POSSIBLE SYSTEMIC ADVERSE EFFECTS IN CLOSTRIDIUM HISTOLYTICUM COLLAGENASE (CCH) TREATMENT OF DUPUYTREN’S CONTRACTURE

Moritz Scholtes, Joachim Ganser
Department for Hand- and Plastic Surgery, Kantonsspital Münsterlingen, Switzerland

INTRODUCTION
Treatment for Dupuytren’s contracture in one or more finger rays with Collagenase Clostridium Histolyticum (CCH) becomes increasingly popular. With the last 4-7 years experience, also adverse effects are being reported. These are local and systemic ones, as well as allergic or non-allergic ones. As Dupuytren’s contracture is a localized disease (even in its manifestation as Morbus Ledderhose or Peyronie disease) and in itself not life-threatening, this study’s focus was set on systemic adverse effects possibly threatening the patient’s life or general medical condition.

MATERIALS AND METHODS
63 patients were treated for Dupuytren’s contracture in one or more finger rays by injection of CCH between November 2014 and September 2017. Since January 2017, the majority of patients received two concurrent doses of CCH. A retrospective study was performed based on patient charts, complete photo documentation and a subjective questionnaire. Initial follow-up was performed until 6 weeks post injection. Patients were contacted in September 2017 and invited to clinical follow-up.

Besides local complaints after CCH injection, the questionnaire focused on general complaints and observations in the extremity and whole body: pain, swelling, ecchymosis, weakness, fever and shivering, dizziness, distress, abnormalities in urine and faeces, psychological distress, and even any medical consultation (and its reason) days or weeks after the CCH injection.

RESULTS
Of the 63 patients, 47 (75%) returned the questionnaire and 17 (27%) followed invitation to clinical follow-up.

Adverse effects, mainly seen within 2 days after injection, included either isolated or in combination: extensive ecchymosis up to the axilla and even two distant ecchymoses (eyelid and other hand; see Figures 1-3), severe aseptic inflammation of the lymphatics, headache, pain in all extremities, chill, and dizziness. These complaints lasted up to 2 weeks. 1 frozen shoulder after CCH injection into the ipsilateral hand took 8 months to heal. 1 pulmonary embolism from a deep venous thrombosis of the lower leg occurred 3 weeks after injection (see Figure 5). A bilateral basal pneumonia in an otherwise healthy and active patient, retrospectively diagnosed as probable pulmonary embolism, occurred 6 weeks after injection. 1 patient with known coronary heart disease died 6 weeks after injection, the cause of death was not further investigated.

DISCUSSION
As a clearly visible effect, at least the local and distal ecchymosis after Collagenase Clostridium Histolyticum (CCH) injection could be related to affection of the vascular wall or to a disturbance of the blood coagulation system. Pulmonary embolism and unexpected death several weeks after injection can possibly be explained.

Most of the adverse effects were not related to allergic reactions. On the other hand, the nature, the extent and the degree of the adverse effects was not related to the amount of CCH (one or two doses). Nevertheless, patients afflicted by a more severe adverse effect were not offered a second or third CCH injection of another or recurrent Dupuytren cord. Confronted with the major adverse effects we saw after CCH injection, we would like to propose further research regarding its systemic effects on vessels and the coagulation system. Regarding the high recurrence rate in our personal experience with CCH injection therapy and the yet unexplained adverse effects (figure 6), we are currently reconsidering treatment recommendations for our patients.

CONTACT
joachim.ganser@stpg.ch
+41 (0)71 686 29 65

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