Onycholysis Associated with Weekly Administration of Paclitaxel

Stefanie M Flory, Dominic A Solimando Jr, Guy F Webster, Charles J Dunton, Julia M Neufeld, and Mary B Haffey

OBJECTIVE: To report an unusual reaction associated with weekly administration of paclitaxel.

CASE SUMMARIES: Onycholysis was seen in four women with recurrent ovarian cancer being treated with low-dose, weekly paclitaxel. Two of the patients had previously received higher doses of paclitaxel on an every-three-week schedule without similar reactions. Onycholysis developed between weeks 10–13 of treatment in three of the patients. In the fourth patient, it developed shortly after initiation of weekly paclitaxel. None of the reactions required dose adjustments or discontinuation of therapy. Direct toxicity to the nail bed or inhibition of angiogenesis are possible mechanisms for this reaction.

DISCUSSION: Onycholysis, separation of the nail from the nail bed, is an infrequent adverse effect of drug therapy. Antineoplastic drugs have previously been reported to cause onycholysis, pigmentation, bands, thickening or thinning of the nail bed, and nail shedding. Nail changes with the taxanes, primarily docetaxel, are reported in up to 30–40% of patients. Paclitaxel is not commonly associated with dermatologic reactions, although localized skin reactions and tissue necrosis have been reported. Nail changes, pigmentation or discoloration of the nail bed, occur in 2% of patients receiving paclitaxel.

CONCLUSIONS: Onycholysis is an uncommon reaction that may occur in some patients receiving weekly, low-dose paclitaxel therapy. The reaction is not life-threatening and does not warrant discontinuation of therapy. However, clinicians should be aware of the possibility of this effect and be prepared to advise patients who develop signs of nail changes.

KEY WORDS: onycholysis, paclitaxel.

CASE REPORTS

CASE 1
A 50-year-old African-American woman was diagnosed with advanced, low malignant potential ovarian cancer at age 25 and initially treated with whole abdominal radiation. She developed recurrent disease, which was treated with multiple courses of chemotherapy (including melphalan, megestrol, tamoxifen, alretamine, etoposide, topotecan, gemcitabine). In 1997 she began weekly infusions of paclitaxel 80 mg/m² (130 mg). Concomitant medications included gabapentin, furosemide, potassium supplementation, and transdermal fentanyl. After 11 weeks of paclitaxel treatment, the patient developed purpuric nail beds followed by onycholysis. She continued on the weekly paclitaxel regimen and developed no further similar reactions.

CASE 2
A 57-year-old white woman with a history of breast cancer diagnosed in 1991, which was treated with lumpectomy, radiation, and chemotherapy, was diagnosed with ovarian cancer in 1995. She received numerous chemotherapeutic regimens, including paclitaxel, cisplatin, tamoxifen, etoposide, and topotecan, for her ovarian cancer. Treatment with weekly infusions of paclitaxel 80 mg/m² (115 mg) began in May 1997. Concomitant medications included filgrastim and epoetin alfa. After receiving paclitaxel for 13 weeks, the patient reported nail bed purpura that led to onycholysis. The patient experienced this reaction on the right forefinger, middle finger, little finger, and left thumb. The patient was referred to a dermatologist for further evaluation. The dermatologist prescribed a two-week course of therapy with ciprofloxacin. The patient continued to be treated with weekly paclitaxel with no further complications.

CASE 3
A 55-year-old white woman with recurrent ovarian cancer, diagnosed in May 1993, was previously treated with numerous antineoplastic agents, including cisplatin, paclitaxel, etoposide, doxorubicin, cyclophosphamide, tamoxifen, topotecan, and carboplatin, prior to receiving weekly paclitaxel 80 mg/m² (120 mg). Filgrastim was the only other medication that the patient was taking. After 13 weeks of treatment, the patient reported changes in the nail and oozing of blood, which led to a bruised appearance in the fingernails and nail beds of both great toes. Paclitaxel was discontinued for 16 weeks. Due to an increasing CA125 concentration, suggesting progressive disease, paclitaxel was discontinued and single-agent cisplatin therapy began in January 1998. Her nails subsequently grew back without further complications.

CASE 4
A 65-year-old white woman with ovarian cancer diagnosed in February 1992 had a three-year history of progressive systemic sclerosis. Recurrent ovarian cancer was diagnosed in 1995, and she was treated with paclitaxel, tamoxifen, and topotecan. With subsequent progression of the ovarian cancer, she was begun on weekly paclitaxel 80 mg/m² (120 mg). Concomitant medications included penicillamine, vitamins, omeprazole, gabapentin, and furosemide. According to the patient, onycholysis developed on the fingernails shortly after beginning weekly paclitaxel. The patient continued to receive 23 cycles of weekly paclitaxel until January 1998.

Discussion
Antineoplastic drugs have previously been reported to cause reactions such as onycholysis, pigmentation, bands, thickening or thinning of the nail bed, and nail shedding. The patients described here experienced nail bed purpura, followed by pus formation and onycholysis. None had reported nail changes prior to therapy with paclitaxel. Three patients experienced the reactions on the fingernails, while one patient experienced this reaction on both finger- and toenails. Two patients were referred to a dermatologist and one sought the attention of a dermatologist on her own. All patients received the same pretreatment regimen prior to paclitaxel administration (dexamethasone, cimetidine, diphenhydramine, ondansetron).

The reactions were not dose limiting and none of the patients required a change in therapy as a result of the reaction. There was a similarity in the time course of the reaction in three of the patients, with an onset of the reaction at approximately 12 weeks from the beginning of treatment. The reactions gradually resolved over several weeks and did not require discontinuation of therapy.

The risk of developing nail reactions may be related more to the dosing interval than to the dose administered. Despite paclitaxel’s widespread use, onycholysis has not been reported when higher doses are given on a three- to four-week schedule. The two patients previously treated with paclitaxel did not develop the reaction until they started weekly therapy. One possible mechanism for this reaction may be direct toxicity to the nail bed. An alternative is inhibition of angiogenesis, a crucial process in wound healing and tumor growth. Such impaired healing may have caused these reactions. The premedications were unlikely to be responsible for the reactions since an extensive literature search failed to identify similar reactions reported for these medications. Additionally, this regimen has not been associated with this reaction when used with other paclitaxel regimens. Our experience indicates that this reaction is not life-threatening and does not warrant discontinuation of therapy. To our knowledge, this is the first report of onycholysis following administration of paclitaxel.

References
Quatre femmes atteintes d’ónicólisis se desarrolló entre la décima a la decimotercera semana de tratamiento, y en la cuarta paciente se desarrolló al principio del inicio del tratamiento. Ninguna de las reacciones requirió que se descontinuara o que se modificaran las dosis. Los mecanismos posibles de esta reacción pueden ser toxicidad directa a la matriz de la uña o inhibición de angiogénesis.

**DISCUSIÓN:** O Nicoleís, la separación de la uña del lecho ungual, es un efecto secundario poco frecuente. Se ha informado previamente de drogas antineoplásicas que causen onicólisis, pigmentación, bandas, engrosamiento o adelgazamiento del lecho ungual, y mudada de la uña. Se ha informado de cambios en las uñas en hasta 30–40% de pacientes a los que se les ha administrado taxanos, principalmente docetaxel. El paclitaxel no se ha asociado comúnmente con reacciones dermatológicas, aunque sí se ha informado de reacciones localizadas en la piel y de necrosis de tejido. Cambios en las uñas (pigmentación o descoloración) ocurren en el 2% de pacientes bajo tratamiento con paclitaxel.

**CONCLUSIONS:** Onicólisis es una reacción poco común que puede ocurrir en algunos pacientes que reciben paclitaxel semanalmente y en dosis bajas. Esta reacción no es amenazante para la vida, y no requiere que se descontinue la terapia. Los clínicos deben estar al tanto de la posibilidad de este efecto y prepararse para aconsejar a los pacientes que desarrollen cambios en las uñas.

**RÉSUMÉ**

**OBJECTIF:** Rapporter une réaction rare associée à l’administration hebdomadaire de paclitaxel.

**RÉSUMÉ DES CAS:** Quatre femmes atteintes d’un cancer ovarien récurrent qui ont été traitées avec du paclitaxel hebdomadaire à faible dose ont présenté de l’oncholyse. Deux des quatre patientes avaient reçu antérieurement des doses élevées de paclitaxel à toutes les trois semaines sans réaction similaire. L’oncholyse s’est développée entre la dixième et la treizième semaine de traitement chez trois des quatre patientes, tandis qu’elle est apparue “peu de temps” après le début du paclitaxel hebdomadaire chez la quatrième patiente. Aucune de ces réactions n’a nécessité un ajustement de la dose ou un arrêt du traitement. Les mécanismes possibles de cette réaction indésirable sont une toxicité directe au niveau des ongles ou une inhibition de l’angiogénèse.

**DISCUSSION:** L’onycholyse, qui se défini par la separation spontanée de l’ongle et de la pulpe unguaire, est un effet indésirable rare des médicaments. Certains antineoplastiques ont déjà été associés à des altérations au niveau des ongles, notamment une pigmentation des ongles, un épaississement ou un amincissement des ongles, la chute des ongles, et l’onycholyse. Pour ce qui est des taxanes, principalement le docetaxel, des changements au niveau des ongles sont rapportés chez 30–40% des patients qui en reçoivent. Le paclitaxel n’est généralement pas associé à des réactions dermatologiques malgré le fait que des réactions cutanées localisées et des nécroses tissulaires ait été rapportées. Des altérations des ongles (pigmentation ou décoloration de la pulpe unguaire) surviennent chez 2% des patients recevant du paclitaxel.

**CONCLUSIONS:** L’onycholyse est une réaction peu fréquente pouvant survenir chez certains patients recevant un traitement hebdomadaire de paclitaxel à faible dose. Puisque cette réaction ne met pas la vie du patient en danger, un arrêt du traitement n’est généralement pas nécessaire. Toutefois, les cliniciens devraient être conscients de la possibilité d’une telle réaction afin d’en aviser leurs patients.

**Luz Labrada-Ravelo**

**Esthel Rochefort**