patients with inoperable DF treated with moderate-dose radiotherapy.

Chemotherapy is an alternative for inoperable DF, especially for recurrent cases. The application

of methotrexate and vinblastine to inoperable cases was first reported in 1989.[15] A phase II study by Azzarelli et al[16] found that 30 inoperable cases treated with low-dose methotrexate and vinblastine showed a 67% 10-year actuarial progression-free interval (follow-up, 75 months). Other regimens, such as pegylated liposomal doxorubicin, also were reported to be effective and with acceptable toxicities.[17] Almost 1 in 2 patients with DF was likely to respond to cytotoxic chemotherapy.[18] Moreover, the toxicity of low-dose chemotherapy was far lower than that of standard-dose chemotherapy, which also might be appropriate for pediatric patients with benign tumor. Hormonal agents, such as antiestrogens and aromatase inhibitors, were applied to patients with DF alone or in combination with nonsteroidal anti-inflammatory drugs, and the overall response rate varied.[18] Hormonal therapy was less toxic, but only certain patients showed a response. Overall, high-level evidence, such as randomized clinical trials, to support the role of chemotherapy or other therapy for DF is lacking. Systemic treatments should be considered in relation to efficacy versus toxicity.

The present case of pediatric DF of the head and neck was treated with very low-dose rate (VLDR) brachytherapy. The tumor showed a locally aggressive pattern and relapsed 3 months after initial surgical treatment with gross residual tumors. Positive margins after surgery indicated a high risk for disease recurrence.[5,10] In contrast, Gluck et al[19] concluded that there was no clear association between surgical margin status and local control and that tumor of the head and neck predicted a higher risk for recurrence.

There are some reports on brachytherapy for DF, but most concern high-dose rate brachytherapy. Furthermore, few articles on brachytherapy for DF of the head and neck have been published. Fontanesi et al[20] reported on 6 cases of extra-abdominal DF treated with afterloaded iridium-192 (^{192}Ir) or manually loaded californium-252 brachytherapy alone and treatment failed in 3 cases. Thus, they did not advocate the application of brachytherapy alone. In contrast, Schmitt et al[21] reported that radiotherapy for 24 cases of DF, 2 of which received irradiation with ^{192}Ir implantation alone, achieved a 75% 10-year recurrence-free survival rate. Similarly, Assad et al[22] reported on 14 patients with DF who underwent surgery and brachytherapy with temporary ^{192}Ir afterloading or permanent ^{125}I implantation, and 10 were free of recurrence at a follow-up longer than 2 years. As a modality of radiotherapy, brachytherapy seemed to be effective against DF.

Most early toxicities of radiotherapy include delayed wound healing, dermatitis, myositis, wound infection, and dehiscence. Late toxicities of radiotherapy can occur in the pediatric population and include skin fibrosis, decreased mobility of joints receiving radiation, and increased risk of fracture.[23] The pediatric population has the additional side effects of growth and developmental abnormalities. Brachytherapy has the advantage of providing a high dose of radiation to the CTV and delivering a lower dose to the surrounding normal tissue. When used as first-line treatment for certain pediatric malignancies, brachytherapy increases local control with a decrease in the probability of toxicities compared with external beam radiotherapy.[24]

Because of locally aggressive growth patterns, there are challenges in the treatment of DF and a multidisciplinary approach is necessary. To the authors' knowledge, this is the first case of ^{125}I interstitial brachytherapy for pediatric DF of the head and neck. VLDR brachytherapy as the sole modality could be a reasonable alternative for the treatment of inoperable DF of the head and neck, which avoids the risk of cosmetic deformity caused by surgery, especially in pediatric patients. In addition, long-term follow-up is recommended.

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