Intralesional Fluorouracil Injection in Infantile Digital Fibromatosis

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The Cutting Edge: Challenges in Medical and Surgical Therapeutics

REPORT OF A CASE

A 7-year-old Korean girl presented with an 8-month history of an erythematous hard plaque on her left hand. There was no history of trauma. On physical examination, a 1.4 × 0.8-cm firm plaque was observed on the ulnar surface of the left hand at the metacarpophalangeal level (Figure).

Histopathologic examination showed moderately cellular fibroblasts throughout the dermis. Hematoxylin-eosin staining revealed eosinophilic intracytoplasmic inclusion bodies in fibroblasts. The inclusions stained bright red with Masson trichrome and deep purple with phosphotungstic acid–hematoxylin. They were negative for alcian blue and periodic acid–Schiff.

THERAPEUTIC CHALLENGE

In the past, infantile digital fibromatosis (IDF) was considered potentially malignant, leading to amputation of affected digits.1 However, reported cases of spontaneous regression suggest a more benign biologic behavior, and metastases have never been reported.1-3 Therefore, a conservative approach is now advocated. However, deformities of the affected digits have developed in a number of untreated cases, with functional impairment after regression of tumor.1-3 Moreover, up to 60% of cases recurred even after standard wide local excision.1-2 Thus, an effective, nonsurgical treatment with low morbidity is desirable.

SOLUTION

We treated the lesion with 5 monthly intralesional injections of fluorouracil. At each session, undiluted fluorouracil (50 mg/dL) was injected into the lesion using a 30-gauge needle without any local or general anesthesia. At each treatment, the total 10 mg (0.2 mL) of fluorouracil was injected at 2 or 3 sites. Systemic adverse effects were not observed, and local adverse effects included only pain on injection. Partial response was noted after 1 injection, and the lesion regressed with flattening after 5 injections (Figure). No recurrence was noted during a 2-year follow-up period.

Figure. Plaque on the ulnar surface of the left hand. A, Well-defined erythematous firm plaque before treatment. B, One month after first injection. C, One month after second injection. D, Seven months after fifth injection.
Infantile digital fibromatosis is a rare benign fibrous tumor that develops on the fingers and toes of infants and children. In this case, intralesional injection of fluorouracil was effective in inducing regression of IDF. Fluorouracil, a pyrimidine analogue with antimetabolite activity, is widely used in cancer chemotherapy. Interestingly, it inhibits dermal fibroblast proliferation and collagen synthesis in cell culture. Recently Wendling et al demonstrated that fluorouracil inhibited transforming growth factor β-induced type I collagen synthesis through the inhibition of transforming growth factor β–SMAD–driven COL1A2 transactivation in human fibroblasts.

Fluorouracil has previously been used to reduce scarring. In the early 1980s, it was investigated as an adjunct to glaucoma-filtering surgery, as failure of glaucoma filtration surgery often occurred as a result of scarring at the surgical site. In 1999, Fitzpatrick reported his 9-year experience with the use of intralesional injection of fluorouracil for the treatment and prevention of inflamed hypertrophic scars and keloids. Favorable responses were noted in most patients. The best responses were obtained with scars that were very red, symptomatic, inflamed, and indurated. Old, uninflamed, asymptomatic scars did not respond very well. Keloids responded, but frequently recurred. Fitzpatrick’s success has been confirmed by others. Uppal et al reported that a single application of fluorouracil solution after extralesional excision of keloids resulted in significant reduction of scar size and recurrence. Gupta and Kalra further demonstrated the efficacy of intralesional fluorouracil as an individual therapeutic agent for the treatment of small keloids. They reported that approximately half of the patients showed more than 50% flattening of the treated keloid. Although hypertrophic scars, keloids, and IDF express different clinical phenotypes, they share myofibroblastic features on histologic examination. These similarities may explain our success with intralesional injections of fluorouracil.

The safety of fluorouracil as an adjunct to glaucoma-filtering surgery in children has also been established. We used 10 mg of fluorouracil as an intralesional dosage according to previous keloid therapies. Although this dosage of fluorouracil is much lower than tolerable intralesional doses, careful attention needs to be paid to both short- and long-term safety in children. The common adverse effects of intralesional fluorouracil treatment were pain, purpura, ulceration, burning sensation, and pigmented disturbance. The main disadvantages of fluorouracil treatment were pain and the need for repeated injection. Therefore, another alternative technique, such as topical fluorouracil application after excision surgery or shave removal, might also be useful to minimize these disadvantages. Nevertheless, intralesional fluorouracil injection appears to be a safe, effective treatment for IDF that warrants further investigation.

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