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Systemic contact dermatitis caused by acupuncture – a neglected route of allergen entry

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CONFLICTS OF INTEREST

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Systemic contact dermatitis (SCD) caused by acupuncture had never been reported. We report a case of SCD caused by acupuncture in a woman who is allergic to chromium and cobalt, to illustrate that acupuncture induced SCD may be under-recognized.

Case report

A 70-year-old female, a retired railway transportation technologist, presented with a 2-month history of a generalized eczematous rash involving her arms, legs and trunk. In September 2015, she began to receive acupuncture for the treatment of recurrent urticaria, which had manifested over the prior year. Electroacupuncture was used during the treatment, in which electrical stimulation was applied to the needles to generate a small electric current¹. After one week of acupuncture, skin erythema appeared at the location of the acupuncture treatment. One week later, a maculopapular rash developed on her limbs. While she continued the acupuncture treatment, the rash spread from her limbs to her entire body, with severe itching that affected sleep (Figure 1A). The rash did not respond to antihistamines or corticosteroids. The patient has a history of hypothyroidism. Physical examination showed a maculopapular rash widely distributed on the body and limbs, multiple scratches and scabs, and an enlarged left cervical lymph node (2.8×1.1cm). Laboratory tests showed an absolute eosinophil count of $1.25 \times 10^9/L$ (normal range: $0.02 \sim 0.5 \times 10^9/L$) and her total IgE level (T-IgE) was 2900 KU/L (normal range <60KU/L). Specific IgE to dust mite, mold, egg, milk, peanut, soybean, wheat, fish and shrimp were negative. Autoimmune screening was negative except for ANA low titer positivity.

Initially, she was misdiagnosed as bullous pemphigoid and hypereosinophilic syndrome. Skin biopsy showed a nonspecific perivascular lymphocytic infiltrate in the entire dermis accompanied by a large number of eosinophils (Figure 1C). The patient refused lymph node biopsy. Patch test was performed with the European baseline and metal series. Allergens were applied on the back with IQ-ultra Chambers (Chemotechnique Diagnostics, Vellinge, Sweden) on Scanpor tape. The tests showed positive reactions on day 3, according to ICDRG criteria, to cobalt chloride hexahydrate 1.0 pet. and potassium dichromate 0.25 pet. (Figure S1 in the Supporting Information). The acupuncture needle (Changchun Aikang Medical Devices Co., Ltd, China) was made of 304 stainless steel. We performed micro-X-ray fluorescence (μ -XRF) microspectroscopy to investigate the component of the needle and metal ion release from the needle into artificial sweat (methods are described in the Online Repository). The results showed that the needle contained chromium, cobalt and iron (Figure S2 in the Supporting Information), and that concentrations of chromium, cobalt and iron were clearly increased in the artificial sweat in which the needle was immersed (Artificial sweat 1 in Figure S3) compared to sweat in which the needle was not immersed (Artificial sweat 2 in Figure S2 in the Supporting Information).

She recalled that when she was 30-year-old, her wrist wearing a metal watch would be itching after sweating in summer. But she never did patch test before and was never diagnosed with a contact allergy to metals before. Acupuncture treatment was discontinued. The lymph node decreased in size, the rash gradually resolved (Figure 1B), and her T-IgE and eosinophil count returned to normal (Figure 1D). At a five-year follow-up, she had no further rashes.

Discussion

Systemic (allergic) contact dermatitis (SCD) is by definition a skin condition occurring in previously sensitized patients after allergens are administered systemically². The prevalence of chromium and cobalt allergy is estimated to be 1-3%². Chromium is ubiquitous in water, soil, food and household supplies, and cobalt is a common component of paints, jewelry, prosthetics and other common household products². As early as decades ago, it was reported that a subset of chromium or cobalt sensitized individuals develop systemic skin

reactions to dichromate or cobalt sulphate when exposed through the oral route^{3,4}. In the literature, only a few cases of chromium and/or cobalt induced SCD have been reported, all of which were caused by implants, oral intake or inhalation (see Table S1 in the Supporting Information). To the best of our knowledge, this is the first report of SCD caused by acupuncture, a special route of allergen entry. In Chinese Traditional Medicine, acupuncture has been widely used for thousands of years. During an acupuncture treatment, the needles are inserted into precise acupoints and are usually retained between five and 30 minutes. In China, acupuncture is often used to treat skin diseases, including eczema and urticaria⁵. The theory behind this may be that the activation of hypothalamus-pituitary-adrenal axis during and after acupuncture increases the secretion of glucocorticoids and results in the suppression of immunological reaction, but there was only meager evidence^{6,7}. It is not well recognized to most physicians that acupuncture itself can be a cause of an eczematous appearing rash. We performed μ -XRF to prove that chromium, cobalt and iron were released from the needle into artificial sweat, which was consistent with other studies^{8,9}. Therefore, we suspect that free metal ions were released into the body during acupuncture treatment. Electrical stimulation applied on the needles probably accelerates the release of metal ions¹⁰. Then, hematogenous spread of trace amount of chromium and cobalt triggered a generalized eruption. Although iron was also released into artificial sweat, it was not considered a cause of SCD. This is because human body consists of considerable amount of iron, as iron is a major component of hemoglobin.

The precise mechanism behind SCD remains unknown. The skin biopsy of this patient suggested type-IV delayed-type hypersensitivity (Figure 1C). Interestingly, the T-IgE and eosinophil count of the patient increased significantly, which is seldom described in other SCD cases shown in Table S1 in the Supporting Information. However, in a study of chromium induced contact dermatitis, chromium exposed workers with contact dermatitis had high T-IgE levels and eosinophilic counts¹¹. Eosinophilia and elevated T-IgE levels are also reported in several cases of SCD^{12,13}. Her eosinophil count returned to normal within three weeks after the pacemaker was removed. In addition, tannery workers who were occupationally exposed to chromium and developed rough, itchy and decolorized skin had significantly higher levels of IgE than controls¹⁴. High T-IgE level indicates that the SCD in this patient may also involve type I hypersensitivity.

We also suspect that the lymph node enlargement was a reaction to acupuncture since it resolved after stopping acupuncture. One case of chromium induced SCD presented by Bizzotto N et al also had lymph node enlargement and a lymph node biopsy that showed large aggregates of Langerhans cells¹⁵.

This case indicates that acupuncture is a potential cause of contact dermatitis for some patients with metal allergy. This case aims to attach importance to allergic reactions that may occur during treatment with acupuncture, thereby avoiding misdiagnosis and ineffective treatment.

FUNDING

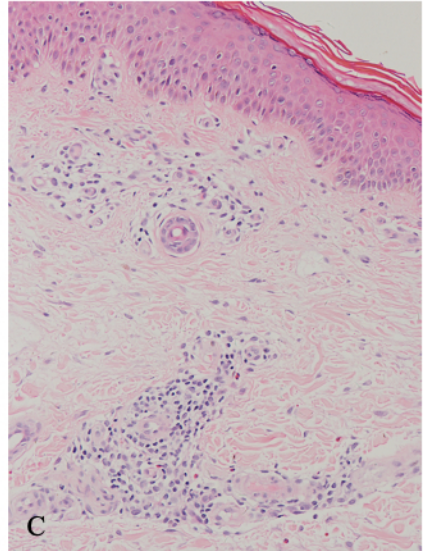
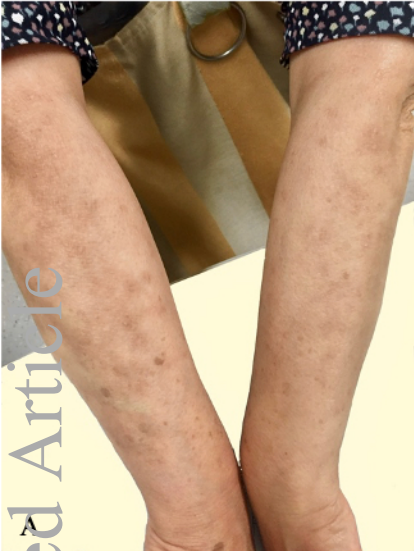
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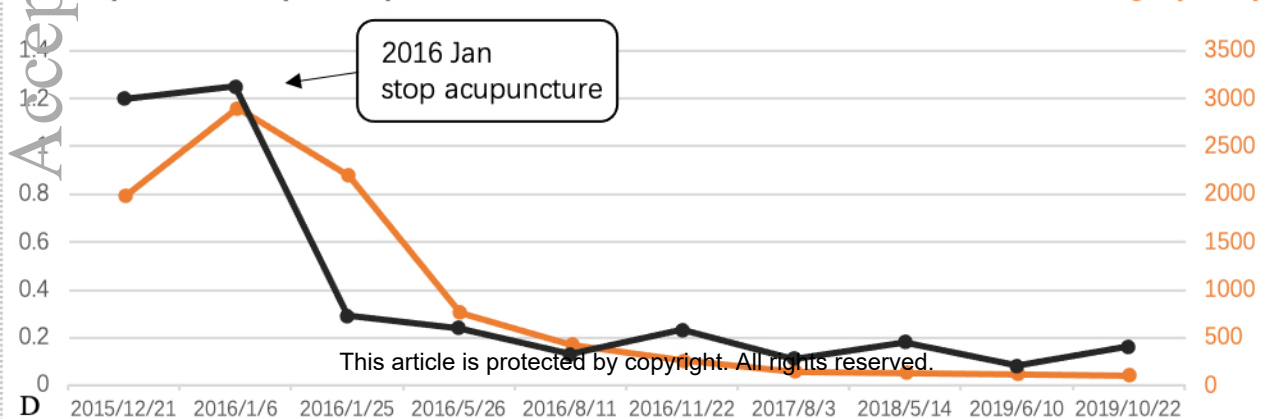
Figure legends

Figure 1. (A) Remnant of the rash and pigmentation on both arms. (B) The rash disappeared after the patient discontinued acupuncture. (C) Skin biopsy of the rash. (D) Eosinophils count and total IgE.



Eosinophils count ($\times 10^9/L$)

Total IgE (KU/L)



Method

Micro-X-ray fluorescence (μ -XRF) microspectroscopy

The micro-X-ray fluorescence (μ -XRF) microspectroscopy experiment utilized a non-destructive analytical technique that is widely used for elemental and chemical analysis. It was performed at 4W1B beamline, Beijing synchrotron Radiation Facility, which runs 2.5 GeV electron with current from 150 to 250 mA. The incident X-ray energy was monochromatized by W/B4C Double-Multilayer-Monochromator (DMM) at 15 keV and was focused down to 50 μ m in diameter by the polycapillary lens. The two-dimensional mapping was acquired by step-mode: the sample was held on to a precision motor-driven stage, scanning 50 μ m stepwise. The Si(Li) solid state detector was used to detect X-ray fluorescence emission lines with live time of 30s. The data reduction and processing were performed using PyMca package¹. Due to the difficulty associated with the preparation of the standard references for artificial sweats, we compared the change of the normalized XRF peak intensities for the metals, without calibration curve applied.

Artificial sweat immersion is a common way to investigate the metal ion release from the material that may cause contact dermatitis²⁻⁴. The composition of the artificial sweat was sodium chloride 0.1g/10mL, ammonium chloride 0.05g/10mL, urea 0.05g/10mL, acetic acid 0.025g/10mL, lactic acid 0.05g/10mL, adjusted to pH 5.5 by addition of sodium hydroxide⁵. One entire needle was immersed in 10mL artificial sweat solution for 48 hours. The μ -XRF microspectroscopy was performed on three random parts of one needle and five random samples of the artificial sweat.

Table S1. A summary of cases of chromium and/or cobalt induced systemic allergic contact dermatitis.

Year	Author	Cause	Allergen(s)	Route of allergen entry
2011	Gao X ⁶	Total knee arthroplasty	Chromium	Joint implants
2015	Bizzotto N ⁷	Metal hip arthroplasty	Chromium	Joint implants
2017	Cobb HK ⁸	Metatarsophalangeal joint hemi implant and tattoo	Cobalt, nickel and palladium	Joint implants
2014	Wong CC ⁹	Metal-on-metal right total hip replacement	Cobalt	Joint implants
1992	Merle C ¹⁰	Knee osteotomy and insertion of a plate and screws	Cobalt	Joint implants
2017	Suwarna O ¹¹	Bone plate fixation as a management for mandibular fracture	Cobalt and nickel	Bone implants
2001	Kanerva L ¹²	The fibula and tibia were surgically realigned and retained by metal plates and screws	Chromium and nickel	Bone implants
1983	Hubler WR ¹³	Chromium dental plate	Chromium	Dental implants
1994	Guimaraens D ¹⁴	Dental crowns	Chromium	Dental implants
2018	Ling DH ¹⁵	Alloy denture frameworks	Chromium and cobalt	Dental implants
1994	Veien NK ¹⁶	Orthodontic appliance made of steel	Chromium	Dental implants
2014	Meyer MD ¹⁷	Flaxseed ingestion	Cobalt and nickel	Oral intake
2017	Panaszek B ¹⁸	A meal containing cobalt and/or palladium	Cobalt and palladium	Oral intake
2000	Fowler JF ¹⁹	Chromium picolinate	Chromium	Oral intake
2010	Ozkaya E ²⁰	Multivitamin/multimineral tablets	Chromium	Oral intake
2007	Adachi A ²¹	Mother's milk. The mother had been taking a lot of chocolate and cocoa.	Chromium	Oral intake
2014	De Marchi S ²²	Food supplement	Chromium	Oral intake

1964	Shelley WB ²³	Welding fumes	Chromium	Inhalation
1982	Zugerman C ²⁴	Welding fumes	Chromium	Inhalation
2009	Asano Y ²⁵	Hard-metal powder	Cobalt	Inhalation

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Supporting Figures



Figure S1. Patch test showing that cobalt chloride and potassium dichromate were positive.

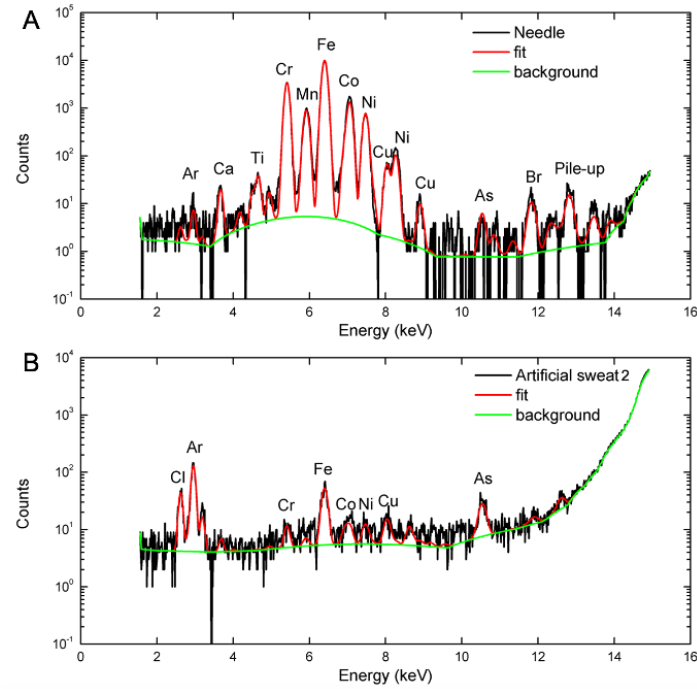


Figure S2. XRF spectrum analysis of the needle and artificial sweat 2. **(A)** The results showed the needle did contain Cr. **(B)** The artificial sweat 2 showed a strong peak for Fe, but weak peaks for Cr and Co. Artificial sweat 2: sweat without needle immersion.

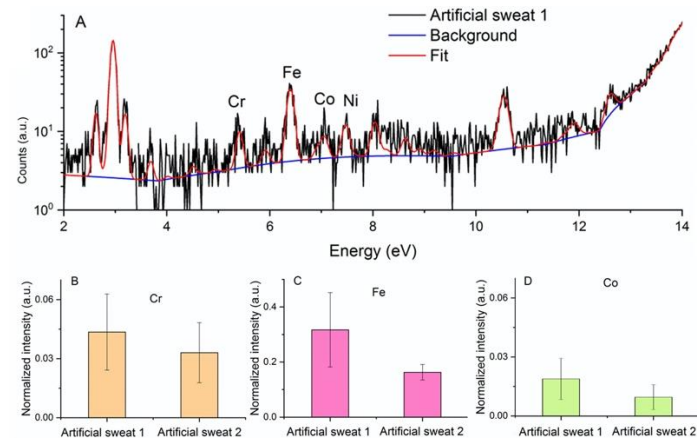


Figure S3. **(A)**: Representative XRF spectrum analysis of artificial sweat 1. **(B-D)**: Statistical results on the normalized peak intensity changes for chromium (Cr), iron (Fe), and cobalt (Co). The intensity for Fe is displayed at a higher level. Artificial sweat 1: sweat in which needle was immersed; artificial sweat 2: sweat without needle immersion.