
CASE REPORT



Imipenem Induced Dental Stains

Carrie Ku and Donna O'Neill

INTRODUCTION

We present three cases of suspected imipenem-induced staining of teeth. A MEDLINE literature search did not yield any previously reported cases but enquiries to Merck Sharp & Dohme did reveal that they had received 19 reports on this adverse effect. Since 1986, between zero and four reports have been received each year. Fifteen reports were from the United States, one from Belgium, two from France, and one from Germany.

In the 19 cases reported to the company, tooth discoloration occurred in nine males and nine females (the sex of one patient was not identified) ranging in age from six to seventy-seven years old. The onset of discoloration occurred in less than one week in three patients, between the second and fourth weeks of therapy in three patients, after more than one month in one patient, and the onset could not be determined in twelve other patients. The adverse event was described as a brownish-black or grayish discoloration of the teeth and tongue. The outcome in most cases reported to the company was unknown.

The three cases presented here are similar to those reported to Merck Sharp & Dohme.

Case 1

L.O., a 13 year-old girl, presented with fever and ongoing left foot pain (no trauma). She was diagnosed with osteomyelitis of the left 4th metatarsal. After two days treatment with cefazolin and gentamicin, she was switched to IV imipenem 500 mg q8h and discharged home on this antibiotic under the Hospital-In-The-Home program. She was not on any other medications except for Tylenol #3 and had no known drug allergies. Approximately two weeks after discharge, her parents noticed a yellowish-brown stain on her teeth which they felt was due to the antibiotic as they noticed the same colour stain when a few drops of imipenem were spilled on white clothing.

The patient saw her dentist approximately one month later and he felt that the stain was superficial and was caused by the antibiotic in her saliva. The stain gradually faded over the next four months and after her dentist cleaned and scaled her teeth, they were of normal colour.

Case 2

M.S., a 52 year-old woman, presented with a cat bite. Antibiotics that were tried for the cellulitis included cephalixin,

ciprofloxacin (to which she developed a rash), and ceftriaxone 1 g daily IV for 10 days before switching to imipenem. She received 500 mg imipenem q8h IV as a home antibiotic patient on two separate occasions (one four-day course and one 28-day course). She also received 500 mg IV q6h for two days as an inpatient. Her second course of imipenem as a home patient was combined with metronidazole 500 mg po tid for 11 days before the metronidazole was discontinued and cotrimoxazole DS bid for three days was continued. M.S. noticed staining, which she likened to nicotine staining, approximately two to three weeks after her first course of imipenem. As well, the visiting home nurse observed a brown, oily substance which discoloured the IV tubing.

M.S. visited her dentist who gave her teeth a thorough cleaning but was unable to remove all the stains. An acrylic coating was needed to whiten her teeth again.

Case 3

J.M., a 33 year-old woman, was on a respirator with chronic tracheitis. She had multiple drug allergies including erythromycin, tetracycline, cloxacillin, cefaclor, cotrimoxazole, ampicillin, and

Carrie Ku, B.Sc.Pharm., M.Sc., at the time of writing this paper was the Pharmacy Manager, Clinical Services, The Mississauga Hospital, Mississauga, Ontario. Carrie is now a Regulatory Affairs Associate at Miles Canada, Inc., Etobicoke, Ontario.

Donna O'Neill, M.D., was an Infectious Disease Specialist and Medical Microbiologist at The Mississauga Hospital. She is now working in Ann Arbor, Michigan.

Address Correspondence to: Carrie Ku, Regulatory Affairs Associate, Miles Canada Inc., 77 Belfield Road, Etobicoke, Ontario M9W 1G6

ASA. She received a total of five courses of imipenem for her tracheostomy infections. In her first course, she received 500 mg IV imipenem q8h (for 11 days) along with clindamycin 450 mg po q8h, fluconazole 100 mg po daily, vancomycin 500 mg IV q8h and 125 mg po qid. For her second course of treatment, she received imipenem 500 mg q8h IV (for 28 days) vancomycin 500 mg IV q12h and 125 mg po qid and ceftazidime 1.5 g q12h IV. She subsequently received three other courses.

By the second week of the first course, both J.M. and her family noticed yellow staining on her teeth. However, imipenem was continued due to the patient's allergies to other antibiotics. The stains could not be removed by regular brushing but were removed by the dentist.

DISCUSSION

There were similarities noted between all three cases: the onset of teeth stains seemed to be approximately two weeks after treatment with imipenem and could not be removed by regular brushing. In two out of the three cases, the stains were successfully removed by dentists. Teeth stains have not been associated with any of the other antibiotics used by these patients. None of these cases involved children with developing teeth and the stains were reversible.

Therefore, the mechanism of action is not likely to be that of forming a calcium complex in bone-forming tissue (like tetracycline). As well, although imipenem is a small molecular size antibiotic, it is

unlikely that it is small enough to be incorporated into the tooth like fluoride.

Chlorhexidine gels and mouth rinses are known to discolour teeth and dentures a brownish colour; this staining is reversible and does not seem to be dose-related. Binding of food dyes to the chlorhexidine has been postulated as the cause of these teeth stains.¹⁻³

This could be a possible explanation for the staining due to imipenem. None of these patients reported the use of chlorhexidine gels or mouth rinses.

Imipenem is widely distributed and potentially therapeutic levels have been measured in the sputum. One to two hours after a 500 mg dose of imipenem IV was given, a concentration of 1.6 mg/L was measured in sputum⁴. Similarly, one hour after a 1 g dose of imipenem was given, the concentration in the sputum was 2.7 mg/L⁵. MacGregor and colleagues measured imipenem concentrations after multiple doses of imipenem 500 mg q6h were administered to patients with serious infections. Mean concentrations measured within two hours after the end of infusion were 4.4 mg/L in the sputum (seven patients) and 0.38 mg/L in saliva (ten patients). Therefore, sufficient concentrations may accumulate in sputum to cause superficial staining of the teeth. The fact that the colour of the stain was noted to be similar to the stain from IV fluid supports this idea.

It is not known whether these teeth stains are dose-related or temporally related since all three patients received a dose of 500 mg

q8h and the teeth stains were noticed approximately two weeks after first receiving the drug.

Another possible influencing factor may be the storage of imipenem at home since all three patients were on the home antibiotic program at one time or another. In this program, weekly medication supplies are dispensed from the inpatient pharmacy to the patient. However, the third patient, J.M., received her first two courses of imipenem as an inpatient.

To the authors' knowledge, these cases are the first to be reported in the literature. Although this adverse effect is uncommon, it can be bothersome for the patient. ☒

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