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CLINICAL CASE REPORT

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Acute Submandibular Swelling Complicating Arteriography With Iodide Contrast

A Case Report and Literature Review

Guilian Zhang, PhD, Yaqi Li, MD, Ru Zhang, PhD, Yingying Guo, MD, Zhulin Ma, MD, Huqing Wang, MD, Lei Zhang, MD, and Tingting Li, MD

Abstract: Iodide mumps is an uncommon condition induced by iodide-containing contrast. We present the first reported case of iodide mumps in mainland China, which occurred after carotid artery intervention.

The patient, a 65-year-old Chinese male, had a history of dizziness, hypertension, diabetes, and right arm weakness. He had no history of allergies and had never previously received iodide-containing contrast. The patient's kidney function and other laboratory findings were normal. He underwent stenting of the left internal carotid artery (LICA) opening and received approximately 250 mL of a nonionic contrast agent (ioversol). Approximately 5 hours after angioplasty, bilateral local swellings were noted near the mandible; the masses were moderately firm and nontender.

Iodide mumps was diagnosed in the patient. Intravenous dexamethasone (10 mg) was administered. The submandibular glands had shrunk by 11 hours after angioplasty, and they gradually became softer. The mandibular salivary glands had completely recovered by 5 days after surgery.

Iodide mumps represents a rare late reaction to iodine-containing contrast media. This condition can occur in any patient receiving any iodinated contrast agent and may recur upon repeated exposure, but self-resolution can be expected within 2 weeks. All clinicians who use contrast media or iodide should be aware of this condition.

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Abbreviations: CT = computed tomography, DSA = digital subtraction angiography, LICA = left internal carotid artery, MRI = magnetic resonance imaging.

INTRODUCTION

Iodide mumps is an uncommon condition. A large-scale study of adverse reactions to iodinated contrast media performed in 337,647 patients did not report any cases of sialadenitis.[1] The first reported case of contrast-related sialadenitis was in 1956 and occurred after intravenous urography;[2] subsequently, cases have been reported in patients exposed to iodine in many different countries. There have been approximately 40 cases of iodide mumps reported in the English language literature since the first case was described over 50 years ago. One case was reported in a patient with renal impairment in Hong Kong in 2008,[3] but there have been no other reports from Mainland China. The previous cases were exposed to iodide in different ways, and only 1 previous case of iodide mumps occurred after carotid artery stenting (this case was reported in 2010).[4] Here, we report a patient who presented with contrast-induced sialadenitis after left carotid artery stent-assisted angioplasty in mainland China. To increase recognition of this condition, we also incorporate an analysis of the characteristics of the 36 previously reported cases.

CONSENT

The study protocol was approved by the Ethics Committee of the Second Affiliated Hospital, Medical School of Xi'an Jiaotong University. Informed consent was obtained from the patient's son on behalf of his father, and a copy of the written consent is available for review by the editor of this journal.

CASE REPORT

A 65-year-old Chinese man presented to our department with a 1-year history of dizziness and slight weakness of his right arm. The patient also reported a 1-year history of hypertension and diabetes. He was taking prescribed medications, and his blood pressure and blood sugar were stable. He had no history of allergies and had never previously received iodide-containing contrast. Physical examination showed a slight paralysis of the patient's right arm and leg (grade 4). His kidney function was normal (normal urea, creatinine, and cystatin C). Other laboratory results were also normal, including routine blood and urine tests, liver function tests, blood glucose concentration, blood lipid concentration, a full blood count, blood viscosity, homocysteine, coagulation function tests, erythrocyte sedimentation rate, C-reactive protein, autoimmune markers, thyroid-stimulating hormone, hepatitis B virus antibody/antigen, hepatitis C virus antibody, hepatitis E virus IgM, human immunodeficiency virus antibody/antigen, *Treponema pallidum* antibody, electrocardiography, and ultrasonic cardiogram. Brain magnetic resonance imaging showed multiple lacunar infarctions in the brainstem and basal ganglia. Brain digital

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From the Department of Neurology, Second Affiliated Hospital, Medical School of Xi'an Jiaotong University (GZ, RZ, YG, ZM, HW, TL); Department of Stomatology, Affiliated Children's Hospital, Medical School of Xi'an Jiaotong University, Xi'an (YL); and Department of Neurology, Second Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang, Shaanxi Province, China (LZ).
Correspondence: Guilian Zhang, Department of Neurosurgery, Second Affiliated Hospital, Xi'an Jiaotong University, #157 XiWuLu Street, Xi'an 710004, China (e-mail: zhgl_2006@126.com).
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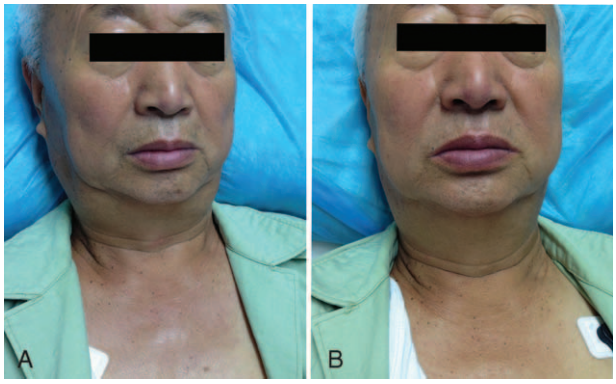

FIGURE 1. Bilateral enlargement of submaxillary glands, at initial onset (A) and 11 h after onset (B).

subtraction angiography (DSA) showed a large ulcerous plaque in the opening of the left internal carotid artery (LICA).

The patient underwent stenting of the opening of the LICA and received approximately 250 mL of a nonionic contrast agent (ioversol). Approximately 5 hours after angioplasty, the patient experienced a foreign body sensation below his left mandible, but he did not have any other discomfort, such as pain, fever, rubefaction, urticaria, itching, nausea, vomiting, or respiratory compromise. At this time, his temperature was 36.5°C, his blood pressure was 120/75 mm Hg, and his heart rate was 58 beats/min. Bilateral local swellings were identified near the mandible; the masses were moderately firm and nontender (Figure 1A). The patient had previously received antiplatelet medication and heparin; thus, the possibility of bleeding in the submandibular region was considered. Color Doppler ultrasound revealed bilateral, swollen, homogeneous glandular tissue without significantly abnormal echotexture. Intravenous dexamethasone (10 mg) was administered. By 11 hours after angioplasty, the submandibular glands had shrunk (Figure 1B), and they gradually softened. Neck computed tomography (CT) 43 hours after surgery revealed mild enlargement of the bilateral submandibular glands (Figure 2A, B). The average CT density of the right gland (17.7 ± 11 HU) differed from that of the left gland (12.9 ± 9.0 HU) (Figure 2C). By 5 days after surgery, the patient's mandibular salivary glands had recovered completely.

DISCUSSION

Cases of iodide mumps have been reported worldwide—from the US, UK, Israel, and Switzerland, for example—but there have been no reports from mainland China. In this study, we reviewed all of the previously reported cases published in English (Table 1 [2–32]); we analyzed the count data using constituent ratios, expressing the age and time of onset as mean ± standard deviation (SD). We identified only 36 cases of iodide sialadenitis[2–32] (22 men, 14 women; mean age, 60.0 ± 13.6 years; age range, 8–78 years). Of these 36 patients, 19 had received intravenous injections,[2,6–13,16,18,24,25,28,32] 10 had undergone arteriography[3,4,17,19,20,22,23,26,27,29] (1 case occurred after carotid artery stenting[4]), 4 had ingested an iodine compound,[5,14,30] 2 had undergone both arteriography injections and ventriculography,[21] and 1 was exposed to oral and intravenous iodide contrast media.[31] We found that iodide mumps can occur after intravenous, intra-arterial, oral, or ventricular iodide administration.

Iodide mumps occurred in bilateral (31, 86.1%) or unilateral salivary glands (5, 13.9%). Gland enlargement was a frequent clinical finding, and the largest mass measured approximately 5 cm in diameter. Nineteen cases involved the submandibular glands, and 12 cases involved the submandibular and parotid glands. Occasionally, the thyroid gland, lacrimal gland, or other glands were also involved. In our case, the patient experienced an accompanying foreign body sensation near his left mandible. Of the 36 previous cases, 8 patients reported pain in their glands; 1 patient developed a skin lesion, choking sensation, and facial paralysis, the most severe complications reported in the literature.[6] None of the cases showed life-threatening airway compromise. The onset varied from several minutes to 5 days after contrast medium administration, and the clinical features persisted for 12 hours to 11 days (mean, 3.83 ± 2.5 days) in 34 of the cases.

Iodide mumps can occur after the administration of any type of iodinated contrast agent, including both ionic and nonionic media.[12,17,18,33,34] Eighteen of the 36 patients had received ionic contrast media, 15 had received nonionic contrast media, and the type of media was not specified in 3 cases. A low-osmolar nonionic contrast agent (ioversol) was used in our case. When ioversol is administered quickly by intravenous injection, it immediately reaches a peak level in the blood; the blood level begins to fall after 5–10 minutes. The iodine concentration in the blood then reaches an equilibrium with the extracellular space. According to Katayama et al,[1] the use of nonionic contrast media significantly reduces the frequency of

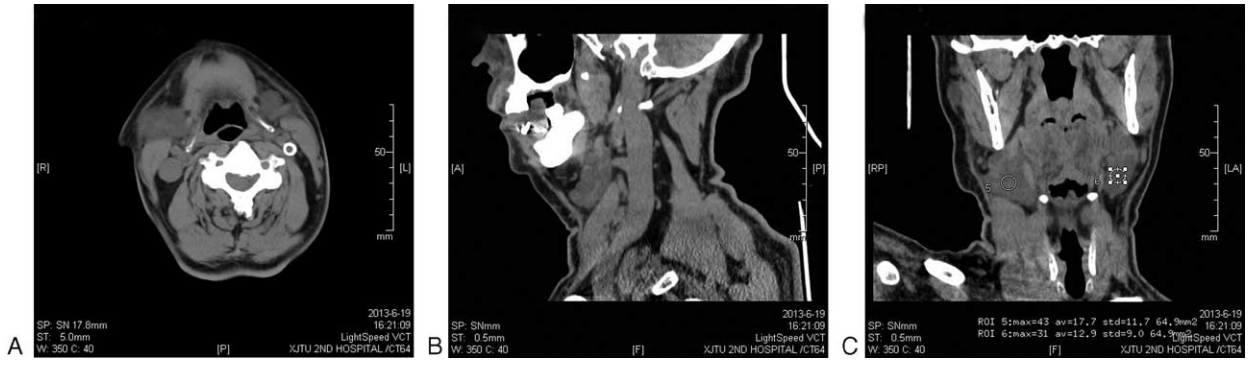

FIGURE 2. Neck CT 43 h after onset (A, axial; B, sagittal; C, coronal views).

TABLE 1. Summary of Iodide Mumps Cases in the Published Literature

Author/Year	Age (yr)/Sex	Onset	Route of Administration	Type of Co- ntrast	Glands Involved	Duration	Renal Disease/Failure	Other clinical Features	Treatments
Sussman RM et al/1956[2]	68/M	2 d	Intravenous	Ionic contrast, (Hypaque, 30 mL)	Bilateral, Submandibular, Parotid	4 d	Nil	Nil	Nil
Sussman RM et al/1956[2]	62/M	2 d	Intravenous	Ionic contrast, (Hypaque, 20 mL)	Bilateral, submaxillary	6 d	Nil	Nil	Nil
Chow KM et al/2008[3]	38/F	3 d	Artery angiography and intervention	Nonionic contrast, (iopamidol)	Bilateral, Parotid	2 d	Lupus nephritis	Ultrasound showed diffuse swelling with abnormal heterogeneous echotexture and surrounding soft tissue inflammation.	Nil
Capoccia L et al/2010[4]	71/M	1 d	Artery angiography and stentting	Nonionic contrast, (Iomeron-350, 50 mL)	Unilateral, Submandibular	7 d	Nil	Sialorrhea	Steroid
Carter JE et al/1961[5]	48/F	Near 12 h	Take orally	Iodinated glycerol 2 tablets	Not mentioned, Submaxillary, Parotid	72 h	Nil	Bronchospasm and cough; Similar history ago	ACTH gel
Carter JE et al/1961[5]	32/F	2 d	Take orally	Ionic contrast, (potassium iodide)	Bilateral, Parotid	2 d	Nil	Throat soreness, mouth swollen, and pain in epigastrium	Nil
Koch RL et al/1969[6]	48/M	0.5 h	Intravenous	Ionic contrast, (Hypaque)	Bilateral, Parotid	5 d	Nil	Painful, facial nerve palsy requiring decompressi	Prednisone, Benadry
Harris et al/1970[7]	64/M	1 d	Intravenous	Ionic contrast, (Hypaque, 125 mL)	Bilateral, Submandibular	6 d	Nil	Nil	Nil
Harris et al/1970[7]	78/M	1 d	Intravenous	Ionic contrast, (Hypaque, 125 mL)	Bilateral, submandibular	7 d	Renal calculus.	Throat soreness	Nil
Harris et al/1970[7]	62/M	1 d	Intravenous	Ionic contrast, (Hypaque, 125 mL)	Bilateral, submandibular	2 d	Renal failure	Nil	Nil
Nakadar AS et al/1971[8]	53/M	4 d	Intravenous	Ionic contrast (Urografin)	Bilateral, Submandibular	3 d	Renal failure	Discomfort	Nil
Talner et al/1971[9]	57/M	3 d	Intravenous	Ionic contrast (Hypaque)	Bilateral, Submandibular	7 d	Renal failure	Slight dysphagia and mild localized postprandial ache	Not mentioned
Imbur et al/1972[10]	64/M	3 h	Intravenous	Ionic contrast (Hypaque)	Not mentioned, Submandibular, Parotid	2 d	Nil	Recurrence later with renal angioplasty	Nil
Davidson et al/1974[11]	8/F	24 h	Intravenous	Ionic contrast (Conray-280)	Unilateral, Submandibular, Parotid	3 d	Nil	Facial pain	Diphenhydramine
Kohri et al/1977[12]	52/F	1 h	Intravenous	Ionic contrast (Hypaque, 100 mL)	Bilateral, Submandibular	3 d	Nil	Nil	Antihistamines, steroids.
Cohen JC et al/1980[13]	76/F	5 d	Intravenous (enhanced CT scan)	Not reported	Bilateral, Parotid	3 d	Renal failure	Jaw pain, repeatedly exposure to contrast material history	Nil
Goldberg RE et al/1987[14]	55/F	Shortly	Take orally (nuclear bone imaging)	Ionic contrast (potassium iodide)	Bilateral, Submandibular	4 h	Not mentioned	Nil	Nil
Wolf et al/1990[15]	57/M	3 h	Intravenous	Ionic contrast (Urografin)	Bilateral, Submandibular, parotid	48 h	Recurrent renal colic	Mild stridor and dyspnea.	Corticosteroids
Wylie EJ et al/1991[16]	68/M	4 h	Intravenous	Nonionic contrast (iopamidol, 100 mL)	Bilateral, Submandibular, parotid	12 h	Nil	A sensation of choking	Indomethacin
Berman HL et al/1992[17]	62/M	24 h	Arteriography	Nonionic contrast (iohexol-350, 60 mL; iohexol-300, 40 mL)	Bilateral, Submandibular, parotid	1 d	Renal failure	Sublingual glands, lacrimal glands, thyroid gland, conjunctival edema and erythema	Diphenhydramine, hydrocortisone
Linn JF et al/1996[18]	70/F	16 h	Intravenous	Nonionic contrast, (iopromide, 100 mL)	Bilateral, Submandibular	6 h	Nil	Recurrent later with oral administration of hypaque	Antihistamine, prednisolone
Chuen J et al/2000[19]	70/M	18 h	Artery angioplasty	Nonionic contrast, (Ultravist-300, 100 mL)	Bilateral, Submandibular, parotid	11 d	Nil	Recurrent later with angiogram	
Kalaria VG et al/2001[20]	63/F	A few hours	Artery intervention	Nonionic contrast, (Ioversol, 100 mL)	Bilateral, Submandibular	2 d	Renal failure	Pain, a history of mumps.	Analgesics and dialysis

Author/Year	Age (yr)/Sex	Onset	Route of Administration	Type of Co- ntrast	Glands Involved	Duration	Renal Disease/Failure	Other clinical Features	Treatments
Ben-Ami R et al/ 2002[21]	77/M,	5 d	Artery angiography and ventriculography	Nonionic contrast, (Ioxoglate)	Bilateral, Parotid	7 d	Renal failure	Painful, recurrent later with angioplasty and stent	Oral hydration and consumption of sour candy
Ben-Ami R et al/2002[21]	66/F	1 d	Artery angiography and ventriculography	Nonionic contrast, (Ioxoglate, 130 mL)	Bilateral, Submandibular	1 d	Nil	Painful, recurrent later with coronary angiography	
Magen E et al/2003[22]	62/M	7 h	Artery angiography	Nonionic contrast, (iopromide, 120 mL)	Bilateral, Submandibular, parotid	36 h	Renal failure	Fever 38.9°C	Continuous Ambulatory Peritoneal Dialysis
Fränkle S et al/2004[23]	63 /F	30 h	Artery intervention	Ionic contrast, (Iomeprol, 500 mL)	Bilateral, Submandibular	2 d	Nil	Minimal dysphagia	Nil
Park SJ et al/2005[24]	73/M	1/6 h	Intravenous (enhanced CT scan)	Nonionic contrast, (Ioxaglate, 140 mL)	Bilateral, Submandibular	1 d	Nil	Nil	Nil
Wyplosz B et al/2006[25]	60/M	1 d	Intravenous injection (enhanced CT scan)	Nonionic contrast, (Iopamidol, iohexol, iopentol)	Bilateral, Submandibular	7 d	Nil	Recurrence with every injection	Nil
Dallo ML et al/2007[26]	72/M	12 h	Artery angioplasty	Nonionic contrast, (Iodixanol, 300 mL)	Bilateral, Submandibular	12 d	Nil	Nil	Prednisone, 80mg
Moisey RS et al/2007[27]	51/M	1 d	Artery angioplasty	Nonionic contrast, (Visipaque-320 300 mL)	Bilateral, Submandibular, parotid	24 h	Renal failure	Nil	Steroid and hemodialysis
Gilgen-Anner Y et al/2007[28]	71/F	2 d	Intravenous injection (enhanced CT scan)	Ionic contrast (Ioxithalamate)	Bilateral, Submandibular	A few days.	Nil	The biopsy of the lump showed normal glandular tissue, mild edema, and no cellular infiltrate. Recurrent later with CT enhanced scan.	Nil
Bohora S et al/2008[29]	56/M	6 h	Artery angiography and stentting	Nonionic contrast, (Iohexhol, 200 mL)	Bilateral, Submandibular	2 d	Nil	Mild local discomfort, swallowing difficulty	Nil
Lei L et al/2012[30]	53/F	2 d	Take orally	radioactive iodine 131	Bilateral, Parotid	5 d	Nil	Pain, facial swelling, difficulty jaw opening.	Well hydrated, take ibuprofen.
Chau AM et al/ 2013[31]	66/M	24 h	Take orally and intravenous injection (enhanced CT scan)	Not mentioned	Bilateral, Submandibular glands	several days	Nil	Painful, recurrent after annual contrast-enhanced CT scan	Pretreated with low dose prednisone
Acosta-Ochoa MI et al/2014[32]	65/M	48 h	intravenous injection (enhanced CT scan)	Not mentioned	Unilateral, Submandibular, parotid	6 d	Renal failure	Nil	Nil
Current case/2014	65/M	5 h	Artery angiography and stentting	Nonionic contrast, (Ioversol, 250 mL)	Bilateral, Submandibular	5 d	Nil	Nil	Dexamethasone

According to primary literature, contrast media were divided into ionic and nonionic. D = day; F = female; H = hour; M = male.

severe and potentially life-threatening adverse reactions. Nevertheless, minor complications, such as sialadenitis involving the parotid[21] and submandibular[19,26,35] glands, have been reported.

At present, the mechanisms behind sialadenitis are not completely known. An idiosyncratic reaction is 1 possible mechanism; indeed, Ben-Ami et al[18,19,21] found that repeated exposure to iodinated contrast media could induce iodide mumps in susceptible patients. Of the 36 cases, 9 experienced recurrence when iodinated contrast was administered again. However, these patients did not have personal/family histories of allergic diseases or drug/food allergies. The patients were from different countries, so sialadenitis is not race-specific. A second possible mechanism is that sialadenitis may be directly related to the toxic accumulation of iodide in the ductal systems of the salivary glands; serum iodide levels >10 mg/100 mL may impair salivary gland function.[36] However, other authors disagree with this view.[8] Indeed, in previous studies, different doses of contrast media were administered among the cases. The third possible mechanism involves the kidneys. Ninety-eight percent of injected iodide is eliminated by the kidneys; inorganic iodide is also removed from the plasma by the breasts, thyroid, stomach, lacrimal glands, and salivary glands.[37] As a result, renal impairment may be a risk factor,[8] potentially leading to impaired iodide elimination and resulting iodide accumulation in vivo, thereby causing salivary gland intoxication and inflammatory swelling. Eleven of the 36 cases exhibited renal failure.

It was not until 2007 that Gilgen-Anner et al[28] used histological analysis, skin tests, controlled reexposure, premedication, and imaging studies to establish that salivary gland lesions in affected patients represented rare noninflammatory edema elicited by iodine. Sialadenitis is associated with elevated serum iodide levels, often in combination with severe renal impairment.[21] In our case, CT images obtained 43 hours after surgery did not show obvious inflammation and edema, but the average CT density in both submandibular glands was lower than normal (20–40 HU), supporting the presence of noninflammatory edema. However, a detailed understanding of the mechanisms involved in this type of sialadenitis requires further study.

Most studies have shown that iodide mumps is a self-limiting condition that does not necessitate any intervention. Some patients have been treated with corticosteroids or antihistamines, but there have been no controlled trials confirming their efficacy. It is worth mentioning that recurrence is common if susceptible patients are subjected to further iodinated contrast media.

CONCLUSIONS

Iodide mumps is a rare late reaction to iodine-containing contrast media. This condition can occur in any patient, regardless of sex, age, or race, route of administration, in association with any iodinated contrast medium, and it may recur after repeated exposure, but self-resolution can be expected within 2 weeks. Given the widespread use of imaging and interventional techniques that utilize iodinated contrast, clinicians should be aware of this condition.

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