Diffuse punctate keratitis in a patient treated with cetuximab as monotherapy

A 62-year-old man without any prior particular ophthalmologic history was treated with chemotherapy [cisplatin and 5-fluorouracil (5-FU)] combined with weekly cetuximab from April 2005 till September 2005 for a local recurrence of squamous cell cancer of the oropharynx. After six cycles, a confirmed partial response (Response Evaluation Criteria in Solid Tumors) was documented and chemotherapy was stopped. Weekly cetuximab continued. From December 2005 onward the patient had increasing complaints of a decreased visual acuity of the left eye. There was no mentioning of any pain.

On 15 February 2006 the patient was examined by the ophthalmologist, who described small epithelial punctate lesions covering the entire surface of the left cornea (Figure 1A), limiting the visual acuity to 0.5. The right cornea was completely normal. Shirmer test without anesthesia was normal in both eyes, suggesting a normal tear production. The corneal sensibility was reduced when compared with the sensibility of the right cornea. Artificial hyaluronic acid containing eye drops were prescribed but as patient remarked no improvement of the visual acuity, he stopped this treatment.

Repeat photographs and examination of the cornea on 19 April 2006 were virtually unchanged as compared with 15 February (Figure 1B).

The patient had only slight trichomegaly of the eyelashes, certainly having no connection with the corneal lesion.

On 3 May 2006, progression of the tumour was documented and cetuximab was discontinued. Thereafter, the cornea lesions gradually decreased in number and almost completely disappeared within 5 weeks (Figure 1C). He resumed with chemotherapy (docetaxel, cisplatin, 5-FU) in combination with cetuximab on 14 June 2006. After 6 weeks, his visual acuity decreased again and keratitis reappeared (Figure 1D). Now also his right eye was affected.

The finding of cornea lesions possibly related to treatment with cetuximab should not be a complete surprise as at least two members of the epidermal growth factors receptor (EGFR) family are known to play an important role in the cornea healing process [1–3].

Ocular side-effects have been described in patients treated with the EGFR downstream pathway inhibitor gefitinib [4]. Cetuximab has been reported to cause trichomegaly of the eyelashes [5]. We are unaware of cases of cetuximab-linked keratitis in the literature.

Shah et al. [4] suggested to check patients under treatment with gefitinib for excessive eyelash growth and to refer them to an ophthalmologist in case of symptoms of corneal irritation. Our suggestion is to extend this advice to patients treated with cetuximab and to consider cornea lesions also in patients with decreased visual acuity, even without pain.

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references


Figure 1. Fluorescence photographs of the cornea. The small green dots represent punctate corneal lesions.

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