FATAL COMPLICATION FOLLOWING INSULIN THERAPY IN RHEUMATOID ARTHRITIS

BY

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In this hospital, over fifty cases of rheumatoid arthritis have been treated with insulin, as first reported by Kersley and others (1950). In their series, the occurrence of spontaneous hypoglycaemia in two cases shortly after cessation of treatment was the only complication reported (Kersley and others, 1951). Our series has also been free of all major complications with the exception of the one case here described.

Case Report

A fishmonger, aged 71, was first seen in July, 1951, when he complained of pain and stiffness of all the limb joints and the neck for the past 8 weeks. He had also lost 1 st. in weight.

History.—He had suffered from haematemesis in 1949, with recovery on medical treatment. Examination showed the changes typical of rheumatoid arthritis, and the erythrocyte sedimentation rate was 19 mm./hr (Wintrobe). Symptomatic physiotherapy was given, but after 6 weeks he became worse and was admitted to hospital.

On admission, moderate rheumatoid arthritic changes were found in all limb joints, with pain and limitation of movement. The loss of weight was now 2 st. Other systems appeared normal and the urine was clear at all times.

Blood count (September 11, 1951): Hb 59 per cent., R.B.C. 3·2 million/c.mm.; erythrocyte sedimentation rate 47 mm./hr (Wintrobe).

Therapy.—Soluble insulin, 60 units daily, increased after 3 days to 70 units daily, was administered for 5 days in each week for a total of 3 weeks. Hypoglycaemia was stopped after 2½ hrs by oral glucose and a normal breakfast. On no occasion did intravenous glucose prove necessary. Full physiotherapy was also given during this stay in hospital. He showed considerable improvement and was discharged after a further 2 weeks' physiotherapy, walking well.

Relapse.—Two months later his condition had relapsed, and, on December 19, 1951, the erythrocyte sedimentation rate was 54 mm./hr (Wintrobe), and Hb 69 per cent.

Re-admission.—He was re-admitted to hospital on January 14, 1952, and, by this time, was unable to walk, all joints being severely affected. Erythrocyte sedimentation rate was 49 mm./hr (Wintrobe), Hb 59 per cent. Urine normal on routine examination.

Therapy.—A course of soluble insulin was given, and before, for 2 weeks. Again, on no occasion was intravenous glucose necessary. Full physiotherapy was also given during this time. On January 19, 1952, he had a manipulation of shoulders, neck and knees under pentothal anaesthesia. Insulin treatment was stopped on January 25 for the usual weekly interval of 2 days without treatment.

Further Developments.—Thirty-six hours after this last dose of insulin, the patient told his wife he was thirsty, but did not inform us. He had never before complained of excessive thirst. The following noon, twenty hours later, he felt unwell, but no abnormal signs were found. He started to vomit at 8 p.m. on January 27, 1952; at 10 p.m. he was drowsy, the smell of acetone was noticeable in his breath, and no urine had been passed since the vomiting started. At 11.30 p.m. he was catheterized, and the urine was found to contain sugar +++; acetone +++. A diagnosis of diabetic coma was then made, and treatment started.

Intravenous soluble insulin 300 units, and subcutaneous soluble insulin 280 units was given immediately, and saline transfusion commenced; 6 hrs later (6 a.m.) another 200 units insulin were given, and 4 hrs later (10 a.m.) another 200 units. The urine test remained orange with Benedict's.

From 12 noon on January 28 further intensive treatment was given (see Table), but the patient died at 5.20 a.m. the following day.

Post-mortem Examination.—Marked cerebral oedema was found, together with oedema of all connective tissues, with moderate pulmonary oedema. Apart from this, no abnormality was detected. Histology of the pancreas, adrenals, and pituitary proved normal.
**FATALLY AFTER INSULIN IN RHEUMATOID ARTHRITIS**

**Table**

**INTENSIVE TREATMENT IN THE LAST HOURS OF LIFE**

<table>
<thead>
<tr>
<th>Time</th>
<th>Soluble Insulin (units)</th>
<th>Other Treatment</th>
<th>Urine Tests</th>
<th>Sugar</th>
<th>Acetone</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 noon</td>
<td>400 subcutaneous</td>
<td>2nd litre saline started</td>
<td></td>
<td>Orange</td>
<td></td>
</tr>
<tr>
<td>2 p.m.</td>
<td>400 subcutaneous</td>
<td></td>
<td></td>
<td>Orange</td>
<td>+</td>
</tr>
<tr>
<td>3 p.m.</td>
<td>400 subcutaneous</td>
<td>Blood sugar 1,1,000 mg. per cent.</td>
<td></td>
<td>Red</td>
<td>+++</td>
</tr>
<tr>
<td>5 p.m.</td>
<td>400 intravenous</td>
<td></td>
<td></td>
<td>Red</td>
<td>+++</td>
</tr>
<tr>
<td>6 p.m.</td>
<td>400 intravenous</td>
<td></td>
<td></td>
<td>Red</td>
<td>+++</td>
</tr>
<tr>
<td>11 p.m.</td>
<td>1,1,000 intravenous</td>
<td>Saline completed</td>
<td></td>
<td>Orange</td>
<td>+</td>
</tr>
<tr>
<td>12 midnight</td>
<td>1,1,000 intravenous</td>
<td>5 per cent. dextrose started</td>
<td></td>
<td>Red</td>
<td>+</td>
</tr>
<tr>
<td>1 a.m.</td>
<td>1,1,000 intravenous</td>
<td></td>
<td></td>
<td>Red</td>
<td></td>
</tr>
<tr>
<td>2 a.m.</td>
<td>1,1,000 intravenous</td>
<td></td>
<td></td>
<td>Orange</td>
<td></td>
</tr>
<tr>
<td>3 a.m.</td>
<td>1,1,000 intravenous</td>
<td></td>
<td></td>
<td>Orange</td>
<td></td>
</tr>
<tr>
<td>4 a.m.</td>
<td>1,1,000 intravenous</td>
<td>Serum urea 200 mg. per cent.</td>
<td></td>
<td>Orange</td>
<td>Insufficient urine</td>
</tr>
<tr>
<td>5 a.m.</td>
<td>1,1,000 intravenous</td>
<td>2nd litre dextrose started</td>
<td></td>
<td>Orange</td>
<td></td>
</tr>
<tr>
<td>5.20 a.m.</td>
<td>Patient died</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Comment**

This patient appeared to die in an insulin resistant diabetic coma, 8,000 units of insulin in 30 hrs having had no effect. It would appear unlikely that a diabetes of this type would be due to the production of ACTH by insulin therapy, and coma due to depression of endogenous insulin production should have reacted to the large doses of insulin administered.

We cannot find any record of a similar case in the literature, although such a complication might be expected to have occurred in view of the large number of psychiatric patients who have been given insulin therapy.

**Summary**

A case is reported of a patient who died in an insulin resistant diabetic coma after two courses of insulin therapy for rheumatoid arthritis. Cerebral and pulmonary oedema and oedema of the connective tissue were found post mortem.

It is a pleasure to record our thanks to Dr. G. D. Kersley and Dr. J. B. Walker for helpful advice, to Dr. N. E. Rankin and Dr. W. Brumfitt for the pathological investigations, and to Professor Newcombe for his opinion on the histology of the pituitary.

**REFERENCES**


Complication mortelle de la thérapie insulinique de l'arthrite rhumatismale

**RÉSUMÉ**

On relate le cas d'un malade mort d'un coma diabétique résistant à l'insuline, survenu après deux séries de thérapie insulinique instituée pour traiter son arthrite rhumatismale. A l'autopsie on trouva de l'oedème du cerveau, du poumon et des tissus conjonctifs.

Complicación letal de la terapia insulinica de la artritis reumatoïde

**SUMARIO**

Se relata el caso de un enfermo muerto de coma diabético resistente a la insulina; el coma sobrevino después de dos curas de insulina al tratar su artritis reumatoide. La necropsia reveló un edema cerebral, pulmonar y de los tejidos conjuntivos.