

FATALITIES FOLLOWING ELECTRIC CONVULSIVE THERAPY

A REPORT OF 2 CASES WITH AUTOPSY FINDINGS

FRANKLIN G. EBAUGH
CLARKE H. BARNACLE

AND

KARL T. NEUBUERGER
DENVER

In this paper we wish to discuss fatal cases of patients receiving electric convulsive therapy. While, according to the United States Public Health Service, Shock Therapy Survey, October, 1941, four fatal cases have occurred in mental hospitals, no data as to neuropathological findings have yet been described in the literature.

The first patient, a 58-year-old male, had a depressive psychosis and was given electro-shock convulsive therapy, having twelve grand mal seizures and one petit mal. Following the last shock (grand mal) he complained of pain suggesting angina pectoris and died within one and a half hours after the treatment. Autopsy showed a severe coronary sclerosis, with occlusion of the left descending branch and recent infarction of the left ventricle. The brain was examined by routine histological methods. The cortex showed "areas of devastation" which were entirely devoid of nerve cells or showed a small number of ghost cells; this was accompanied by some proliferation in glia and microglia. In addition, diffuse slight degenerative changes of the neurons were observed throughout the cortex, particularly on the surface of the convolutions. The changes were accentuated in the hippocampus. The extracortical gray matter was slightly involved. No evidence of arteriosclerosis was observed; and, while there was a fairly large amount of lipid pigment in the nerve cells, silver stain failed to reveal early signs of the presence of senile changes (argentophil plaques or fibrillary alteration).

The second case, a 57-year-old male, was treated for a manic reaction. He died following the third electro-shock treatment, immediately after his first grand mal. A complete autopsy failed to give any evidence in the various organs and systems that would result in sudden death. Thorough examination of the brain showed a number of cortical areas of "paleness" or beginning necrosis. This was in some instances associated with early glial reactions (presence of red cells, swelling of astrocytes). The polymorph layer of the hippocampus showed a marked swelling and increased number of astrocytes. Early ischemic changes or paling of cells were occasionally found in the corpus striatum, thalamus, dorsal nucleus of the nervus vagus, substantia reticularis and nucleus arcuatus; this was sometimes accompanied by satellitosis, neuronophagia and the pres-

ence of "gliarosen." These changes were of no greater intensity in the areas where the electric current is supposed to pass. No changes attributable to vascular disease or early senility were ascertained. (Since in both cases the bodies had been embalmed before removal of the brain, the benzidine stain for vessel contents was not applicable.)

The pathogenesis of the changes described will be discussed, with respect to the direct effect of the electric current upon the brain parenchyma, and its effect upon the cerebral circulation. The significance of the histological findings in regard to the advisability of electric shock treatment in older patients will also be considered.

DISCUSSION

BERNARD J. ALPERS: I think it is fair to point out that discussion of these different changes comes pretty close to being academic, because regardless of what we concluded about the changes in the brain, there is no doubt that we will continue to use electrical shock treatment.

Now there seem to be two groups, the hemorrhagic ideology, which I represent, and the group which states that there are no changes or that there are very few changes in the brain substance. At the expense of muddying up what has been clarified, I should like to report a case in a patient in which we found hemorrhages, just as we did in the animals.

This was a forty-five-year-old woman, with involutional melancholia, who was in good condition, who had had treatments over a period of about five months and had in all 62 convulsive shock treatments, of which 46 resulted in convulsions. The patient died about three months after the last treatment, and when she came to autopsy showed a number of hemorrhages in the brain substance.

Now there must either be a significant difference in the technics employed or the hemorrhages and the other changes which have been described have nothing whatever to do with the electric shock. We have not found either in our animals or in the human case any other cause for the convulsions. I do not mean to say that the electrical current itself was responsible for the convulsions, but there was no other reason to assume that there was another cause. There was no evidence of any focus or embolic hemorrhages and there was no evidence to assume they were agonal. So we must assume that the electrical current had something to do with it.

Now the question of technic comes into consideration. The statement has been made, or at least the inference has been drawn that in the cases with hemorrhages there must be something wrong with the technic. The technic used, in so far as I can see, is exactly that employed by others, namely, a current which is just sufficient to produce a convulsion, 200 milliamperes in strength, given for one-tenth of a second; in the human being which Hughes et al. reported, the current was no larger than that used in other cases. So that the threshold stimulus appears to me to be in consonance with what is used by other investigators. I do not think that the strength of the current can be blamed for the findings which were discovered in our animals and in human individuals.

The crucial factor is the amount of shock delivered. One would expect a direct proportion between the number of the shocks and the total time of the convulsions and the brain changes, and we found no such correlation whatever. As Dr. Barrera pointed out, we are just as apt to find changes in animals which had received half a dozen shocks as we are in animals which had received 15 shocks, and in animals which had a total time of convulsions of ten minutes as compared with a total time

of convulsions of perhaps thirty minutes. So that I do not think the amount of current delivered over a long period, or the total time of the convulsions can be the crucial factor.

It seems to me that to say that the electrical shock or that the electrical current has nothing to do with the changes in the brain, if one assumes that there are changes in the brain, is simply begging the question. Let us assume that they are not responsible and that the current is not responsible for the brain changes. The current has been produced and whatever has taken place has been indirectly the result of the current and probably would not have been there if electrical shock had not been used. So that looked at it in a little more oblique sort of way, the electrical current is in some sense responsible for the brain changes, at least, which we found.

I think that there must be some other responsible factor. There may be a difference in species, or there may even be a different susceptibility of human beings to the electrical shock. There may be some X factor which, as Dr. Moore has pointed out, is present in such cases which develop changes in the brain. I do not think that we are in a position to say definitely what happens at the present time, but I think it is a good plan to speculate about it. It may be that the patients with some degree of inanition, or patients who seemingly are in good health but who have some obscure ailment are more susceptible to brain changes than are others. I do not see from the evidence which we have at hand that we can say that the electrical current is not responsible in any sense nor can we say that the changes which have been produced have not been produced by physiological methods.

HARRY C. SOLOMON: It is undoubtedly very important to have records of human beings who have died after electric shock, thus only can we get any real material from which to draw conclusions of what happens in the human being. However, I think we can heed carefully what Dr. Barrera has told us, that it is very difficult to draw conclusions and make too close connections.

May I refer to several points about Dr. Ebaugh's cases? One case that died of coronary disease is one of those accidents that are bound to occur. He may have died at the same day or a week later without the shock; but he did go through a convulsive period which was a drag.¹ We all, I think, have known patients who had marked coronary disease and have been given electric shock therapy without having any bad results therefrom.

The second case, as I gather it, died of an anoxia and it would seem fair to assume that some of the cellular changes were the result of the anoxia. So perhaps had he not died of an anoxia, such axis-cylinder changes would not have taken place. What also is interesting was the diffuse location of the pathological findings which would seem to suggest at any rate that they were not due to the current, although they may have been due to the convulsions and to the changes that take place in the body with anoxia, with convulsion, and so on.

I would like again to emphasize that it is very difficult to draw the conclusion that these findings were the result either of any particular factor, electric shock, convulsion, anoxia or anything else; but with the accumulation of more such cases, we will have a very much better basis upon which to reach a conclusion. I think we must all constantly give homage to the great god coincidence, particularly when we only have a couple of cases to our credit.

I would like to add one more case of death following electric shock which occurred in one of our Massachusetts institutions, of which I am able to tell you something. This was a young man in the early twenties who had previously had a course of ten metrazol convulsions, with some improvement of his symptoms, a relapse, ten electric shock convulsions with again some improvement, followed by a relapse and return to the hospital, and then eight or nine more electric shocks.

¹ Ebaugh

¹ den probe Zfall Goldes

Fifteen hours subsequent to the last shock, he died of pulmonary edema. Microscopic studies have not yet been made. Grossly there were no brain changes to be seen, certainly no gross or meningeal hemorrhages. He had an early but definite glomerular nephritis and the assumption (again being an assumption) is drawn that the combination of the glomerular nephritis plus the weight of the convulsive therapy upon his economy was sufficient to break him down and lead to pulmonary edema and death.

ABRAHAM MYERSON: I am going to stress what Dr. Solomon said about the great god coincidence. People have died of coronary thrombosis outside of the waiting room of the cardiologist just after they have been examined by competent cardiologists and have had electrocardiograms taken.

The number of deaths from coronary thrombosis which occur suddenly without any exciting cause that can be found makes one say that the burden of proof is not on the man who gives the electric shock or the general use of electric shock treatment, but upon the individual who states that a coronary thrombosis following treatment had anything to do with the electric shock treatment.

The second thing I want to express is perhaps more radical. I believe there have to be organic changes or organic disturbance in the physiology of the brain for the cure to take place. I think the disturbance in memory is probably an integral part of the recovery process. I think it may be true that these people have for the time being at any rate more intelligence than they can handle and that the reduction of intelligence is an important factor in the curative process. I say this without cynicism. The fact is that some of the very best cures that one gets are in those individuals whom one reduces almost to amentia. It is impossible to conceive of that amentia without an organic base; there must be at least temporarily organic changes in the brain, and the cure is related to these organic alterations. Possibly there is occasioned, in some instances, more or less irreversible pathology, but in the vast majority of individuals this is not true. In these cases and for the time being something happens to the brain which interferes with its function sufficiently so that mood becomes altered in the proper direction. I think that we need not be afraid of this particular phase of the situation. We need not be worried lest we be producing permanent organic changes in the brain. Every surgical operation in an interference with normal physiology and is a mutilation and likewise this particular type of drastic therapy is associated, I believe, with reversible and transitory organic changes in most instances, possibly with irreversible organic changes in a very few.

NATHANIEL W. WINKELMAN: Dr. Myerson has touched upon something which is very interesting, but I think there is something else we must consider. I would like to ask those who have been interested in the pathology of the nervous system over a period of many years whether or not they couldn't duplicate what Dr. Ebaugh has shown in a 57- or 58-year-old man, irrespective of electric shock. I would like also to ask them also whether or not they have found hemorrhages in the brain in status epilepticus. I have seen a good many cases of patients who have died in status; no hemorrhages were found. I have seen gross hemorrhages only where patients in a convulsion have fallen down the stairs or hit their heads against radiators. Where there has been this direct relation between trauma and the convulsion, there is a different story. I think the case that Dr. Alpers quoted as proof of his hemorrhage theory is reported in full in the last number of the *Neuropathologic Journal*. I think that is right. I think Dr. Alpers reported that death occurred two months after the last treatment and that the hemorrhage in that case was *fresh* blood. I certainly would not by any stretch of imagination attribute that lesion to a therapeutic convulsive course completed two months before death.

The changes that Dr. Barrera reported are significant and I agree that there are and must be changes of a reversible nature.

We have recently tried the very interesting experiment of giving patients with involutional depressions daily doses of electricity. We gave one patient seven doses and the resident called me and said, "I think we have produced a case of Alzheimer's disease." Well, we did, temporarily, there was no doubt about it, but in the course of about a week or ten days, that patient cleared up completely; she had good insight and she has gone home, having made a very satisfactory recovery from her psychosis.

I believe that the reversible changes which Dr. Myerson has stressed are important, and they are not the changes that should deter us from using this method of treatment in those cases in which some good can be accomplished.

LEO ALEXANDER: It is important to keep in mind that there are two factors which are conceivably the source of pathological changes. One is the direct action of the passage of the electric current. We have to postulate that those changes which are attributed to the current must be present either only within the direct path of the current, that is along the almost straight or slightly outwardly curved lines between one electrode and the other, or should predominate there. We can accept, as caused directly by the current, only those pathological changes which are within these only slightly curved, essentially straight boundary lines.

The other pathological changes are only indirectly related to the electroshock. Every convulsion causes an upheaval of the circulation, and electroshock treatment certainly creates a great deal of demand on the efficiency of the circulation throughout the body; but so does a hundred yard dash too, in an equally unspecific way. Patients with coronary disease or otherwise poor circulatory mechanisms may break down under either strain.

I am quite sure we will learn more about the types of cases which should not be treated with electric shock. So far, at Duke, Dr. Lyman and Dr. Lowenbach, who have, for a long time, carried out the electroshock treatments, have not so far, fortunately, had any fatalities. Of course, one cannot be sure whether some may not occur at any time. I think all the reported fatalities are only indirectly related to the electric shock.

The changes which are caused directly by the passage of current are temporary and reversible. They consist of blanching of the frontal lobes between the electrodes, lasting for half an hour. This temporary ischemia may damage a few cells but probably not permanently; it is conceivable that ischemic cells may appear, although we have not seen them in our experimental animals. I quite agree with Dr. Barrera that significant irreversible changes in the Nissl picture are absent, even after fairly large shock doses. I am not quite sure, however, whether the two pictures which Dr. Barrera has shown are definitely comparable and from exactly the same region. I thought the normal control section was from the area entorhinalis with its normal gaps between its distinct cellular groups, while the other from the electroshock animal came from the ribbon of the Ammon's horn, where such gaps are not present normally. At any rate, I should like to register the opinion that no lasting or irreversible changes are caused by the electroshock treatment, and that the organic aspects of the effects of electroshock may be on the level of a physical-chemical change. We know that during the half hour when the blanching of the frontal lobes occurs, there is a slight swelling of the frontal lobes and we know that under conditions of edema, permeability of the cells changes. I think that the organic biological change produced in the frontal lobes, which is possibly the way the treatment works, must be of the nature of a subtle physical-chemical change, possibly related to cell permeability. This change still awaits investigation.

EUGENE ZISKIND: Controlled studies present an opportunity for contrasting the hazards of convulsive therapy. At the American Psychiatric Association meeting last week, Dr. Esther Somerfeld and I reported a 3-year study of 74 untreated and 59 treated cases of affective psychoses. There were 9 deaths from suicide and

exhaustion in the untreated controls and only 1 death in the treated series, a patient who committed suicide 9 months after his treatment was completed. Some hazards of therapy are therefore warranted in face of the resulting improved mortality rate.

In view of the controversy as to brain damage based on animal experimentation, as clinicians we might well revert back to our patients for data bearing on this problem. This is particularly pertinent since clinical evidence of disturbed cerebral functions may well be a more subtle indicator of organic impairment induced by the treatments than histologic change. Three years ago we reported on the frequent occurrence of memory defects during convulsive therapy pointing out that recovery occurred in every instance and that the first appearance of memory impairment might be utilized as one of the early clinical signs that the phase of reversible brain damage, referred to here today, had been reached.

There is ample evidence that with the induction of a large enough number of convulsions organic cerebral injury can occur. The problem of utmost significance to those of us working with the procedure is; are there margins of safety within which no permanent impairment of cerebral function occurs? Future studies on this problem of cerebral trauma should attempt to delimit the number of treatments within the margins of reversible impairment. Perhaps a better index will be obtained than the early memory impairments, but until then we recommend their utilization as a warning signal of approaching hazard.