CASE REPORTS

Essential Cold Urticaria:
A Potential Cause of Death While Swimming

C. SIGAL, M.D.,* *Portland, Ore., U.S.A.*, and J. C. MITCHELL, M.D.,†
Vancouver, B.C.

THE conditions characterized by cold hypersensitivity states may be considered in three main classes as cold urticaria, cold hemoglobinuria and cryoglobulinemia.[1] Essential cold urticaria is a syndrome characterized by histamine-release phenomena occurring as a result of local or general cold exposure and may be congenital or acquired.[2, 3] The disorder is of current interest because of recent work on the role of the mast cell and basophil leukocyte in urticarial reactions.[1] Horton, Brown and Roth[4] in 1936 reported that immersion in cold water may be followed by collapse and drowning. The following case report illustrates the risk to any swimmer who suffers from this disorder.

During the summer of 1961 a 25-year-old white male store manager experienced an attack of itching of the skin shortly after leaving a heated swimming pool. He noted some itching and redness of the pinnae on exposure to cold during the following winter. In June 1962 he bathed in a lake, and after 15 minutes' immersion he noted that the skin of the entire body had become bright red. A large amount of blossom from nearby cottonwood trees was floating on the surface of the lake. He left the water, and while drying by rubbing with a towel, he noted the onset of weakness, vertigo and difficulty in getting his breath. He reported that he "fainted slowly over a few minutes". He was carried to a seat and, in the supine position, regained consciousness and "shivered and shook but could not keep warm".

About 15 minutes later he was examined by a physician, who found that the patient was in a physical condition which resembled anaphylactic shock or a vasovagal attack. The pulse was regular, 88 per minute, and the blood pressure was 90/70 mm. Hg. The patient could hear but he could not speak; peripheral cyanosis was present. While the physician was preparing an injection, the patient appeared to make some further recovery and it was noted that the pulse had fallen to approximately normal and that the blood pressure had risen to 130/70 mm. Hg. Intramuscular injections of 0.5 ml. of 1:1000 adrenaline and of 10 ml. trimeprazine (Panectyl) were administered. Marked improvement occurred and the patient was driven to the hospital, where, during the next few hours, he experienced sweating, shivering and rigors. During the evening he vomited a large amount of coffee-ground material which was positive for blood.

During the first night in hospital he had an attack of trembling and shaking followed by sweating and by incontinence of feces. Thereafter, recovery was uneventful and he was discharged from hospital after four days.

During the remainder of the summer of 1962 he noted attacks of redness, itching and swelling of the skin after any exposure to cold. On one occasion he walked through the spray of a garden water-sprinkler and observed that a red spot appeared on his skin where each drop of water had settled; this exposure was followed by weakness and fatigue which passed off when he lay supine.

Since he was fond of swimming, he persevered in attempts to overcome the disability and discovered that he could swim in the lake only if he carried out a careful preparative technique. If he immersed his body a part at a time, making four or five entries into the water and withdrawals during the course of half an hour, the symptoms did not appear or, if they did, were tolerable. He also tried an increase in duration of exposure to the water on successive days and found that, with a gradual increase, the symptoms successively diminished. Ingestion of an antihistamine before swimming markedly reduced the itching but did not prevent the appearance of swelling and redness of his skin.

During the following winter he experienced more attacks. When he washed his car he noted swelling of the hands and stiffness of the fingers accompanied by difficulty in making a fist. Immersion of his hands in hot tap-water relieved these symptoms and speeded recovery. He noted that he could suck ice-cubes until they melted, without any swelling of the mouth.

On a fishing trip he was affected by a cold wind which entered his clothing around the legs, the skin of which became red and itchy. During a hunting trip he sat down on a wet, cold, tree-stump and his buttocks became red, swollen and itchy. If he was exposed to cold when "nervous", the dorsa of the hands reddened and itched but the palms did not.

He discovered that he could bring on the changes in the skin at will by tub-bathing. The symptoms brought on by tub-bathing were identical with those brought on by lake-swimming, and, by use of a thermometer in the bath-water, he found that the critical temperature was 72° F. At a temperature above 72° F. he was not affected but below that temperature he experienced redness and itching of the skin accompanied by tiredness, fatigue, and dizziness similar to "the fatigue one feels when taking a very hot bath".

During the early months of 1963 he noted that if he went out of the store into the open air his face and ears swelled but that these symptoms were experienced

*Resident, Division of Dermatology, University of Oregon Medical School, Portland, Oregon, U.S.A.; lately, Assistant Resident in Medicine, Vancouver General Hospital.
†Clinical Assistant Professor, Faculty of Medicine, University of British Columbia.
750 West Broadway, Vancouver 9, B.C.

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only on the coldest days, probably at an outdoor temperature below 20° C. If his hands were uncovered they became beetroot-red, but if the hands were gloved they remained unaffected on a cold day.

Previous History

From early childhood to age 15 he had had attacks of urticaria. Ingestion of hen's egg had been followed by the appearance of hives. With avoidance of eggs, no attack of hives were noted until about the age of 20; then occasional bouts of hives were noted until the age of 25, but no definite eliciting factor was identified.

At the age of 10, he noted attacks of redness and watering of the eyes with sneezing and running of the nose. These symptoms were perennial, but exposure to hay and grain dust would precipitate an attack.

In September 1957 he reported recurring attacks of right flank pain, often accompanied by fever, during the previous several years. Pyelography revealed right hydronephrosis, and on October 1, 1957, right nephrectomy was performed. The pathological diagnosis was acute and subacute non-specific pyelonephritis with pyonephrosis.

In the spring of 1962, after stepping upon a rusty nail, he received an injection of tetanus toxoid, and at about the same time he was given oral poliomyelitis vaccine, without any unusual reaction.

Family History

The patient's mother had seasonal bronchial asthma which was attributed to exposure to tree pollens. After a change of residence and with avoidance of propinquity to birch trees, asthma did not recur.

Physical Examination

When the patient was examined on May 6, 1963, an eruption of papular acne and seborrhea was present on the face but the skin and mucous membranes were otherwise unremarkable. The hemoglobin value was 14.5 g. per 100 ml. and the white blood cell count was 9000 per c.mm. with 55% neutrophils, 38% lymphocytes, 4% monocytes, 1% eosinophils, 1% basophils, and 1% staff cells. Morphology of the stained erythrocytes was normal. The erythrocyte sedimentation rate was 1 mm. per hour (Westergren). The urine was negative for albumin and glucose; the urinary sediment showed no abnormality. A V.D.R.L. precipitation test was negative. Serum electrophoresis showed normal mobility of all fractions without evidence of cryoglobulins. Cold agglutination of erythrocytes was not observed.

Application of ice to the volar surface of the forearm for 20 seconds resulted in erythema which faded in 60 seconds. Application of ice for 30 seconds resulted in erythema as before, but two to three minutes later, erythema reappeared and a wheal appeared and was followed by a flare and by pruritus. The wheal was sharply marginated, without pseudopodia. By applying beakers containing water at different temperatures for two minutes to the patient's back it was found that whealing occurred following exposure to a temperature of 16° C. Erythema and slight pruritus but no whealing occurred following exposure to 20° C.

Progress

During the summer of 1963, the patient persevered in his attempts to go swimming. He found that he was able to stay in the water for about 45 minutes provided he desensitized himself as previously described. After three or four short immersions, each followed by drying, he was able to swim without ill-effect during the next seven or eight hours. If he entered the water without preliminary trials he experienced a reaction, the course of which was not affected by oral antihistamine therapy. Such therapy, however, prevented any itching.

DISCUSSION

Lewis[5] showed that histamine-like substances are liberated from the skin when it is irritated by physical agents, particularly by cold. This systemic reaction to cold is similar to that which is produced by either subcutaneous or intravenous injection of histamine. The systemic effects described in our patient are explicable by histamine release. Sensitivity to cold occurs in cryoglobulinemia and in syphilitic paroxysmal cold hemoglobinuria, but the presence of cold agglutinins in the blood is not associated with such sensitivity.

The various eliciting stimuli for cold urticaria enumerated in the literature include prophylactic injections and previous atopy. An atopic family history was recorded in one-third of those patients in whom such enquiry had been made.[3] Desensitization to cold may be attempted. Kierland[6] recommended immersion of the patient's hand or foot in water at 17° C. for from two to five minutes, once or oftener daily, and gradually reducing the temperature of the water to a minimum of 7° C. over a period of from three to four weeks. This procedure was not successful in our patient. Using blood from two patients with acquired essential cold urticaria, Juhlin and Shelley[1] demonstrated that basophils and mast cells underwent degranulation when chilled. Congenital or familial cold urticaria is inherited as a dominant trait, and the basophil cold-sensitivity test may prove to be of use in exploring the genetic background of the autoimmune state.

Acquired cold urticaria could be regarded as based on an antigen-antibody mechanism if it is postulated that low temperatures facilitate the reaction between an antibody and a pre-existing antigen present in human skin.

The crucial test in this respect is the demonstration of circulating antibody or reagin by passive transfer (Prausnitz-Kustner test). This test involves the possible transmission of serum hepatitis to a healthy individual. Enquiry from our patient's family physician revealed that there had been a recent "flurry of cases of hepatitis at random throughout the district" and accordingly passive transfer tests were not performed.

SUMMARY

A 25-year-old white man, who gave a personal and family history of atopy, began to develop urticaria from exposure to cold and after swimming collapsed with evidence of hypotension and partial loss of consciousness followed by hematemesis. In subsequent urticarial reactions to cold, antihistamine therapy prevented itching but did not prevent whealing. A wheal could be produced by application of cold to the skin. The hazards of swimming for patients with essential cold urticaria are emphasized.

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Thrombocytopenic Purpura During Pregnancy Associated with an Abnormal Protein in the Serum

M. LACOMBE, M.D., F.R.C.P.[C],* G. D'ANGELO, M.T., A.R.T.,†
B. LARAMEE, M.D.‡ and M. LAMOUREUX, M.D., F.R.C.S.[C],§
Montreal

IN RECENT years, it has become apparent that the syndrome, "idiopathic thrombocytopenic purpura", consists of a complex of disorders[1] resulting from the action of possibly many different etiological factors. The occurrence of this syndrome during pregnancy, although fortunately rare, represents a very serious condition which has a fatal prognosis in a high proportion of cases.[2-4]

The purpose of this communication is to report one such case and comment on an unusual feature in this condition, namely the presence of an abnormal serum protein component, migrating with the beta globulins on paper electrophoresis, and having the sedimentation constant of mesaglobulins on ultracentrifugation.

The patient, a 23-year-old woman, was admitted to hospital on December 12, 1961. Two months prior to admission, while in the thirtieth week of an apparently normal pregnancy, she began to have frequent epistaxis, spontaneous bleeding from the gums, and slight blood vaginal discharge, and became covered with petechiae and ecchymoses. Physical examination at that time was otherwise negative, and hematologic tests revealed a severe degree of thrombocytopenia with a slight degree of anemia. Corticosteroids were administered both intravenously and by mouth, along with antihistaminics and vitamins, without any improvement in her condition. She was then transferred to the Maisonneuve Hospital.

Repeated questioning on admission failed to reveal evidence of any exposure to toxic agents, or intake of drugs other than prenatal vitamins, and no history of recent allergic or infectious disease could be elicited. Past history was negative, except for one previous pregnancy and delivery, without incident.

Physical examination revealed a healthy looking woman, slightly pale. There were numerous petechiae and ecchymoses over the whole body and mucous membranes. The pulse was 96 per min., and regular; the blood pressure was 120/95 mm. Hg; and a gravid uterus, 36 cm. in height, could be palpated. The liver and spleen were not enlarged and the examination was otherwise negative.

Laboratory procedures gave the following results: Urinalysis, normal. Blood: hemoglobin, 13.0 g.; hematocrit, 40.5%; leukocyte count, 13,700 per c.mm.; neutrophils, 74%; lymphocytes, 20% and monocytes, 5%; reticulocytes, 6.2%; platelets, 3000/c.mm.; bleeding time (Ivy), longer than 30 minutes; coagulation time (modified Lee and White), 16 minutes (normal: 10-20 min.); clot retraction, nil after 24 hours; sedimentation rate (Wintrobe), 45 mm. after one hour; blood urea nitrogen, 29.2%; blood sugar, 82 mg. %; fibrinogen, 578 mg. %; blood group, A positive; Coombs' test (direct and indirect), negative.

A bone marrow aspiration was found to be rich in cellular elements. No morphological abnormality could be demonstrated except for megakaryocytes, which were numerous but generally devoid of platelets at their periphery.

Protein electrophoresis performed on her admission showed a striking peak in the beta globulin fraction (Fig. 2a). The Sia test for macroglobulin was negative but an ultracentrifugation analysis (performed by the Institute of Medical Physics, Belmont, Calif., U.S.A.) gave the following report: proteins of the S4 class (albumin), 3.7 g./100 ml.; proteins of the S7 class (gamma globulins), 1.8 g./100 ml.; mesaglobulins of the S10 class, 0.253 g./100 ml.; macroglobulins of the the S19 class, 0.120 g./100 ml.

Upon arrival, the patient was put on a high dosage of corticosteroids (Fig. 1) without any change in her platelet count, which remained between 5000 and

From Maisonneuve Hospital, Montreal, Que.
*Hematologist in Charge, Division of Hematology, Department of Laboratories.
†Chief Technologist, Division of Hematology.
‡Assistant, Service of Gynecology and Obstetrics, Department of Surgery.
§Director, Department of Surgery.