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Nakamura, S. ; Kajita, S. ; Takagi, A. ; Hashimoto, Y. ; Ishida
–Yamamoto, A. ; Takahashi, H. ; Iizuka, H.

Improvement in docetaxel-induced nail changes associated with cyclooxygenase-2 inhibitor therapy

Satoshi Nakamura*,**, Satoshi Kajita**, Akiyoshi Takagi**, Yoshio Hashimoto*, Akemi Ishida-Yamamoto*, Hidetoshi Takahashi*, Hajime Iizuka*.

*Department of Dermatology, Asahikawa Medical College, Asahikawa, Japan

**Takagi Dermatological Clinic, Obihiro, Japan

Reprint requests to; Satoshi Nakamura, M. D., Department of Dermatology, Asahikawa Medical College, Midorigaoka Higashi 2-1-1-1, Asahikawa, Hokkaido, Japan

Postal code. 078-8510

Phone. +81-166-68-2523

Fax. +81-166-68-2529

E-mail. namu@asahikawa-med.ac.jp

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Docetaxel is a semi-synthetic chemotherapeutic drug from the European Yew (*Taxus baccate*) and belongs to the family of taxoids. Nail changes related to taxoids have been reported ¹⁻³⁾, where a neurological mechanism was suggested ²⁾. We used selective cyclooxygenase (COX) 2 inhibitor (meloxicam) for docetaxel-induced nail changes with favorable results. This is the first report of the beneficial effect of meloxicam for taxoids-induced severe nail changes.

A 50-years-old Japanese woman referred to our clinic with a two-week history of nail pain and subungual haemorrhage. She had advanced breast cancer (Stage III) and had been under six courses of docetaxel therapy (60mg/kg every 3weeks). At the time of dermatological examination, her finger and toe nails showed painful subungual haemorrhage, paronychia and partial onycholysis. In view of a recent report showing a beneficial effect of COX inhibitor for docetaxel-induced nail changes ²⁾, we started a selective COX2 inhibitor (meloxicam, 10mg/day). Although her nail changes with marked onycholysis progressed for 6-weeks following the meloxicam therapy (Fig. 1-a), they gradually improved with pinkish nail beds and normal growing nails. Skin culture was positive for *Acinetobacter species*, the significance of which remains unknown. Meloxicam therapy was continued and all the mails returned normal at 20-weeks (Fig. 1-b). Docetaxel therapy of every 3-weeks were continued with no remarkable nail changes.

Taxoids-induced nail changes including onycholysis, nail bed haemorrhage, nail pain, and paronychia occurs in about 0-44% of cases ³⁾. Many therapeutic modalities, which include topical corticosteroid, antibiotics, and sunlight screening, had been used

with little or no benefit ^{1,2)}. Although on theoretical grounds, clipping of the nails or the use of iced gloves might be expected to be useful, there are no reports of these approaches being employed. Recently, nociceptive C-fibre-mediated neurogenic inflammation and sympathetic inflammation were proposed for the mechanism of taxoids-induced nail changes ²⁾. Beneficial effect of COX inhibitors, which prevent prostaglandin-dependent inflammation, has also been suggested. In fact, diclofenac (150mg/day) was shown to be effective for the nail changes ²⁾. Diclofenac shows a low to moderate preference to inhibit COX2. Because COX2 is expressed on inflammatory cells, and in order to minimized the gastrointestinal side effects of COX, we used the selective COX2 inhibitor, meloxicam, in this case with favorable results.

Several recent reports suggest the relation between taxoids and COX2. Preliminary studies showed enhanced anticancer activity by the addition of COX2 inhibitors to taxoids treatment ⁴⁾. Taxoids also induce COX2 by stimulating transcription and by stabilizing mRNA ⁵⁾. Our case highlights the possibility that meloxicam could be beneficial for the taxoids-induced nail changes. The addition of COX2 inhibitor might be recommended for the potentiation of therapeutic efficacy of taxoids as well as for the prevention of adverse side effects including nail changes.

References

- 1 Vanhooteghem O, Richert B, Vindevoghel A, Vandenbossche L, Vandeveire A, de la Brassinne M : Subungual abscess: a new ungual side-effect related to docetaxel therapy. Br J Dermatol 2000 ; **143**: 462-464.
- 2 Wasner G, Hilpert F, Schattschneider J, Binder A, Pfisterer J, Baron R : Docetaxel-induced nail changes – a neurogenic mechanism: a case report. J Neuro-Oncol 2002 ; **58**: 167-174.
- 3 Minisini AM, Tosti A, Sobrero AF, Mansutti M, Piraccini BM, Sacco C, Puglisi F : Taxane-induced nail changes: incidence, clinical presentation and outcome. Ann Oncol 2003 ; **14** : 333-337.
- 4 Olsen SR : Taxanes and COX-2 inhibitors: from molecular pathways to clinical practice. Biomed Pharmacother 2005 ; **59**: Suppl2:S306-10
- 5 Subbaramaiah K, Marmo TP, Dixon DA, Dannenberg AJ : Regulation of cyclooxygenase-2 mRNA stability by taxanes: evidence for involvement of p38, MAPKAPK-2, and HuR. J Biol Chem 2003 ; **278**: 37637-47

Legends to Figures

Figure 1-a.

The sixth week. Bilateral fingernails show subungual haemorrhage, abscess, and paronychia.

Figure 1-b.

The 20th week. All finger nail beds show pinkish color and become flat. Note the tips of the nails, which had been floated, are fractured.

(a)



(b)

