

- [4] Frémeaux-Bacchi V, Guinépain M-T, Cacoub P, et al. Prevalence of monoclonal gammopathy in patients presenting with acquired angioedema type 2. *Am J Med*. 2002;113:194–199.
- [5] Cicardi M, Zingale LC, Pappalardo E, Folcioni A, Agostoni A. Autoantibodies and lymphoproliferative diseases in acquired C1-inhibitor deficiencies. *Medicine*. 2003;82:274–281.
- [6] Gelfand EW. Intravenous immune globulin in autoimmune and inflammatory diseases. *N Engl J Med*. 2012;367:2015–2025.
- [7] Auricchio L, Vitiello L, Adriani M, et al. Cutaneous manifestations as presenting sign of autoimmune lymphoproliferative syndrome in childhood. *Dermatology*. 2005;210:336–340.

Radiocontrast-induced iodide sialadenopathy and neutrophilic dermatosis

Iodinated radiocontrast medium (iRCM) can cause immediate or delayed hypersensitivity reactions; however, iodine itself rarely causes acute sialadenitis (iodide mumps) and painful neutrophilic cutaneous nodules (iododerma). We describe a case of acute sialadenitis associated with a Sweet syndrome–like eruption after administration of iRCM.

A 78-year-old man with a medical history of hypertension, chronic renal insufficiency (estimated glomerular filtration rate, 28 mL/min/1.73 m²), diabetes mellitus, and hypothyroidism presented with sudden-onset abdominal pain radiating to the back. Physical examination revealed a pulsatile, nontender central abdominal mass.

Plain computed tomography revealed a large saccular aneurysm (87 × 94 mm) below the level of the renal arteries to the aortic bifurcation. Computed tomographic angiography of the abdomen was performed 2 days later, during which the patient received 100 mL of Ultravist 370, containing 769 mg/mL of iopromide (equivalent to 370 mg/mL of iodine).

Sixteen hours later, he experienced submental and parotid area pain, severe enough that light touch or movement was excruciating. During the ensuing hours, these areas swelled markedly. The following day multiple, painful, tender, dark purplish nodules appeared on his scalp. On the third day he had painful blistering swellings on the palms and fingers with hand edema. He was febrile (temperature, 38.2°C). Aneurysm repair surgery was postponed because the patient was acutely unwell (Fig 1).

Vasculitis and endocarditis were considered; autoimmune screening, serum complement, cryoglobulin, blood culture, and echocardiography results were normal. A test result for mumps virus IgM was negative. Eosinophil count was normal throughout. The C-reactive protein level was elevated. A diagnosis of iodide mumps secondary to iRCM exposure and iododerma or Sweet syndrome was made. Treatment with prednisolone, 50 mg, was commenced; by the second day of treatment, he was no longer febrile, the parotid and submandibular swelling had substantially reduced and was less tender, and mastication was tolerable. The scalp lesions subsided almost completely, leaving faint hyperpigmentation. The bullous lesions on the hands turned to a dark purplish discoloration. Some of the hand lesions discharged serosanguineous fluid. The C-reactive protein level, which peaked at 210 mg/L, decreased to 39 mg/L. Aneurysm repair surgery was scheduled.

In the evening of day 5 of prednisolone treatment, the patient experienced sudden pain and collapsed within a few minutes. The resuscitation team found him to be pale and clammy with a distended abdomen, unrecordable blood pressure, and absent pulse. Cardiopulmonary resuscitation failed.

A skin biopsy specimen (taken 2 days after commencing prednisolone therapy) available after his death revealed heavy dermal neutrophil infiltration with superficial dermal edema and early vesicle formation in the papillary dermis. The epidermis was acanthotic and hyperkeratotic with focal spongiosis. Eosinophils were not identified. The overall

appearances were consistent with Sweet syndrome. Dermal microabscesses, a cardinal feature of iododerma, were not seen.

Iodide mumps (sialadenopathy) is generally a benign and self-limiting condition. It has been described after urography or angiography with ionic and nonionic iRCM and is reproducible on repeat exposure.¹ Some cases are painless, whereas others appear to be associated with inflammation, pain, and tenderness. Whether this reaction is idiosyncratic or immunologically mediated remains unclear, but the result of immediate and delayed skin testing with iRCM was negative in one patient.² Importantly, iodide mumps has been reported after exposure to iodide salts, indicating that this is not a reaction to the molecular carrier of iodine but to the iodine or iodide itself.² Iodine is largely excreted by the kidneys; most reported cases of iodide mumps had renal insufficiency.^{3–5} These factors imply that iodide mumps is a physicochemical reaction to excessive iodine, probably in the form of the iodide ion.

Cutaneous hypersensitivity reactions to intravenous iRCM include acute or delayed urticaria, morbilliform rash, and Stevens-Johnson syndrome. These are considered to be caused by hypersensitivity to the iRCM carrier molecule rather than iodine itself. Iododerma is a rare pustular cutaneous reaction that has been reported in association with iRCM but can also be induced by iodide salts.³ Sweet syndrome (febrile neutrophilic dermatosis) has been reported in one individual who received iRCM for intravenous pyelography.⁶

Our patient had cutaneous lesions that might have been consistent with iododerma or Sweet syndrome. Histopathologic findings revealed a heavy neutrophilic infiltrate characteristic of Sweet syndrome. Sweet syndrome typically presents with tender, edematous, and inflamed papules, plaques, and nodules. Less common manifestations in the form of bullous or targetoid lesions have also been described. Our patient displayed these clinical features and fulfilled all criteria for drug-induced Sweet syndrome proposed by Walker and Cohen. There have been no previous reports of glandular swelling occurring simultaneously with Sweet syndrome.

Because iododerma has been reported after iodide salts in patients with renal failure, it is considered likely that it is mediated directly by an inflammatory response to high concentrations of iodides.⁷ In contrast, drug-induced Sweet syndrome is considered a hypersensitivity reaction, although the mechanism is not well elucidated. A cell-mediated immune reaction to antigen with production of cytokines promoting neutrophil activation and infiltration has been suggested.⁸ Pichler et al⁹ have proposed the extended Gell and Coombs hypersensitivity scheme in which type IVa is predominantly mediated by macrophages, type IVb by eosinophils, type IVc by cytotoxic T cells, and type IVd by neutrophils; one example of type IVd is acute generalized exanthematous pustulosis, but drug-induced Sweet syndrome may also be mediated by this mechanism. Therefore, although iododerma and Sweet syndrome are both neutrophilic dermatoses, the inciting mechanism appears to be distinct.



Figure 1. Hand and scalp lesions on day 5 after computed tomographic angiography. Note the multiple palmar bullous lesions and finger edema.

In this case, we have a patient with renal insufficiency who experienced a rare adverse reaction (inflammatory iodide mumps) undoubtedly caused by a direct reaction to iodine and a simultaneous rare reaction (Sweet syndrome) probably mediated by hypersensitivity to iRCM. Paradoxically, potassium iodide can be an effective treatment for Sweet syndrome in other circumstances.

The patient unfortunately died of a ruptured abdominal aortic aneurysm (AAA). There is no evidence that systemic corticosteroids constitute an additional risk factor in critical AAA. The size of the AAA and the presentation with abdominal pain clearly constituted a high risk of incipient aneurysmal rupture, and it is likely that the reason for the tragic outcome in this case was the unfortunate but inevitable delay in the surgical repair procedure.

Should the patient have survived, iRCM would have been contraindicated in future investigations because, based on similar cases in the literature, both iodine mumps and drug-induced Sweet syndrome are likely to be recurrent on subsequent exposure.

Jie Shen Fok, MBBS, MRCP (UK)*
Thavenesh Ramachandran, MBChB†
Michael Berce, MBBS, FRACS (vasc)†
William B. Smith, FRACP, FRCPA, PhD*

*Department of Clinical Immunology and Allergy

†Department of Vascular Surgery
Royal Adelaide Hospital
South Australia, Australia
JieShen.Fok@health.sa.gov.au

References

- [1] Wyplosz B, Scotte F, Lillo-Le LA, Chevlot A. Recurrent iodide mumps after repeated administration of contrast media. *Ann Intern Med.* 2006;145:155–156.
- [2] Gilgen-Anner Y, Heim M, Ledermann HP, Bircher AJ. Iodide mumps after contrast media imaging: a rare adverse effect to iodine. *Ann Allergy Asthma Immunol.* 2007;99:93–98.
- [3] Vaillant L, Pengloan J, Blanchier D, De Muret A, Lorette G. Iododerma and acute respiratory distress with leukocytoclastic vasculitis following the intravenous injection of contrast medium. *Clin Exp Dermatol.* 1990;15:232–233.
- [4] Boudoulas O, Siegle RJ, Grimwood RE. Iododerma occurring after orally administered iopanoic acid. *Arch Dermatol.* 1987;123:387–388.
- [5] Perroud H, Delacrétaz J. Vegetating iodism. *Ann Dermatol Venereol.* 1977;104:154–156.
- [6] Alper Y, Sprecher E, Bergman R, Birnbaum RF. Sweet's syndrome-like neutrophilic dermatosis resulting from exposure to a radiocontrast agent. *J Acad Am Dermatol.* 2008;58:488–489.
- [7] Stone OJ. Proliferative iododerma: a possible mechanism. *Int J Dermatol.* 1985;24:565–566.
- [8] Cohen PR. Sweet's syndrome – a comprehensive review of an acute febrile neutrophilic dermatosis. *Orphanet J Rare Dis.* 2007;2:34.
- [9] Pichler WJ, Adam J, Daubner B, Gentinetta T, Keller M, Yearly D. Drug hypersensitivity reactions: pathomechanism and clinical symptoms. *Med Clin North Am.* 2010;94:645–664.