

Seguin (E. C.)

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(ULCUS ELEVATUM) OCCURRING
DURING THE USE OF BRO-
MIDE OF POTASSIUM

BY

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ON A PECULIAR CUTANEOUS LESION (ULCUS
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USE OF BROMIDE OF POTASSIUM.

By E. C. SEGUIN, M.D.

IN the last few years, more especially since the publication of Trousseau's lecture entitled "*Exanthèmes sudoraux*,"¹ much attention has been paid to toxic or medicamentous eruptions.

Among these, the cutaneous lesions produced by the various bromides, when taken internally, have been particularly well studied, and quite a variety of eruptions have been observed and recorded by dermatologists and neurologists.

In the last edition of Prof. Duhring's excellent work² we find a section devoted to this subject, and the following bromic eruptions are described under the head of *dermatitis medicamentosa*.

1. Acne-form pustules.
2. Brownish discoloration of the skin.
3. Simple papular eruption.
4. Confluent or molluscoid acne.
5. Maculo-papules.
6. Carbuncular acne.
7. Bullæ.
8. Rupia.



¹ *Clinique médicale de l'Hotel-Dieu*, 2me éd., 1865, i, p. 199.

² "Practical Treatise on Diseases of the Skin," 3d ed., Phila., 1882, p. 348.

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Ulcers are not named in this list, and I do not know that they have ever been described; unless it be in the shape of isolated ulcerated carbuncular acne.

It has been my fortune to observe this year two cases of large, elevated ulcers upon the legs, occurring in epileptic patients using the bromide treatment, and I desire to place on record this new form of cutaneous lesion, probably medicamentous in origin.

CASE 1.—Miss C., aged 25 years, epileptic since her fourteenth year. The disease has been fairly well controlled by moderate doses of various bromides, under the supervision, in the last few years, of her physician, Dr. P. C. Barker of Morristown, N. J. Very little facial acne has appeared, and at no time has severe bromism been apparent. Some ten years ago, while the patient was in Germany with her family, there appeared some "boil-like" sores upon the lower part of each leg, which soon coalesced into ulcers, one on each leg, presenting very much the same appearance as those of later development about to be described. On the left leg there was an "ulcer," also below the head of the fibula. In a few months these ulcers healed. So far as the mother of Miss C. knows, there was no increase in the amount of bromides, or change of bromide, prior to the appearance of the eruption, nor does she remember any special treatment, other than the application of some herbs to the sores, which determined their healing. The patient, continuing the bromide (various formulæ) treatment steadily, had no further serious eruption or ulceration, indeed no special bromic symptoms, until about fifteen months ago, when large, purplish papules, like "boils," appeared upon the outer side of each leg, about four inches above the external malleolus. These discharged, leaving ulcerated spots which coalesced, forming an ulcer which increased quite steadily in size until the early spring of this year, when I saw the patient. This account of the early appearances and development of the sores is derived from the patient's mother, whose qualifications as an observer are fair. Still, the lack of professional study of the early stages of the lesion is a *hiatus* much to be regretted. It is doubtful if the ulcer was ever a common excavated one; Mrs. C. thinks that for months prior to my examination its surface was distinctly raised above the level of the healthy skin.

When I saw Miss C., in March of this year, there was a large ulcer on each leg, almost encircling it, leaving a bridge of healthy skin over the anterior surface of the tibia. The rest of the leg, at a level about four inches above the malleoli, was covered by an irregular ulcerated patch, raised from 2 mm. to 4 mm. above the skin. Its area was irregular, somewhat pear-shaped, with its largest development posteriorly. Its greatest width, vertically measured, was perhaps 8 cent. The surface of this "ulcer" was different from any thing I had ever seen. As stated above it was raised quite uniformly above the healthy skin; its edges were abrupt, almost vertical, and showed no signs of cicatricial action. The elevated floor of the ulcer was firm, grayish-red in color, with here and there an adherent crust; it secreted a fetid, sanious, puriform liquid, and bled upon being touched with moderate violence. It did not look like ordinary granulation tissue; it was much firmer, composed of larger masses, and, in fact, at several points it presented a slightly villous or rather papillomatous appearance. There was no burrowing of pus under the ulcer, and the rest of the leg was normal,—perfectly free from "boils" or papules. This description, insufficient as I feel it to be, applies to both legs; the ulcers upon them were almost precisely alike; the lesion was a symmetrical one. (On the left leg, just below the head of the fibula, was an irregularly-shaped, smooth, white and coppery cicatrix of the ulcer which appeared ten years ago, and healed in a few months.) The patient's face and neck presented hardly a trace of bromic acne, and I was told that her body was free from ulcers or other eruptions; she showed none of the other symptoms of bromism, and her epileptic attacks were still recurring in a mild form occasionally.

I was so much impressed with the firmness and elevation of these patches that I could not avoid a suspicion of epithelioma, in spite of the symmetry of the lesion which indicated its toxic or systemic origin. Prof. Henry B. Sands, to whom I then sent Miss C., decided that there was nothing malignant about the ulcers, and he looked upon them as eruptions connected with the patient's condition or with her medicines, and he sent her to Prof. William H. Draper, who also looked upon it as medicamentous eruption. Dr. Draper has recently written me as follows concerning the case:

" . . . I remember Miss C.'s case perfectly, even though I have no notes of it. . . . I examined some scrapings from the ulcer and found only granulation cells. I think it was unquestionably a bromic acne. The lesion begins, I believe in the fol-

licular structures, it is said in the sweat follicles, but I suspect in the sebaceous ones as well. . . .”

Acting upon Dr. Draper's suggestions, Dr. Barker applied pyro-ligneous acid to the ulcers and they at once began healing. I saw the patient a fortnight ago and found the ulcers almost entirely healed, with copperish smooth cicatrices such as we see after common ulcers of the legs.

It is interesting to note that the bromide treatment was continued unchanged.

CASE 2.—Annie L., aged twelve years was brought to me at the Manhattan Eye and Ear Hospital on February 24, 1882, to be treated for peculiar attacks which I considered epileptic, and of a form intermediate between petit-mal and psychical epilepsy. In many seizures there were hallucinations of vision. The first attacks, which appeared about eighteen months ago, after a fever, were distinctly spasmodic. In the last few months more attacks of both sorts; right internal strabismus has appeared. Much complaint of headache, principally over the right eye; grasp of right hand less strong than that of left. Further details concerning the neurosis are unnecessary for my present purpose.

The child's health seemed good; she was fairly well-colored, and her skin was everywhere normal.

She was put upon our regular bromide treatment, taking from three to four grammes a day at various times. The indications of coarse cerebral disease were so strong that I also gave her .75 grammes of iodide of potassium three times a day, and applied a few blisters behind the ears.

The epileptic attacks were at once controlled, and the child seemed to bear the medicines well. Owing to some annoyance at having to wait very long one day, the mother ceased bringing the child to the hospital; this was some time in March, and there was then no bromism or eruption.

Rather accidentally, Annie again came under my care in June, by being brought to my clinic at the College of Physicians and Surgeons. I at once recognized her, and upon inquiry found that she had had private treatment since leaving the hospital, and had taken bromide of potassium only (no iodide). The attacks had been few and slight, more of the psychic order: fear of falling down stairs, seeing animals, weeping, calling out to mother, and complete amnesia of attack. She was somewhat stupid from the bromide, but the amount given was impossible to ascertain. There was almost no facial acne; the child's color was clear and healthy.

The mother, however, stated that since leaving the hospital clinic, the child's legs had become the seat of very painful sores, which she wished me particularly to examine. Bandages were removed from both the child's legs, and my surprise may be imagined when I beheld ulcers precisely like those of Miss C., seen a few months before.

The lower part of each leg, some 5 cent. above the malleoli, was encircled by a large ulcerated patch, distinctly elevated above the surrounding healthy skin. The outline of the sores was very irregular, varying in vertical width from 3 to 8 cent.; the largest surface of each sore being on the fibular side of the leg. The edges were sharply defined and nearly vertical. The surface of the sores, raised 2 or 3 mm. above the healthy skin, was covered with brownish-black scabs and a most offensive sanies. On removing some of these scabs a rough granulating surface, easily bleeding, was revealed. I use the word granulating, but the appearance was that of a firmer, more villous, in places almost papillomatous formation, than the delicate translucent and uniform surface of ordinary granulations.

The mother, a not over-intelligent Irish woman, stated that this local trouble began in April, while using the bromide prescribed by the physician she consulted after giving up the hospital. At first the right leg was affected with large pimples or boils, which "broke," ulcerated, and coalesced into an open sore. In about a fortnight the left leg was similarly affected. It is interesting to note that this woman's account of the beginning of the ulcers agrees precisely with that given by the very intelligent mother of Miss C.

I directed that the ulcers be gradually cleaned of scabs by frequent washing, and that a strongly carbolized ointment be used twice a day. The dose of bromide of potassium was fixed at two grammes night and morning. The mother, having other children to attend to in the midst of the difficulties of tenement-house life, did very little toward cleansing the sores, and did not apply the ointment as carefully as necessary. Besides, the child dreaded to have the legs dressed, and cried violently each time they were washed. I was away a great part of the time in the months of July and August, and during that time there was no material change in the size or appearance of the ulcers. The child remained free from ordinary bromism, and her complexion was good. The seizures occurred but rarely.

On July 28th I gave her ether, and after removing nearly all

the scabs from the left ulcer, I applied to it Paquelin's cauterly quite freely, and ordered a carbolized lotion for a few days, to be followed by applications of balsam of Peru ointment. At the same time I cut out a strip of the ulcer and adjacent sound skin for histological study; this was pinned on a cork and placed in bichromate of potassium solution. In cutting away this little flap I demonstrated that there was no appreciable lesion of the subcutaneous connective tissue; the derma seemed hypertrophied, but the whole piece was easily dissected away with the scalpel. I reduced the bromide one gramme night and morning, and gave five drops of Fowler's solution after each meal.

I saw the child again Aug. 21st. The ulcer which I had cauterized, that on the left leg, was nearly half healed over; the right leg presented the same appearance as at first, and in spite of my urgent orders had not been well cleaned of scabs and sanies. I directed that to be done before the child was brought again, intending to use the cauterly again, or to apply nitric acid. The same amount of bromide was to be taken night and morning, and eight drops of Fowler's solution were to be given after each meal.

I have met with a third case, in which the legs were affected in a way not unlike what the mothers of Cases 1 and 2 describe as the first or carbuncular stage of the ulcer; and probably, if the bromide treatment had been persevered with, ulcers might have formed in this case also.

Miss A. B., aged 17 years, a handsome girl, with a very fresh complexion, of German parentage, consulted me on November 1, 1880, for epileptiform attacks. She was a healthy child. At 8 years had an attack of typhoid fever lasting several weeks. On getting out of bed at the end of eleven weeks, found that she could not walk. It was nearly spring (fever in August) before she walked freely. Arms were unaffected; mind normal. In her ninth year had a convulsion one morning, biting her tongue. During the day legs became quite weak, especially the right. There seemed well-marked paralysis, but it is not certain whether there was any muscular wasting. Under galvanism and strychnia she gradually regained the use of her legs, but ever since she has had convulsions at very irregular intervals—every two or three weeks, or at interval of months. In the last two years three or

four severe attacks, last one in September. Has had occasional doses of bromide, but no systematic treatment. Patient states that in night attacks she wakes dizzy, has time to call some one, hears a loud noise as of a wheel going faster and faster, until she loses consciousness; hears no voices or bell-sounds. A cousin who has witnessed seizures, says that there is a severe convulsion, in which patient's eyes are open; after attack, she is stupid, and wants to rise; talks and weeps violently. Then she falls into a heavy sleep.

Last summer, was exposed to severe solar heat and had a profuse nose-bleed. Ever since has been liable to petit-mal; a whirling dizziness, followed by "faintings" in some instances. Further questioning shows that ever since first spasm she has had a third sort of attack, consisting in the sudden appearance of "balls before the eyes," followed by temporary diplopia; no drowsiness.

In 1877 Dr. Brown-Séguard was consulted, and gave Miss B. his bromide mixture. This was faithfully employed for six months. The patient then had large sores with scabs upon her legs, mostly on right. It is difficult to ascertain whether these sores were like those described above, or discrete scabbed sores, such as I have seen in other patients and termed rupia-like. There was no facial acne, and the epileptiform attacks were suspended. The bromides were stopped and the sores quickly healed.

Examination showed some anæmia and symptoms of gastric catarrh. The case was so clearly epileptic, that in spite of the former bad effects of bromides, I persuaded the patient to try them again; giving her my solution of chloral and bromide,¹ three teaspoonfuls (twelve grammes) at bedtime, well diluted. Treatment and diet were also ordered for the gastric catarrh. In eight days a "boil" appeared on the right leg, constituting a small abscess, which ruptured spontaneously on the twelfth day, near a scar of the former eruption three years ago. Dose of bromide solution reduced to two teaspoonfuls at night. On the fifteenth day several large indurated pimples had appeared around the small abscess. On the nineteenth there was quite a crop of large, purplish papules with evident tendency to suppuration on the right anterior region. This appearance, the patient said, was identical with that observed while using the Brown-Séguard mixture three years ago, and she begged me to stop the bromide. I might add that for a week or ten days arsenic and sulphide of calcium had been

¹ Chloral hydrate, 15.; potassium bromide, 30.; aqua, 200. grammes.

given to control the eruption. There was no bromism, hardly a trace of common facial acne, and the gastric symptoms were better.

I suspended the use of ordinary bromides, and gave bromide of zinc, bromide of camphor, digitalis, valerian, etc., at different times; also, at times, renewed treatment for the dyspepsia, and tonics. The epileptiform attacks have been almost perfectly under control, and there has been no return of the eruption (which passed away in a week or ten days after the bromides were withheld).

Very probably, had I persevered in giving the solution of bromides, the papules would have all undergone suppuration and ulceration, coalesced, and formed an ulcer more or less like those observed in the other cases.

This third case, though incomplete, has this value, that it bears out what the mothers of Cases 1 and 2 claimed as to the early appearances of the ulcers, viz.: at first an acne, undergoing suppuration and ulceration; the resulting ulcers merging into one sore.

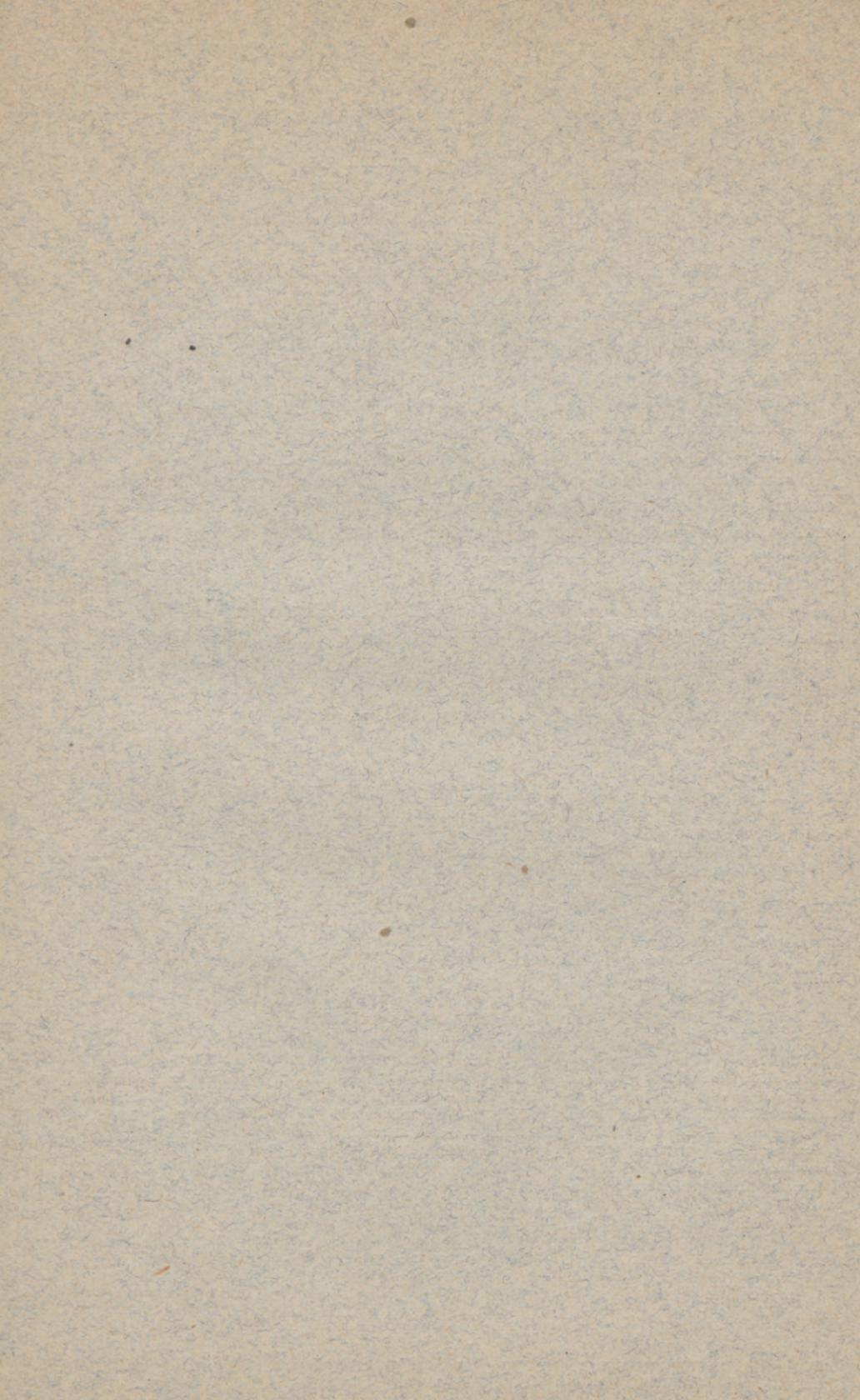
The following points in the clinical history of these ulcers are interesting:

1. Their origin in acne.
2. Their progressive and semi-malignant tendency.
3. The absence of bromism in the patient.
4. The absence or slight development of common facial acne at the same time.
5. The possibility of curing them by energetic local treatment (Case 1) without omitting the bromides.
6. The inefficiency (?) of arsenic and of calcium sulphide (Case 3).

Histology.—Sections of the piece of tissue removed from the ulcer show great increase in the thickness of the rete Malpighii, with hypertrophy of the whole skin in places. In several places villousities visible to the naked eye occur, made up of all the elements of the skin thrown up and out

into a minute mushroom-like or polypoid mass. In other places proliferation of young cells has taken place in the cutis, with atrophy and rupture of the epidermal layer, and partial escape of the newly-formed tissue, constituting a sort of abscess, opening externally. In other localities the patches of inflammation were wholly circumscribed, and sub-epithelial. The deeper layers of the skin, and to a certain extent the subjacent connective tissue, are infiltrated at certain points with young cells. The papillæ, hair-follicles, and sweat-glands do not appear to be the seat of any primary or important inflammatory change. In no part of the section was its surface (edge) covered by granulation tissue, as in a common ulcer.

From these appearances we may conclude that the ulcer resulted from a dermatitis, which was partly suppurative, but largely hypertrophic.



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