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**Case Presentation**

# Systemic allergic contact dermatitis associated with allergy to intraoral metals

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## Abstract

Contact (allergic) dermatitis is a skin disorder related to natural exposure to various allergens. Systemic contact dermatitis (SCD) describes a cutaneous eruption in response to systemic exposure to an allergen. The exact pathologic mechanism remains uncertain. Herein we describe a 36-year-old woman with symmetric systemic allergic contact dermatitis, unresponsive to conventional treatment, associated with dental alloy-contact hypersensitivity. We did skin patch testing and the blood lymphocyte transformation test (LTT) from the dental allergen series to assess contact allergy to restorative dental materials. On patch testing, positive allergic contact dermatitis reactions to metals occurred (nickel, potassium dichromate, and gold). Nickel hypersensitivity was confirmed by LTT, which also revealed silver-amalgam sensitization. Our case report highlights the need to consider adverse reactions to base-metal dental alloys in the differential diagnosis of cases of systemic allergic contact dermatitis.

**Key words: adverse events; amalgam dermatitis; contact hypersensitivity reaction; delayed/chemically induced; delayed-type hypersensitivity; dermatitis/allergic contact hypersensitivity; heavy metals adverse events; mercury dermatitis; mercury exanthema.**

## Introduction

Systemic contact dermatitis (SCD) is an inflammatory skin disease in response to systemic exposure to an allergen and has been reported in patients with adverse health effects linked to dental alloy restorations [1-7], but the exact pathologic mechanism remains uncertain. Herein we report a case of severe systemic allergic contact dermatitis caused by allergy to metals released by galvanic corrosion between a mercury amalgam tooth filling and an endosseous titanium dental implant.

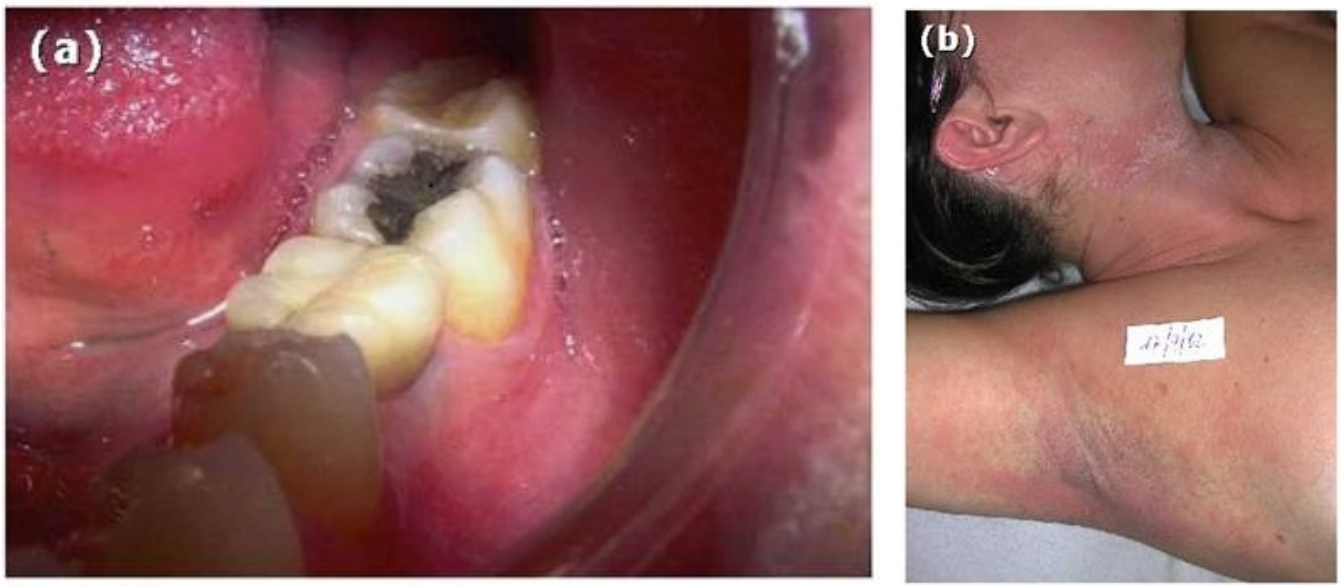
# Case synopsis

A 36-year-old woman reporting severe widespread dermatitis with intractable pruritus was examined in our dermatological department in April, 2002. The gradual onset of dermatitis developed and persisted several months after she had received 2 endosseous root-formed titanium implants, which were implanted in both her maxillary and mandibular bones (Figure 1 e). On imaging studies, titanium endosseous implants appeared to be clinically and radiologically well osteointegrated and they were placed in healed alveolar bone of the maxillary right first molar area (1.6) and mandibular left first molar area (3.6) (Figure 1 a,e), respectively. A single class II mercury amalgam restoration was present on the mandibular left first molar (3.7) (Figure 1 a,e), in close contact to the noble metal-dental alloy implant-supported restoration on 3.6 (Figure 1 a,e). Clinical examination showed extensive dermatitis with erythema, xerosis, and scaling and crusting on face, neck, and bilateral inguinal areas (Figure 1 b,c,d). Facial swelling (especially around eyes) was visible but oral mucosa was unaffected.

Her systemic dermatitis was unresponsive to the usual medical therapies. Medications on admission included a topical class 1 glucocorticoid and emollient moisturizing creams. She had no family history of atopic dermatitis and she had no history of asthma. She did not smoke, drink alcohol, or use illicit drugs; she had no risk factors for occupational and/or non-occupational exposure to chemical substances. The patient's dietary fish intake occurred one time per week. Given that the onset of dermatitis was temporally related to dental work, we hypothesized a hypersensitivity and/or allergic reaction to dental materials. In particular, we suspected a high-rate release of intraoral metal ions owing to galvanic corrosion between the mercury amalgam filling on the mandibular left first molar (3.7) and the titanium implant-supported gold/palladium alloy crown in the mandibular left first molar area, 3.6 area (Figure 1 a). The single metal-ceramic crown restoration was based of noble alloy, consisting in a gold/palladium-based crown (Figure 1 a,e). A small mercury amalgam tattoo (measuring 2 x 2 millimeters, Figure 1 e) was present in the peri-implant mucosa around the titanium dental implant, which was consistent with the previous presence of a mercury dental amalgam restoration. No signs of oral pathology were observed on her oral mucosa.

Skin biopsy was considered but it was not performed. She was patch-tested with a dental allergen series, including mercury allergens for screening for contact allergy to dental amalgam fillings. The 31 allergens from the dental series are listed in Table 1. With regard to the timing of patch test readings, patch test strips were removed at day 2 (48 hours) and readings were performed at day 4 (96 hours). Criteria for scoring of patch test reactions were assessed according to Wilkinson et al [8]. We observed very strongly positive allergic reactions to nickel sulfate 5 percent (score reaction +++), potassium dichromate 0.5 percent (score reaction +++), and gold sodium thiosulfate 0.5 percent (score reaction ++), all in petrolatum (Chemotechnique Diagnostics, Vellinge, Sweden) (Table 1). Sensitization to nickel was subsequently confirmed by the lymphocyte transformation test (LTT-stimulation index, S.I.: 6.7, at a cutoff value of S.I. <2.00 as predictor of response of immune sensitization to metals) and silver reactivity was evident with an LTT-stimulation index, S.I.: 5.5, (cutoff value of S.I.: <2.00).

Mercury dental amalgam contains silver (30-35 percent by weight) and nickel ($Ni^{2+}$) in trace amounts (up to 8-9 micrograms per gram of amalgam metal-matrix alloy) [9]. Both the mercury-containing amalgam filling and the metal-ceramic crown on the dental titanium implant were removed to reduce considerably her intra-oral electrochemical corrosion process, which likely released metal ions (mercury, nickel, and silver) into the saliva and the oral mucosa [10-12]. The systemic contact dermatitis resolved completely within 8 months after the removal of both mercury amalgam tooth filling and a single metal-ceramic crown restoration (gold/palladium – based crown), which were in close proximity to each other (Figure 1 f,g,h). To achieve a complete and stable resolution of the patient's signs and symptoms, it was not necessary to remove her two titanium dental implants. The patient's systemic contact dermatitis reverted completely and did not recur in 12 years of follow-up (Figure 1 f,g,h).



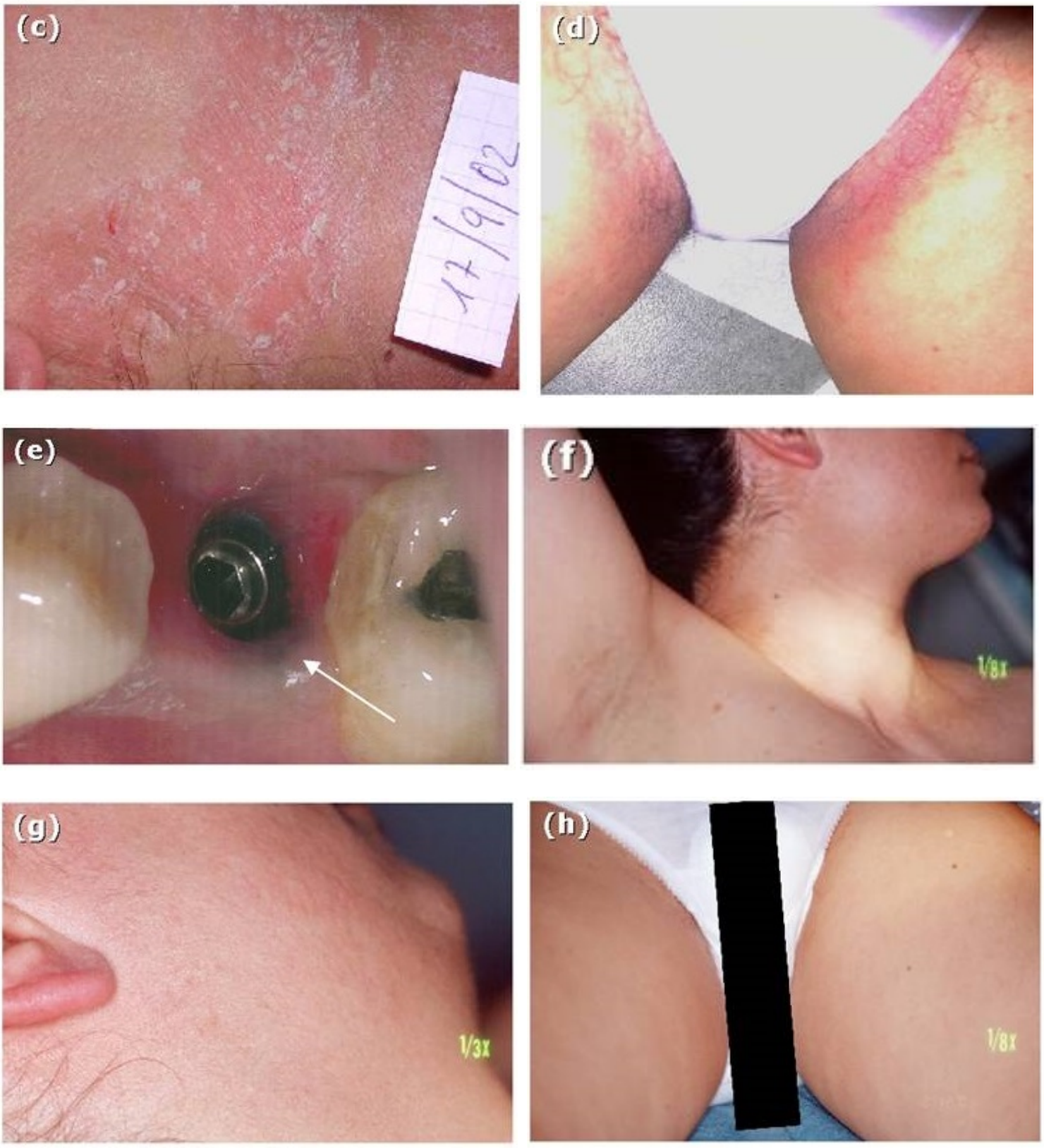



**Figure 1.** Mercury-containing dental amalgam filling (on the mandibular left second molar, 3.7 area) and endosseous titanium implant placed in the mandibular left first molar area (3.6), at presentation (a,e). Erythema, edema, large scaling, crusting, erosions with oozing on the neck area, and adjacent right ear (b), neck and submandibular area (c), left and right inguinal region (d). Eight months after the removal of mercury dental amalgam alloy crown, but with no medications, her signs and symptoms of allergic contact dermatitis completely resolved (f,g,h), and did not recur. The arrow indicates intraoral mercury amalgam tattoo (measuring 2 x 2 millimeters) in peri-implant mucosa around dental endosseous titanium implant (e).

## Discussion

Adverse events in the skin are considered to be the most common amalgam-related clinical adverse reactions [5,13].

The possibility of acrodermatitis enteropathica was raised because of the symmetric scaly erythematous eruption on her perineum, but was ruled out. We also excluded the possibility that there was an exposure to aspartame (formaldehyde-releasing product), a food additive used in the diet, which may cause systemic dermatitis [14]. Our patient was exposed to elemental mercury ($Hg^0$) released from the mercury amalgam filling. The main route of exposure is by inhalation through the

lungs in which 80 percent of mercury vapor is absorbed and, in part, through ingestion of elemental mercury ($Hg^0$) dissolved in saliva [5].

Intra-oral wear and corrosion of dental alloy restorations produce a release of an extensive variety of metals and intraoral metal ions, which are also contact sensitizers. These highly reactive metals are absorbed through the oral mucosa as well as through the intestinal lumen. In patients who have a positive response (contact sensitivity) to metal allergens (e.g., mercury, nickel, cobalt, chromium) that are administrated systemically (orally), generalized pruritus and skin eruption may occur. Nickel, cobalt, palladium, mercury, silver, and gold are contained in mercury amalgam tooth fillings and may create a possible risk of developing allergic reactions to metals.

In our experience, after removal of the inciting metal antigens (mercury or nickel), systemic allergic contact dermatitis resolves within 12 months. Mercury amalgam filling is a well-known contact allergen of local and systemic allergic contact dermatitis. Usually, mercury amalgam-related contact eczematous dermatitis is caused by delayed-type hypersensitivity reaction (DTH)/type IV reactions to metals contained in the mercury dental amalgam (i.e.,: mercury, nickel, cobalt, palladium), according to the Gell and Coombs classification [13,15].

There have been reports of skin disorders associated with exposure to mercury in dental amalgam fillings such as amalgam dermatitis [2,16-18], baboon syndrome [5,19,20], cheilitis [6,11,13], contact eczematous dermatitis [2-4,7,13,18,20,21], contact orofacial granulomatosis [5,7], cutaneous and oral lichen planus [5,7,21], dermatitis [3,4,6,7,18], dermographism [5], edema [18], eczema [3,4,18], erysipelas-like mercury exanthema [22], erythema-multiforme (minor)-like eruption [18,22], exudative facial dermatitis [17], Grover disease (transient acantholytic dermatosis [23], herpes simplex infection (cold sores) [24], hyperpigmentation [23], Kawasaki disease (Mucocutaneous Lymph Node Syndrome) [19], lichenoid contact stomatitis [5,7], mercury amalgam tattoo [19], mercury exanthema [5,16,25], nummular dermatitis (discoid eczema) [5,21], palmo-plantar pustolosis [23], perioral dermatitis [11], pruritus [2,6], salmon and/or pink exanthema [5,19], scleroderma [26], systemic allergic contact dermatitis [6,7,20], and urticaria/angioedema[3-7,18].

Adverse events associated with endosseous (titanium) dental implants are yellow nail syndrome [27], facial eczema [1,21], skin rashes [15,18,25,28], local and peripheral neuropathy [27], burning mouth syndrome (BMS) [11], leukopenia, and exfoliative cheilitis [11]. Even in this case, it seems highly likely that allergy to chromium could have increased the cutaneous adverse events caused by either hypersensitivity to dental amalgam alloy and exposure to elemental mercury ($Hg^0$) as described previously [5]. A number of observations support this hypothesis [5]. In addition, systemic allergic contact dermatitis has been reported with epidermal hypersensitivity to metals contained in mercury amalgam tooth fillings and the patients seldom present with oral mucosa involvement [17]. The prevalence of allergy to mercury-containing dental amalgam is reported to range from 1.4 to 16.5 percent [29].

In our ongoing investigation of 520 case series [11], we have found that the prevalence of systemic contact dermatitis in adult patients with adverse health effects associated with mercury-containing dental amalgam was 3.5 percent (18 of 520 patients): 95 percent confidence interval, 2.0 – 5.0.

The clinical and biologic relevance of patch testing with dental metal allergens was clear, linking the causative relation between exposure to dental metal allergens and systemic allergic contact dermatitis in our case. Dermatologists should consider the possibility of an allergy to metal ions released from dissimilar dental alloy restorations in patients with systemic allergic contact dermatitis.

**Table 1.** Patch-Test Allergens Used and Allergic Reactions to Mercury Amalgam Metal-Matrix Alloy of Proven Relevance in a Patient with Systemic (allergic) Contact Dermatitis (concentrations refer to petrolatum).

| | **Allergen** | **Concentration (%)** | **Result** |
|---|---|---|---|
| 1. | Methyl methacrylate (MMA) | 2% | - |
| 2. | Triethyleneglycol dimethacrylate (TREGDMA) | 2% | - |
| 3. | Urethane dimethacrylate (UEDMA) | 2% | - |
| 4. | Ethyleneglucol dimethacrylate (EGDMA) | 2% | - |
| 5. | BIS-GMA | 2% | - |

| | | | |
|---|---|---|---|
| 6. | N,N-dimethyl-4-toluidine | 5% | - |
| 7. | 2-Hydroxy-4-methoxy-benzophenone | 2% | - |
| 8. | 1,4-Butanediol dimethacrylate (BUDMA) | 2% | - |
| 9. | BIS-MA | 2% | - |
| 10. | Potassium dichromate | 0.5% | +++ |
| 11. | Cobalt chloride | 1% | - |
| 12. | 2-Hydroxyethyl methacrylate (2-HEMA) | 2% | - |
| 13. | Gold sodium thiosulfate | 0.5% | ++ |
| 14. | Nickel sulfate | 5% | +++ |
| 15. | Eugenol | 2% | - |
| 16. | Colophony | 20% | - |
| 17. | N-ethyl-4-toluene sulfonamide | 0.1% | - |
| 18. | 4-tolyldiethanolamine | 2% | - |
| 19. | Copper sulfate | 2% | - |
| 20. | Methyl hydroquinone | 1% | - |
| 21. | Palladium chloride | 2% | - |
| 22. | Aluminum chloride hexahydrate | 2% | - |
| 23. | Camphoroquinone | 1% | - |
| 24. | N,N-Dimethylaminoethyl methacrylate | 2% | - |
| 25. | 1,6-Hexanediol diacrylate (HDDA) | 0.1% | - |
| 26. | 2(2-Hydroxy-5-methylphenyl) benzotriazol | 1% | - |
| 27. | Tetrahydrofurfuryl methacrylate | 2% | - |
| 28. | Formaldehyde | 1% | - |
| 29. | Mercury Ammonium Chloride | 1% | - |
| 30. | Mercury (metallic) | 0.5% | - |
| 31. | Mercury dental amalgam | 20% | - |

**Table 2.** Skin disorders associated with exposure to mercury-containing dental amalgam fillings.

| Skin disorders associated with exposure to mercury-containing dental amalgam fillings |
|---|
| Amalgam dermatitis [2,16-18] |
| Baboon syndrome [5,19,20] |
| Cheilitis [6,11,13] |
| Contact eczematous dermatitis [2-4,7,18,20,21] |

| |
|---|
| Contact orofacial granulomatosis [5,7] |
| Cutaneous and oral lichen planus [5,7,21] |
| Dermatitis [3,4,6,7,18] |
| Dermographism [5] |
| Edema [18] |
| Eczema [3,4,18] |
| Erysipelas-like mercury exanthema [22] |
| Erythema-multiforme (minor)-like eruption [18,22] |
| Exudative facial dermatitis [17] |
| Grover's disease (transient acantholytic dermatosis) [23] |
| Herpes simplex virus infection (cold sores),[24] |
| Hyperpigmentation [23] |
| Kawasaki disease (Mucocutaneous Lymph Node Syndrome) [19] |
| Lichenoid contact stomatitis [5,7] |
| Mercury amalgam tattoo [19] |
| Mercury exanthema [5,16,25] |
| Nummular dermatitis (discoid eczema) [5,21] |
| Palmo-plantar pustolosis [23] |
| Perioral dermatitis [11] |
| Pruritus (neurogenic), itching [2,6,18] |
| Salmon and/or pink exanthema [5,19] |
| Scleroderma [26] |
| Systemic allergic contact dermatitis [6,7,20] |
| Urticaria/angioedema [3-7,18] |

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