CHORIO-EPITHELIOMA FOLLOWING HYDATIFORM DEGENERATION

WITH REMARKS ON THE USE OF RADIUM*

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IT is the general belief that chorio-epithelioma and its frequent precursor, hydatiform mole, is of rather rare occurrence. The fallacy of this belief has been so convincingly brought to me during recent months that I have felt a study of this subject might be of interest.

Although when a medical student I saw three cases of hydatiform mole, all followed by malignant chorioma, during a period of fifteen years since, no more cases came under my observation, at least none were so recognized, until in the past eighteen months during which time I have treated four cases of hydatiform mole, while two other cases have occurred in the practice of my colleagues in St. Vincent's Hospital during the same period of time. Four of these six cases were followed by chorio-epithelioma, the other two being operated at an early stage while still benign moles.

The prevalent idea of the infrequency of these conditions is probably due to the text of authors long since out of date. For instance, Edgar in his book states that placental mole occurred four times in 15,000 cases. Williams observed five in 5000, while Madame Boivin states that the condition occurs once in 20,000 conceptions. My own experience of the past eighteen months, coupled with a study of the more recent literature, would at once show the fallacy of the old teachings, and convince the student of today the necessity for greater familiarity with the subject and a more watchful attitude in the care of all conceptions, both tubal and uterine.

Meyer states that in 348 pathological uterine abortions the incidence of hydatiform degeneration occurred in 43 per cent., while in 104 tubal pregnancies classed as pathologic the hydatid mole followed in 46 per cent. Meyer's numerous and recent writings cover most completely all sides of this study and he finally states, "Indeed, how many cases of hydatiform degeneration one can find in tubal and uterine abortions will depend very much upon the care with which the examination is made, for the condition is undoubtedly extremely *common* and not rare, as heretofore supposed."

The fœtal placenta is developed from the chorion, and through the chorionic villi is derived the nourishment for the fœtal organs. These villi are finger-like projections covered on the surface with the layer of syncytial cells, next beneath the cells of Langhans', and then the stroma containing a small number of capillaries. As the placenta develops the villi show rapid

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growth and great erosive power by which they are able to penetrate through the uterine mucosa into the underlying venous sinuses, where, by selective absorption, they gain nourishment for themselves and for the placenta. When conditions are normal and the fœtus about mature, these villi withdraw from their intra-mural position; the outer layer of syncytial cells covering the villi has long since undergone atrophy; the layer beneath Langhans' cells also undergo degeneration and thus the attachment between mother and fœtus is loosened in preparation for birth. But this does not always happen, for some of the villi may persist in intimate contact with the maternal tissues and maternal blood and may continue to grow in situ after the normal period of gestation has been attained. Continuing to be nourished by the maternal blood and to absorb fluid, they may hypertrophy and become distended by an œdematous mucoid infiltration so as to form a mass or series of clear, grape-like vesicles of varying size, distending the uterus to even as great an extent as a full term fœtus. Such is the hydatiform mole.

When the above condition remains within normal limits the result is nothing more than a benign mole; this is expelled in due time or is surgically removed, and thereby is explained the fairly frequent cases of hydatiform mole which are followed by repeated normal pregnancies. On the other hand the villous growth may proceed beyond the normal limits; the venous sinuses may become filled with an active proliferation of the chorionic elements; the epithelial cells may be swept away by the blood current and deposited in the capillaries of the vagina, pelvic vessels, lungs and other organs, and thus we have a transition from the benign mole to the highly malignant chorio-epithelioma.

I have already referred to the rather common frequency of hydatiform degeneration found in pathological abortions, both tubal and uterine, but of greater importance is the incidence of malignant chorio-epithelioma resulting from the transition of the epithelial elements of the placenta mole. Briquet, in a series of sixty-five hydatid degenerations, found that malignant chorioma followed in thirty-one demonstrable cases. Pollasson and Violet, in the study of 455 cases of chorio-epithelioma, found that mature hydatiform mole or hydatiform degeneration of pathologic abortion occurred as a precursor in 366 instances. To emphasize the importance of careful examination of all placentas it may be added with stress that these same investigators found ninety-seven chorio-epithelioma followed hydatiform degenerations discovered during labor near term.

With the present unrecognized frequency of these conditions it is not surprising to find that the initial symptoms may first appear as the result of metastases in vagina, lungs or brain, producing thereby a vaginal tumor, cough with hæmoptysis or cerebral apoplexy. The lungs seem to be the most common site for metastasis. In the above quoted series of cases metastases occurred in the vagina ninety-three times, in the brain forty times, and in the lungs 133 times. Ewing, in discussing the rapidity with which malignancy follows hydatiform degeneration, states that the transition usually takes

place about five weeks after labor at term, seven weeks after abortions, and about eight weeks after mature mole. In one of my cases (No. 4), well-developed chorio-epithelioma was found in the scrapings removed one week after the mature mole was discharged.

The maternal mortality of simple placental mole is quoted as 13 per cent. by Edgar and 18 per cent. by Dorland. This mortality is usually due to hemorrhage or sepsis, and the rate is entirely too high provided these cases can have hysterectomy performed before molar abortion occurs. After malignant transition occurs the mortality rate is quoted about 100 per cent. by all authorities. Ewing states that with or without hysterectomy the disease permits life for from six to eighteen months, and further states that he has been unable to find any operative cure of chorio-epithelioma. Adami states that the process is rapidly fatal. Schmauch emphasizes the necessarily fatal issue and advises against operation. Since the primary malignant process always develops entirely within the venous sinuses and capillaries, it would seem almost impossible to avoid displacing intra-vascular fragments during hysterectomy and thus hastening metastasis. On the other hand if this susceptible fœtal hyperplasia could be stunned or its growth inhibited by radium, there might be a greater possibility of cure following hysterectomy. This agent was employed on three of my patients, with results in two cases that are both promising and encouraging.

My experiences may be related briefly as follows:

CASE I.—A negress with soft symmetrical uterine tumor, carrying a pre-operative diagnosis of fibromyoma, upon whom hysterectomy was done before molar abortion had occurred. This patient is living and well.

CASE II.—White, age forty-six, came under my care three weeks after expulsion of the larger portion of an hydatid mole. Fragments of the mole could be extracted with the examining fingers through the patulous os. The general condition of the patient was wretched; a grave secondary anemia following continuous hemorrhage for three weeks, with rapid, feeble pulse absolutely precluded operative interference. 1800 mhrs. of radium treatment within the uterus was followed in one week by complete relief from metrorrhagia. In eight weeks the patient was greatly improved with a gain of twenty pounds in weight. At this time bleeding from the uterus recurred, but the general condition of the patient was so good that operative interference was undertaken. Again 1800 mhrs. of radium was given as a pre-operative measure within the uterus and forty-eight hours later pan-hysterectomy was performed. The specimen removed showed a well localized, perforating chorio-epithelioma in a state of regression and degeneration. Eighteen months has elasped since this patient expelled the mole and she is now living and apparently well.

CASE III.—White, age forty-two, presented about the same problem as Case No. II, coming under my care for continuous and depleting uterine hemorrhage following molar abortion five weeks previous.

Fragments of the remaining hydatiform mole removed with placental forceps showed no evidence at that time of malignancy. The same radium dosage was employed and the hemorrhage promptly checked, but returned again in five weeks. Profiting by the experience of Case No. II, I did not wait for better general improvement, but operated forty-eight hours after a second radium application of 1800 mhrs. within the uterus. The specimen removed disclosed a more widespread area of chorio-epithelioma than in Case No. II, but the entire pathological process showed marked destructive and degenerative action from the radium. Eleven months have elapsed since this patient was first treated by radium and she remains well to this date.

CASE IV.—This case is recent. Seven days after expulsion of a huge hydatid mole the scrapings from the uterus showed well-developed chorio-epithelioma and the fact that the accompanying hemorrhage promptly yielded to radium within the uterus. The general condition of this patient is too precarious at this time to permit of radical operative measures.

I have just received data of a case in the practice of one of my colleagues in which a smaller dosage of radium, 400 mhrs., checked the bleeding and apparently relieved the patient of all symptoms following the expulsion of the benign mole four months ago.

CONCLUSION

The frequency of hydatiform degeneration and the ready transition into chorio-epithelioma should counsel every practitioner to be on the alert especially in pathologic abortion, both tubal and uterine. A more extensive experience with radium in these conditions may lend hope in the treatment of the malignant transitions which heretofore have been considered necessarily fatal.

Additional justification for this hope may be found in the recognized susceptibility of embryonal structures to radium, especially if used early, for Ries has reported intact villi in a uterine sinus eighteen years after the last labor and the latency of malignant chorio-epithelioma, one, three, five and even ten years has been established by the literature.