CLINICAL VIGNETTE

A Case of "Iodide Mumps"

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A 56-year-old female with ESRD on hemodialysis presented with acute onset of bilateral painful neck and facial swelling that awakened her from sleep. She also noted mild shortness of breath and some odynophagia. She denied lip or tongue swelling, hives, or rash. Fifteen hours prior to onset, the patient underwent computed tomography and received iodine-containing contrast, iopamidol 100mL IV. She denied other new oral medications, trauma, insect bites, prior exposure to iodine-containing contrast or similar episodes. Routine hemodialysis was performed immediately after computed tomography. Her review of systems was otherwise unremarkable.

The past medical history was significant for anti-neutrophil cytoplasmic antibody-positive vasculitis diagnosed five years prior, not currently on immunosuppression, end stage renal disease (ESRD) on hemodialysis, combined chronic systolic and diastolic congestive heart failure, essential hypertension, allergic rhinitis, restless leg syndrome, and diverticulosis. She reported multiple drug allergies and adverse side effects including hives with cefazolin, diphenhydramine exacerbation of restless leg syndrome, and loratidine which causes diarrhea.

Her physical exam revealed a female in moderate discomfort. Vital signs included: T of 36.9°C, BP 186/97mmHg, pulse of 104/bmp, respiratory rate of 20/min, and oxygen saturation of 97% on room air. There was overt swelling of her bilateral parotid and bilateral submandibular glands with tenderness to palpation. No overlying erythema or fluctuance was noted. She had no lip, tongue, or uvula swelling. Lungs were clear to auscultation bilaterally. She was able to speak in full sentences with moderate discomfort. Oropharynx was free of laryngeal edema or bronchospasm. There was no facial rash or hives and the remainder of the exam was unremarkable.

On admission, laboratory evaluation was notable for a white blood cell 7.0 x 10^9/L, hemoglobin 7.6g/dL, creatinine 3.2mg/dL. Thyroid stimulating hormone 1.5uIU/mL, free thyroxine-4 1.2 mcg/dl (both within normal range). Complement 3 and complement 4 levels drawn 3 days prior were within normal range. Cytoplasmic neutrophil antibody was 1:1280 close to prior baseline. Her remaining labs were unremarkable. Ultrasound of the neck revealed normal appearance of the thyroid gland and marked symmetric enlargement and hypervascularity of the bilateral parotid glands.

The patient was admitted. She was started on oral prednisone 20mg, given that she was reluctant to take intravenous steroids or higher dosage orally. Diphenhydramine and histamine antagonists were avoided given her history of adverse effects. The following morning, she had minimal improvement in her bilateral parotid/submandibular gland swelling and pain and she was amenable to increasing prednisone to 40mg daily. She also received routine hemodialysis that day, which improved her symptoms. On HD2, her swelling and pain were significantly improved, leading to a diagnosis and treatment plan for contrast-induced sialadenitis. She was discharged on prednisone 40mg daily for 3 additional days (to complete a total course of 5 days) with routine HD three times per week. Patient was advised to avoid iodine-containing contrast in the future.

Discussion

Iodide mumps is a rare condition. It is generally characterized by acute painless swelling of the salivary glands following iodine-containing contrast exposure.[1] Inflammation is most often bilateral, but unilateral inflammation may occur.[2] The most common clinical feature is gland enlargement. Presentation is most commonly painless, but tenderness may be present. The submandibular and parotid glands are most often affected, the former being the most susceptible given its mucin-rich secretion.[2] Other glands, including the thyroid, lacrimal, and pancreas may also be affected.[2] Iodine-induced sialadenitis, is an uncommon condition. As of late 2018, 50 cases had been reported in the medical literature worldwide.[2] However, some researchers believe the condition may be underdiagnosed and that the true incidence may be 1-2%. The condition may occur with a variety of iodinated contrast agents, including both ionic and non-ionic media, and with different routes of administration, including oral ingestion, intravenous injection, and arteriography. Cases have been reported following coronary angioplasty.[3] The first case of contrast-induced sialadenitis was reported in 1956 after intravenous urography.[4]

The pathogenesis of iodide mumps is unknown. It may be related to a toxic accumulation of iodide in the gland inducing an acute inflammatory reaction with vasogenic edema and iodide-induced renal function damage leading to decreased iodide excretion. Iodide is eliminated primarily by the kidneys (98%) with the remaining iodide secreted from salivary and lacrimal glands, sweat, and other organs. For this reason, it is thought that renal impairment may lead to increased susceptibility as this likely leads to increased levels of iodide in the salivary glands. However, cases have also been reported in patients with normal renal function suggesting that other

mechanisms also play a role. Most patients, do not have a personal or family history of allergic diseases.

Ultrasound may reveal significant, often symmetric, swelling of the bilateral salivary glands with increased echogenicity and heterogeneity. Color-doppler ultrasound may reveal increased vascularity (hyperemia), particularly in the central part of the glands. Computed tomography may reveal low density (20-40 Hounsfield Units) of the affected glands, which may indicate edema.

A recent meta-analysis reviewing 77 cases of iodine-induced sialadenitis was published in Academic Radiology.[5] Median patient age was 63, with 35% with renal impairment. Median time to onset of symptoms was 16 hours and median resolution of symptoms was 3 days regardless of renal function and therapeutic intervention. Longer duration of symptoms was associated with longer time to onset and older ages.[5] Others report time of onset ranging from as several minutes to five days.

Iodide mumps is distinct from an anaphylactic reaction given the absence of angioedema, bronchospasm, hives, and hypotension. It may also occur as a result of a patient's first exposure to iodine-containing contrast; whereas, anaphylaxis requires prior sensitization to the antigen. This supports the theory that the contrast media itself directly causes release of histamine and other chemicals from mast cells without the involvement of an allergic antibody.[6]

Some believe the reaction is unlikely to be directed at the iodine itself, given it is an essential micronutrient in its purest form. The reaction is most likely caused by another component in the iodinated contrast, such as a filler.[7]

Iodine-induced sialadenitis appears to be a self-limiting condition. Patients often receive supportive treatment with corticosteroids and antihistamines. Hemodialysis has also been proposed to reduce blood levels of iodide in patients that are not improving. However, it is unclear if these treatments are effective. Duration of symptoms vary – with case studies reporting symptom resolution after 4 hours to 14 days. Patients should be advised to avoid further exposure to iodide as recurrence is common. Pre-treating with steroids and antihistamines not been shown effective.

Given our patient's history of ANCA-positive vasculitis, this condition was also on the differential as a cause of her sialadenitis. The literature reports, salivary gland involvement a rare presentation of vasculitis.[8] Patient's normal complement levels and chest X-ray were reassuring. She is also at risk of developing other autoimmune conditions such as IgG4-induced sialadenitis, which is characterized by a prominent lymphoplasmacytic infiltrate consisting of increased IgG4-positive plasma cells and storiform fibrosis on histopathology.[9] The condition requires tissue biopsy for definitive diagnosis and responds well to steroids.

Our patient presented with bilateral submandibular and parotid gland swelling and tenderness approximately 15 hours after her initial exposure to iodine-containing contrast. Neck ultrasound revealed marked symmetric bilateral enlargement of the parotid glands with hyperemia. The ultrasound was limited and submandibular glands were not imaged. Symptoms improved significantly in twenty-four hours on oral steroids and particularly after her routine hemodialysis. Given the temporal relationship to her iodine-containing contrast exposure and how quickly she improved particularly after hemodialysis, contrast-induced sialadenitis is the most likely diagnosis. Furthermore, she had a personal history of multiple drug allergies/adverse effects as well as allergic rhinitis. Her ESRD also likely played a role in her presumed increased levels of iodide in her salivary glands. Of note, she received hemodialysis immediately after her iodine-containing contrast exposure. It is unclear if her presentation would have been more severe had she not been dialyzed immediately after contrast agent was given. Given her rapid clinical improvement, biopsy was not pursued. The histologic appearance of iodide mumps resembles noninflammatory tissue edema elicited by iodine[10] as opposed to a leukocytoclastic vasculitis picture seen in ANCA associated vasculitis, in our initial differential.

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