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Percutaneous sclerotherapy of juvenile nasopharyngeal angiofibroma using fibrin glue combined with OK-432 and bleomycin

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ABSTRACT

The purpose of this study was to determine the appropriate conditions for percutaneous sclerotherapy of juvenile nasopharyngeal angiofibroma using fibrin glue combined with OK-432 and bleomycin. Three patients with juvenile nasopharyngeal angiofibroma were treated with an injection of fibrin glue combined with OK-432 and bleomycin. No major complications occurred in any of the patients. The follow-up period ranged from 12 to 14 months. The following outcomes were obtained: one lesion was completely involuted and two lesions were mostly involuted. All of the patients had normal liver and kidney function. Additionally, none of the patients presented with hematologic toxic effects or signs of pulmonary involvement. Percutaneous sclerotherapy using fibrin glue combined with OK-432 and bleomycin provided a simple, safe, and reliable alternative treatment for juvenile nasopharyngeal angiofibroma.

Juvenile nasopharyngeal angiofibroma (JNA) is a benign tumor of the nasopharynx composed of fibrous connective tissue and an abundance of endothelium-lined vascular spaces [1]. The tumor is characterized by slow progression, aggressive growth, high vascularization and increased rate of persistence and recurrence. Although JNA is usually located in the nasopharynx, it tends to spread to the anterior nasal cavity and maxillary sinus, lateral pterygoidal region, temporal and infratemporal fossae [2], superior orbital fissure, and middle base of the skull [3]. Surgical resection is the most common primary treatment, although chemotherapy and radiotherapy are recommended as other possible options [1]. In 2009, we reported on the use of fibrin glue combined with OK-432 and pingyangmycin for percutaneous sclerotherapy of massive venous malformations of the face and neck [4]. This study was conducted to determine the appropriate conditions for percutaneous sclerotherapy of JNA using fibrin glue combined with OK-432 and bleomycin.

1. Patients and methods

Between October 2007 and January 2008, three male patients with JNA were admitted and treated at the Department of Oral and Maxillofacial Surgery of the Second Affiliated Hospital of Sun Yat-sen University, Guangzhou, China. The Institutional Review Board (IRB) of Sun Yat-sen Hospital has already approved this entire study. Their ages ranged from 16 to 21 years. The diagnoses were based on general characteristics of the patients, and presenting signs and symptoms included abnormalities of the facial contour (Fig. 1), nasal obstruction, epistaxis, headache, and findings of radiologic examinations such as computed tomography (CT) scans (Fig. 2) and three-dimensional CT angiography (Fig. 3). According to the staging system of Radkowski, all of the patients were classified as stage IIA and IIC (Table 1).

Preoperative embolization was not performed in any of the patients. Patients with JNA were treated under general anesthesia with percutaneous sclerotherapy by an injection of fibrin glue (Guangzhou Bioseal Co., Ltd., Guangzhou, China) combined with OK-432 (streptococcal pyrogenic exotoxin A; Shandong Lukuang Pharmaceutical Group, Luya Co., Ltd., Jinan, China) and bleomycin (Nipponkayaku Co., Ltd., Tokyo, Japan).

The components of the fibrin glue were packaged in separate bottles that contained 50–75 mg of freeze-dried fibrinogen powder, 10–70 U of blood coagulation-factor XIII, a solvent containing 6.8 mg of potassium dihydrogen phosphate for the main gel, 400 IU of freeze-dried thrombin powder for the catalyst, and solvent for the catalyst containing 40 mmol calcium chloride. The fibrin glue was packaged in a kit with two syringes. The fibrinogen, blood coagulation-factor XIII, and buffering solution containing potassium dihydrogen phosphate were loaded into syringe A. The thrombin and calcium chloride solution were loaded

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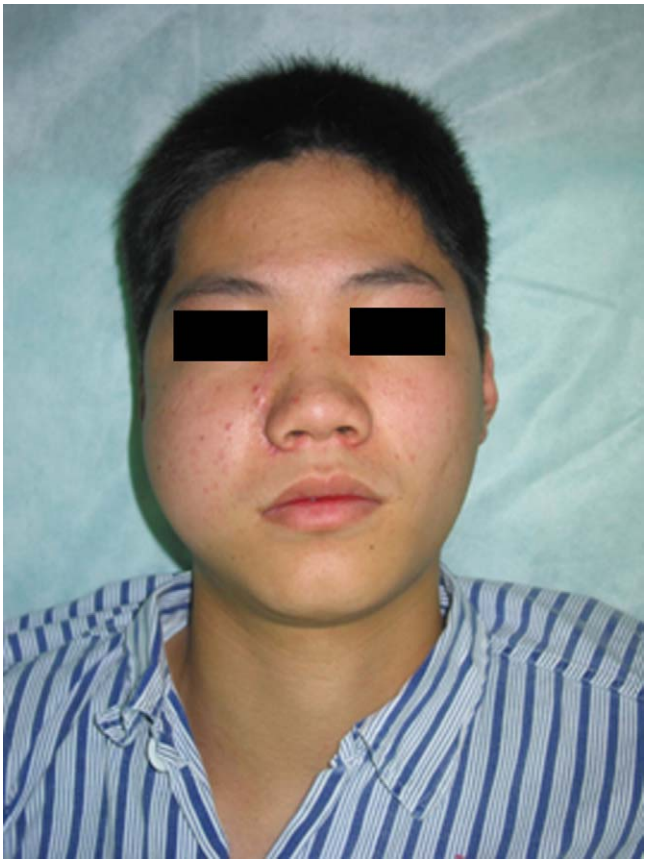

Fig. 1. A 16-year-old boy presented with abnormalities of the facial contour.

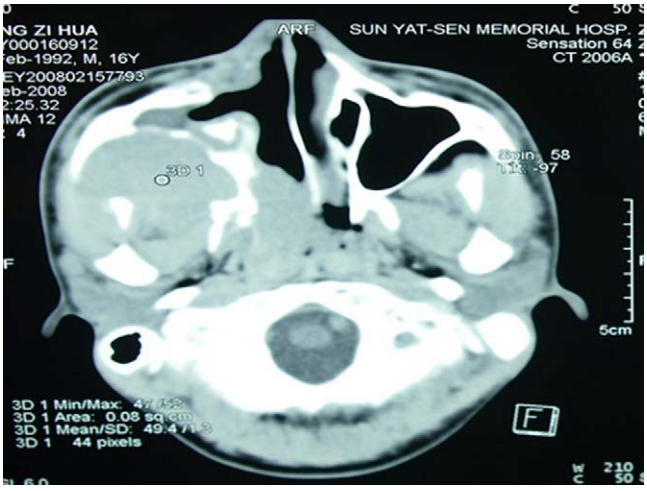

Fig. 2. Coronal views on computed tomography scans revealed a large well-defined nasopharyngeal mass extending into the right nasal cavity with widening of the pterygopalatine fossa laterally.

into syringe B. The fibrin glue was formed by mixing the contents of syringe A and syringe B, and a total of 20 ml was produced.

The injected solution including OK-432 or bleomycin was prepared by diluting lyophilized OK-432 to a concentration of 1 mg (1 KE; '*klinische Einheit*', clinical unit) in 1 ml of normal saline (NS) and lyophilized bleomycin to a concentration of 15 mg in 2 ml NS. Then, 0.5 ml of the OK-432 solution was added to syringe A, and 1 ml (7.5 mg) of the bleomycin solution was added to syringe B. The reagents in the two syringes, which were fitted with 18-gauge needles, were simultaneously injected into the lesions. The needle

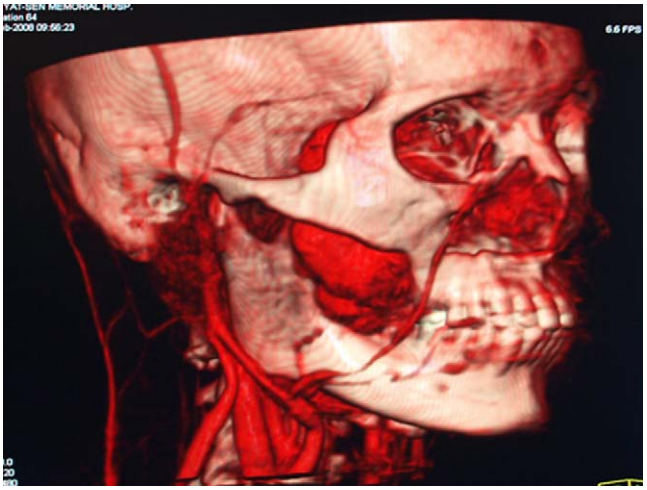

Fig. 3. Three-dimensional computed tomographic angiography revealed a large well-defined nasopharyngeal mass extending into the right nasal cavity with widening of the pterygopalatine fossa laterally.

was introduced through normal skin and advanced into the lesions. Once the lesion was identified, the percutaneous sclerosant along with the fibrin glue containing OK-432 and bleomycin was injected into the lesions at 3–4 sites from several directions (Fig. 4). Intravenous dexamethasone (0.1 mg/kg) and NS (60 ml/kg) were given for 3 days postoperatively.

All of the patients were given an injection of the percutaneous sclerotherapy using the fibrin glue (20 ml) combined with OK-432 (4 mg) and bleomycin (30 mg) in a single sclerotherapy procedure. The injections, which were performed every 5–6 weeks, were repeated three times and administered to all patients under general anesthesia on an inpatient basis. The total doses of fibrin glue, OK-432, and pingyangmycin were 60 ml, 12 mg, and 90 mg, respectively (Table 1). All patients had a preoperative CT scan and follow-up CT scan 12–14 months after surgery.

The outcome was assessed by a panel of three surgeons, and the response rate was graded as follows: complete involution implying a >90% reduction in size, mostly involuted implying a reduction in size of 75–90%, a partial involution implying a reduction in size of 50–75%, a small involution implying a reduction in size of 25–50%, and non-involution implying a reduction in size of <25% [4].

2. Results

All the patients had moderate swelling postoperatively for a period of 2–3 weeks with no major complications. The mean follow-up was 12.6 months, with a range of 12–14 months. Obvious improvements were seen in the facial contour abnormalities. The patients' symptoms, including nasal obstruction, epistaxis, and headache, disappeared. The following outcomes were obtained: one lesion was completely involuted (Figs. 5 and 6) and the other two lesions were mostly involuted. None of the patients experienced a recurrence, or presented with hematologic toxic effects or signs of pulmonary involvement such as pulmonary fibrosis or pulmonary embolism. All of the patients had normal liver and kidney function based on a blood chemistry analysis, and normal liver and kidney function and normal lung fields based on chest X-ray.

3. Discussion

JNA is a tumor for which surgery is often complicated by the possibility of hemorrhage. The most common surgical approaches used to treat this tumor are the midfacial degloving, the lateral