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CASE REPORT

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A painful large ganglion cyst of the ankle treated by the injection of OK-432

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Abstract Despite its benign nature, a ganglion can be problematic. We successfully treated a patient with large painful ganglion in his ankle by OK-432 (lyophilized incubation mixture of group A *Streptococcus pyogenes* of human origin) injection. OK-432 injection seems to be a safe, convenient, and effective alternative to surgical treatment for either symptomatic or recurrent ganglia.

Key words Ganglion · OK-432 · Sclerotherapy

Introduction

Ganglia are common and benign tumoral conditions in soft tissue. If ganglia are developed in the foot or ankle, they can be problematic. Both the pain and mass effect associated with the cystic space can make wearing shoes difficult. There is a multitude of existing therapies and complications including painful scaring and nerve damage, and recurrences are also not uncommon.[1,2] Recently Tanaka et al. successfully treated a patient demonstrating symptomatic small ganglions of the big toe with OK-432 (lyophilized incubation mixture of group A *Streptococcus pyogenes* of human origin).[3] Although the mechanism of action of OK-432 has not been clearly explained, it has been used as a therapeutic agent for immunotherapy in patients with malignant tumors. The injection of this agent intrathoracically and intraperitoneally to reduce fluid accumulation has been effective particularly in patients with malignant pleural effusions and ascites. Injection of OK-432 causes the induction of inflammatory cells, such as neutrophils, macrophages, and lymphokine activated killer cells, and probably induces a slow process of fibrosis.[4–7] We have successfully treated one large ganglion of the ankle with OK-432 injections.

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Case report

A 55-year-old man presented with a recurrent ganglion cyst of the left ankle joint. During the 3-year period before presentation, the mass had been treated more than 10 times by aspiration. He reported mild pain and difficulty in wearing shoes. On physical examination, a large soft mass measuring 8 × 6 cm was found in the lateral aspect of the left ankle. The skin color was normal. Magnetic resonance imaging revealed a well-circumscribed soft tissue mass without any evidence of bone involvement (Fig. 1). Although the patient was offered surgical treatment, he opted to continue undergoing nonsurgical therapy.

We decided to treat the patient with OK-432 after obtaining his written informed consent. After administering local anesthesia to the skin, a 15-ml gelatinous content was aspirated using an 18-gauge needle with a disposal syringe (Fig. 2A,B). This was followed by the injection of 0.05 mg of OK-432 (Picibanil; Chugai Pharmaceutical, Tokyo, Japan) in 2 ml of normal saline (Fig. 2C). Thereafter, temporary pyrexia (38°C), mild pain, and redness of the skin on the ganglion were noted 24 h after the injection, and this lasted for 3 days. A subsequent shrinking of the lesion was achieved. After 2 weeks of injection, his complaints, including mild pain and difficulty in wearing a shoe, were totally resolved. There was no evidence of skin damage or effects on surrounding vital structure. Ten months after the injection of OK-432, the cyst recurred. After 10 ml of gelatinous content were again aspirated, a second injection using a higher dose (0.1 mg dissolved in 2 mal of normal saline) was administered. No significant complications occurred after this injection. A subsequent shrinking of the lesion was also achieved. One year after the second injection, the patient remains free from symptoms and there has been no recurrence of the cyst (Fig. 2D).

Discussion

Ogita et al. reported the intralesional injection of OK-432 as an alternative treatment for lymphangioma in 1987.[5] OK-432 is a sclerosing agent consisting of lyophilized powder containing the *Streptococcus pyogenes* strain treated with benzylpenicillin potassium. It stimulates several immunocompetent cells and induces the production of multiple cytokines.[4–7] This sclerosing treatment is much easier than surgery, leaves no scar, and carries no risk of causing nerve damage, and it should therefore be considered as the primary method of treatment for lymphangioma.[7]

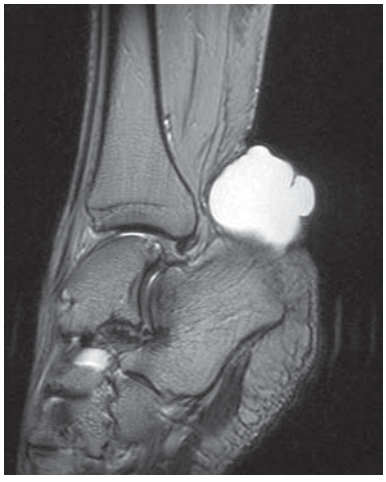

Fig. 1. T2-weighted magnetic resonance image showing cystic tumor around the ankle joint

Although little information is available regarding the management of ganglion cysts on the foot and ankle, one series reported a 43% recurrence rate after surgery on these regions. The surgical management of cysts after recurrence also tends to be more difficult than the initial treatment, thus resulting in increased postoperative pain, high rates of recurrence, and lower patient satisfaction.[1,2]

Some trials of conservative treatment for ganglia with aspiration and the injection of steroids has been reported.[8,9] Varley et al. found no difference in the success rate of aspiration alone or aspiration and injection of steroids (both with success rate of 33%).[9] Carp and Stout showed that ganglion resolved in over half of their cases after 3 years.[10] However, Varley et al. reported that almost all ganglia that recurred after one aspiration did not resolve with further aspirations.[9] Conservative treatment for recurrent and symptomatic ganglion, whether it be that of steroid injections with aspiration of the lesions or use of orthotic devices, will only offer temporary comfort and at best, may retard further development of the cyst.[2] Tanaka et al. reported excellent results with OK-432 sclerosing therapy for recurrent symptomatic ganglia of the hallux after surgical treatment.[3] Although two of four ganglia recurred after the injection of OK-432, an additional injection of OK-432 resulted in a complete cure of the recurrent ganglia. They considered that OK-432 induced inflammatory response in ganglion cyst and induced regenerative process to adhere the cystic space. All ganglia of Tanaka's report were very small. Sclerotherapy for ganglia using sodium tetradecyl disulfate had been previously reported, success rates varying from 100% to 6%.[11,12] Up to now we have been unable to use this agent in Japan.

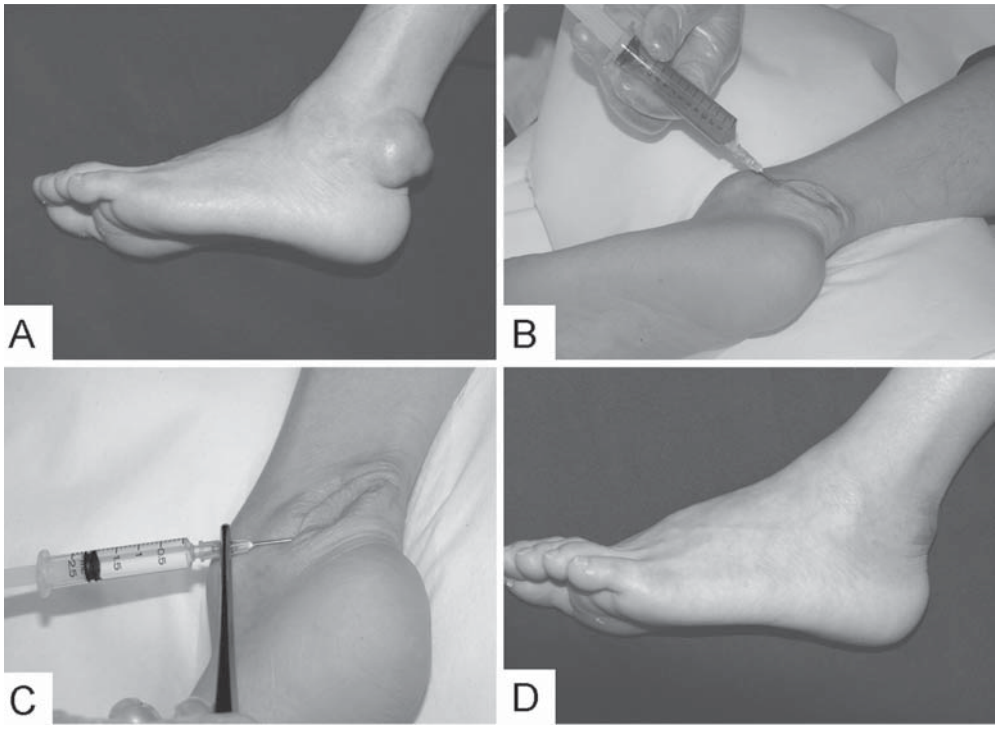

Fig. 2. **A** Photograph showing a large ganglion on the left ankle. **B** Photograph showing the aspiration of gelatinous material. **C** Photograph showing the injection of 0.05 mg of OK-432 in 2 ml of normal saline into a ganglion cyst. **D** Photograph showing the disappearance of the ganglion 6 at months after the OK-432 injection

Recently, Taniguchi et al. reported good results of 57 ganglia treated with OK-432 injection.[13] Pain and fever for several days were the only complications observed, and 56.6% of cases had complete cure. In their report, there was no complication around the injected soft tissue or adjacent joint. Although they did not report the size of ganglia, our case indicated that a large ganglion could be successfully treated with OK-432 injection. On postmarketing surveillance, the side effects of OK-432 were reported as shock (0.05%) and fever (21.9%). Shock seems to be associated with the penicillin that is used in extraction.[13] Therefore OK-432 is contraindicated for those patients with penicillin allergy. Even considering the risk of recurrence, we feel OK-432 injection is a safe and convenient alternative to surgical treatment for symptomatic or recurrent ganglia.

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