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Single Case

Efficacy and Safety of Intralesional Methotrexate in the Treatment of a Large Keratoacanthoma of the Dorsal Hand in a 99-Year-Old Woman

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Keywords
Keratoacanthoma · Intralesional methotrexate · Squamous cell carcinoma

Abstract
Several case reports and retrospective studies have demonstrated that intralesional methotrexate (MTX) could be a very effective and safe alternative treatment of keratoacanthoma (KA). Here, we report a rapid clinical efficacy of two intralesional MTX injections (total dose 40 mg) that were performed 1 week apart in the treatment of a large KA lesion of the dorsal hand in a 99-year-old woman. The lesion, with a 3-cm major axis diameter and a thickness of 2 cm with a central ulceration had rapidly appeared on the right dorsal hand. A 3-mm punch biopsy confirmed the diagnosis of a well-differentiated KA-type spinous cellular carcinoma. Due to the presence of comorbidities (arterial hypertension and atrial fibrillation) and chronic treatment with antihypertensive and oral anticoagulant drugs, treatment with intralesional MTX was proposed to the patient. Two intralesional MTX injections of 20 mg each were performed 1 week apart. A very fast resolution of the lesion was observed after the first injection. A week after the second injection a full resolution of the skin lesion was observed, with a nearly complete resolution of the central ulceration. The treatment was very well tolerated. No local or systemic side effects were observed. This case report confirms that intralesional MTX could be considered an effective and safe treatment of KA also in very old subjects.

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Introduction

Keratoacanthoma (KA) is a fast-growing cutaneous tumor, which commonly occurs as solitary lesion [1]. KA is generally considered a well-differentiated squamous cell carcinoma, and it is characterized by rapid growth and possible spontaneous involution [2]. This skin tumor is common in elderly subjects. Some KAs could exhibit aggressive behavior leading to metastasis and death [3]. Standard excision, Mohs excision, curettage, and electrodesiccation represent first-choice treatment options [4]. However, invasive procedures could have several contraindications or limitations, mainly in the very old [5]. Several case reports and retrospective studies have demonstrated that intralesional methotrexate (MTX) could be a very effective and safe alternative treatment of KA, mainly in elderly patients with multiple comorbidities [6]. Here, we report the rapid efficacy of two intralesional MTX injections (total dose 40 mg) that were performed 1 week apart in the treatment of a KA lesion of the dorsal hand in a 99-year-old woman.

Case Description

A 99-year-old woman with an 8-month history of a rapidly growing skin lesion on the right dorsal hand presented for a dermatological consultation. The lesion appeared as a nodule with a major axis of 3 cm and a minor axis of 2 cm in diameter, with a thickness of 2 cm and a central ulceration (Fig. 1a). A 3-mm punch biopsy confirmed the clinical diagnosis of a well-differentiated KA-type spinous cellular carcinoma. No significant liver or renal dysfunctions were present at the moment of the first clinical visit. However, due to the presence of concomitant diseases (arterial hypertension and atrial fibrillation) and chronic treatments with antihypertensive and oral anticoagulant drugs, resulting in a postprocedure high hemorrhagic risk, a treatment with intralesional MTX was proposed to the patient. A first 20-mg MTX injection (total volume of 0.5 mL; Velos™, Cantabria Labs Difa Cooper) was performed. The drug was injected using a 30-gauge needle into four quadrants of the base of the tumor and at the central lesion. A second injection was performed 1 week apart following the same procedure. A rapid resolution of the nodular lesion was observed soon after the first injection. After 2 months, there was a complete healing of the lesion (Fig. 1b). The treatment was very well tolerated. No local or systemic side effects were observed. No modification of blood formula was detected 1 month after the last intralesional MTX injection.

Discussion

KAs are skin tumors classified as well-differentiated squamous cell carcinoma [7]. The most common clinical presentation is a rapidly growing, well-demarcated nodular lesion. These kinds of tumors are common in elderly subjects, with a peak incidence between 60 and 70 years of age, especially in sun-exposed areas [8]. Typical locations are the face, neck, and dorsal hands. The lesion erupts rapidly, and it is often tender. The rapidly growing phase could be followed by an involution phase [2]. In the past, KAs were believed to be benign lesions. They are now considered as a variant of well-differentiated squamous cell carcinoma [3]. Some KAs could have aggressive behavior, leading to metastasis and possible death. For this reason, KAs should be treated as squamous cell carcinoma [9]. The option of surgical excision could be limited or contraindicated in some cases by the high morbidity associated with the

procedure and the required extensive surgical reconstruction [10]. Due to the fact that KA is common in elderly subjects, concomitant diseases or concomitant pharmacological treatments (i.e., drugs influencing the hemostasis) could represent relative or absolute contraindications to invasive treatment strategies such as surgery, Mohs surgery, and curettage. Topical 5-fluorouracil [11] and intralesional MTX [12] have been successfully used when invasive strategies are contraindicated or when cosmetically sensitive areas are involved. In scientific literature, several case reports and retrospective studies [13–15] have demonstrated that intralesional MTX could be a very effective and safe alternative treatment of KA. The pharmacological rationale of the use of this molecule is that MTX inhibits DNA synthesis in actively dividing cells [16, 17]. Pregnancy, active infections, liver diseases, and blood dyscrasias are contraindications for the use of MTX [18]. Looking at the published data, the use of intralesional MTX in KA has been reported in more than 50 subjects aged between 53 and 90 years [13–15]. In these patients, MTX was in general use with an average of 2.1 injections with an average cumulative dose of 38.2 mg. Intralesional MTX injections were spaced 22 days. A complete response was achieved in more than 80% of the treated subjects [15]. In general, the treatment is well tolerated. Two cases of pancytopenia have been reported in these case series [15], but they have been observed in subjects with concomitant renal diseases. Pancytopenia could be observed soon after the first MTX injection [19]. The average age of subjects treated with intralesional MTX in these reports was 72 years (range 44–90).

Conclusion

This case report confirms that intralesional MTX could be considered an effective and safe treatment of KA also in the very old.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

M.M. is an employee of Cantabria Labs Difa Cooper, Caronno Pertusella, Italy.

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Fig. 1. **a** Lesion at the initial visit. **b** Two months after the intralesional MTX injection.