

Iodide myxedema with facial swelling simulating angioneurotic edema

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The iodide given as treatment for asthma may cause myxedema with facial swelling simulating angioneurotic edema, and this facial swelling may be erroneously attributed to allergic reactions. In 5 patients with asthma, myxedema developed during iodide therapy. Each patient complained of swelling of the face and eyelids, and this was considered allergic in origin by one or more physicians. However, the diagnosis of iodide-induced myxedema was suggested by the history of regular iodide ingestion, facial and eyelid swelling, and other symptoms, including fatigue, cold intolerance, hoarseness, and dry skin and hair. Physical examination also revealed slowed deep tendon reflexes in 4 patients and diffuse goiter in 4. Laboratory measurements supported the diagnosis of myxedema. In 4 patients, the facial swelling and other symptoms of myxedema disappeared after cessation of iodide therapy. The fifth patient required iodide for control of asthmatic symptoms, and the symptoms of myxedema were controlled by exogenously administered thyroid hormone. Myxedema due to iodide ingestion may develop because of an underlying defect in thyroidal function.

Patients with chronic asthma frequently ingest iodides for prolonged periods, and ultimately a few develop myxedema with generalized facial swelling.¹⁻³ Because the facial swelling appears during treatment for asthma and sometimes varies in severity, it may be erroneously diagnosed as allergic angioneurotic edema. I have seen 5 patients in whom myxedema due to iodide ingestion simulated angioneurotic edema.

CASE REPORTS

Case 1

A 47-year-old Caucasian woman complained of asthma and facial swelling. She had had mild asthma for several years, and for 2 years she had been treated with medications, including 20 to 30 drops of saturated solution of potassium iodide daily on a regular basis. Three to 4 months after the iodide regimen had been started, she had noted facial and eyelid swelling, neck swelling, cold intolerance, hoarseness, and dry skin and hair. She had consulted several physicians and had been told that her facial swelling was due to "angioedema and allergy." She had been given various medications but did not improve. She was receiving a course of hyposensitization injections.

From the Division of Allergic Diseases and Internal Medicine, Mayo Clinic and Mayo Foundation.

Presented in part at the annual meeting of the American Academy of Allergy, Boston, February 5 to 7, 1968.

Received for publication Jan. 5, 1971.

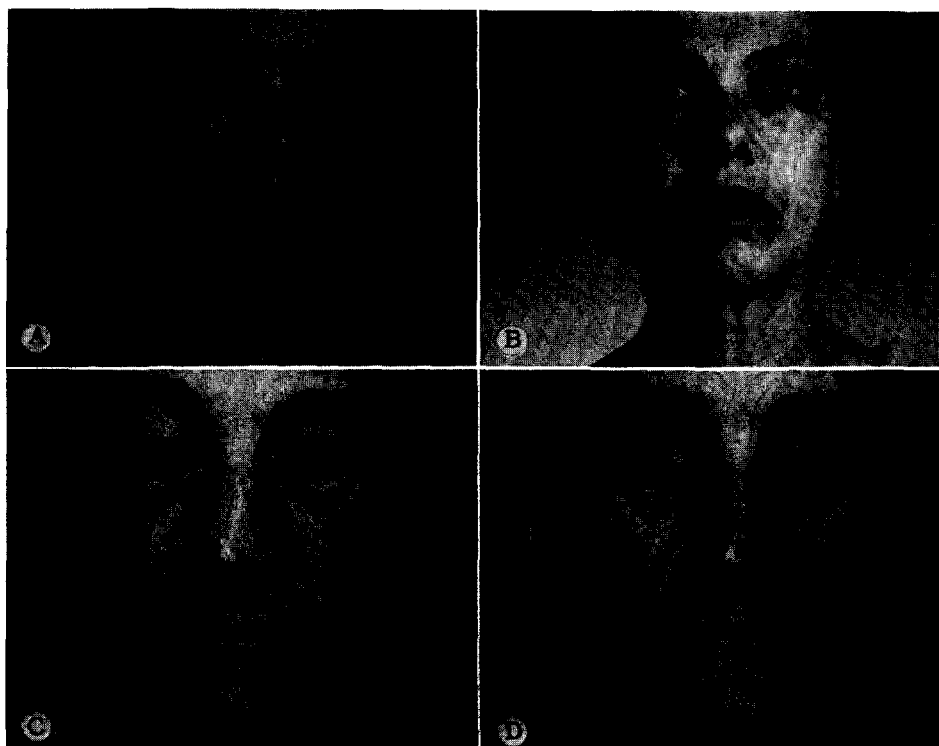


FIG. 1. **A** (Case 1) and **C** (Case 5): Facial and eyelid swelling due to iodide-induced myxedema. **B** (Case 1) and **D** (Case 5): Disappearance of swelling after iodide ingestion was stopped.

On examination, her mentation and actions were slow, her eyes were puffy, her face was diffusely swollen (Fig. 1, A), her skin and hair were dry, her voice was hoarse, and her deep tendon reflexes were slowed. A moderately large, soft goiter was found. The basal metabolic rate, serum cholesterol level, and erythrocyte triiodothyronine uptake supported the diagnosis of myxedema (Table I). Thyroglobulin antibody was present in significant titer. A needle biopsy of the thyroid gland showed small follicles empty of colloid, with cuboidal epithelium, some focal fibrosis, but no evidence of thyroiditis. Iodide ingestion was stopped, and the goiter, facial swelling, and other symptoms of myxedema disappeared within 4 weeks (Fig. 1, B).

Case 2

A 62-year-old Caucasian woman complained of facial swelling, sluggishness, and enlargement of the neck. She had had chronic asthma for 23 years, which at times had required adrenal corticosteroid medication to control symptoms. Therapy with 10 to 30 drops of saturated solution of potassium iodide daily had been begun 9 months prior to her examination. Four months after starting the iodide medication she had developed generalized facial swelling, fatigue, and swelling of the neck. She had consulted several physicians about these complaints and had received various medications, including antihistamines, for "allergic swelling of the face and eyes."

On examination, her hair was coarse, her skin was dry, and a soft goiter was noted. Deep tendon reflexes were slowed. Her face and eyelids were generally swollen, and her voice was hoarse. The basal metabolic rate, serum cholesterol level, and erythrocyte triiodothyronine uptake were suggestive of myxedema (Table I). All iodide medications were stopped, and

TABLE I. Clinical and laboratory data on 5 patients with iodide-induced myxedema

Test	Normal value	Case 1 (F, 47 yr.)	Case 2 (F, 62 yr.)	Case 3 (F, 52 yr.)	Case 4 (F, 69 yr.)	Case 5 (M, 62 yr.)
Basal metabolism (%)	-10 to +10	-15	-22	-19*, -7†	-27	—
Serum cholesterol (mg./100 ml.)	150-250	372	328	398*, 356†	292	277
Serum iodides (μ g/100 ml.)						
Protein bound	3.5-7.5	26.5	—	—	11.7	—
Butanol extractable	—	21.4	—	—	8.6	—
ETVC†	8.7-13.5	7.8	8.3	—	—	—
Achilles tendon reflex (sec.)	0.29-0.46	Slowed	Slowed	0.52*	0.35	0.56
Thyroglobulin antibody titer	0	1:2,500	0	0*	—	0
Total serum thyroxine (μ g/100 ml.)	4-11	—	—	—	—	1.4

*Value while off iodide for 10 days.

†Value while off iodide for 23 days.

‡Erythrocyte triiodothyronine uptake coefficient.

within 4 weeks the facial swelling and goiter, as well as the other symptoms of myxedema, completely regressed.

Case 3

A 52-year-old Caucasian woman complained of swelling of the face, hands, and feet. She had had occasional wheezing for several years and had had chronic asthma for 3 years prior to examination. She had started taking 30 drops of saturated solution of potassium iodide daily 4 months prior to being seen. One month after the iodide medication had been started, she noted swelling of her face and hands. A physician had told her that this was "due to asthma and allergy." She had decided to stop all medication because of fatigue.

She was first seen at the Mayo Clinic 10 days after she had stopped taking iodide. At that time she had generalized facial swelling but felt that this had begun to regress. No goiter was palpable. The deep tendon reflexes were slowed. The basal metabolic rate and serum cholesterol level, measured 10 and 23 days after iodide use was stopped, supported the diagnosis of resolving myxedema (Table I). The Achilles tendon reflex was slowed. The swelling of the face and eyelids continued to regress and disappeared within 4 weeks.

Case 4

A 69-year-old Caucasian woman complained of swelling of the face and eyes, fatigue, and hoarseness of more than one year's duration. She had had chronic asthma for 4 years and had been taking 10 drops of saturated solution of potassium iodide daily for 24 months. The time of onset of her facial swelling and fatigue was uncertain, but the symptoms apparently had been present for at least one year. She had consulted several physicians and had been given various medications. She had been advised that her symptoms were due to "allergy."

On examination, her skin was dry and coarse. There was diffuse swelling of the face and eyelids. Her voice was hoarse, and a firm goiter was present. The basal metabolic rate and serum cholesterol level supported the diagnosis of myxedema (Table I). The Achilles tendon reflex was normal. Because of the severity of the asthma, the use of iodide was continued and thyroid hormone replacement was started. Symptoms of myxedema, including the facial swelling, disappeared within a few weeks after this treatment was started.

Case 5

A 62-year-old Caucasian man complained of swelling of his face, hands, and legs of 11 months' duration. He had had intermittent asthma for 43 years and had been taking a medication containing potassium iodide daily for 2 years. He had been hospitalized for investigation of the facial swelling, and a final diagnosis of "allergy to penicillin and Terramycin" had

been made. The asthma had regressed during hospitalization, and the use of the iodide-containing medication had been stopped for 4 weeks, during which time the facial swelling had receded. The severity of the asthma then increased, so the ingestion of iodide was resumed. The facial swelling had returned within 2 months, and severe fatigue, hoarseness, and disturbed mentation had developed.

On examination, his face and eyelids were puffy (Fig. 1, C) and his skin was dry. His voice was very hoarse, and a diffuse soft goiter was noted. Deep tendon reflexes were markedly slowed. A roentgenogram of the chest showed that the heart was enlarged and globular, but fluoroscopic examination did not demonstrate pericardial effusion. Serum thyroxine level was below normal, and the Achilles tendon reflex was slowed (Table I). Serum cholesterol level was elevated. Iodide ingestion was stopped, and after 6 weeks the facial swelling (Fig. 1, D), hoarseness, and fatigue disappeared and the serum thyroxine increased to a normal level.

DISCUSSION

Excessive iodide intake is known to be goitrogenic and to cause myxedema in some patients.⁴⁻⁸ The 5 patients in this report illustrate this complication and emphasize this possibility in asthmatic subjects treated with iodides. Each patient complained of swelling of the face and eyelids, and this swelling was considered allergic in origin by one or more physicians and was treated as such. The correct diagnosis of iodide-induced myxedema was suggested by the history of regular ingestion of iodide and by the presence of facial and eyelid swelling (which was gradual in onset), fatigue, cold intolerance, hoarseness, dry skin and hair, goiter, and slowed deep tendon reflexes. The facial swelling was not the localized transient type seen in angioneurotic edema but tended to be persistent. The 5 asthmatic patients reported herein had been ingesting iodide from 1 to 13 months before the onset of symptoms of myxedema. Because the patients were being treated for chronic asthma, the insidious onset of the symptoms of myxedema was attributed to allergic causes. The goiter and the symptoms of myxedema regressed promptly when iodide ingestion was stopped. One patient continued taking iodide for relief of asthmatic symptoms, and the goiter and myxedema were controlled by thyroid hormone replacement.

Laboratory tests of thyroid function, which are particularly valuable in the presence of high serum levels of iodide, include the serum thyroxine determination, basal metabolic rate, and erythrocyte or resin uptake of triiodothyronine.⁹ The serum cholesterol level and Achilles tendon reflex also reflect thyroidal function. The protein-bound iodine and butanol-extractable iodine values were not helpful, as both were above the normal range because of the high serum level of iodide bound to protein. Direct serum measurement of the serum thyroxine was not available until Case 5 was seen, and this is now the preferred laboratory measurement of thyroid function.¹⁰

One patient in this series had a needle biopsy of the thyroid, and this showed small follicles empty of colloid and without thyroiditis. The histologic changes in the thyroid in iodide-induced goiter are not uniform. In most cases in which biopsy has been performed, parenchymatous hypertrophy has been seen. However, colloid-rich, flat, unstimulated follicles also have been found in many of the goiters studied.²

Myxedema caused by iodide ingestion is probably caused by inhibition of organic binding of iodide in the thyroid.⁸ Studies of laboratory animals have

shown that the intrathyroidal accumulation of iodide above a critical level interferes with the organic binding of iodide (Wolff-Chaikoff¹¹ effect) and therefore with the production of thyroid hormone. The reason iodide produces goiter and myxedema in certain persons is not clear. These individuals may have a basic underlying defect in thyroid function that allows excessive intrathyroidal concentration of iodide.⁸ Hall and associates¹² have suggested that a latent thyroid autoimmunity may be present in patients with intrinsic asthma because antithyroglobulin antibody has been found in the serum of some patients with iodide-induced goiter. However, the antibody titers are seldom as high as those seen in Hashimoto's thyroiditis. Braverman and colleagues¹³ documented the remarkable susceptibility to the induction of myxedema by pharmacologic doses of iodide in patients euthyroid after radioiodine use or surgical treatment of diffuse toxic goiter. They also postulated an underlying thyroidal abnormality. In any event, physicians must be careful not to attribute iodide-induced facial swelling of myxedema to allergic causes.

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