OXALOSIS IN CHRONIC RENAL FAILURE

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Summary

The incidence and severity of oxalate deposition as a complication of chronic renal failure in a retrospective study of 73 patients is presented.

The reason for this study was the occurrence of a syndrome characterised by multiple shunt-complications, muscle weakness and peripheral ulceration in three haemodialysis patients.

This syndrome seems to be caused by an obliterative vasculitis due to oxalate deposition in the media of peripheral vessels (Figure 1).

Figure 1
Introduction

Oxalosis, first described by Lepoutre [1] is a metabolic state characterised by hyperoxaluria and soft tissue deposition of oxalate salts, leading to chronic inflammation and fibrosis.

Deposition most commonly involves the kidneys [2], the walls of blood-vessels [3], the myocardium [4] and various other organs. A distinction is made between primary hereditary and a secondary exogenous type of oxalosis. Primary oxalosis is a rare metabolic disease, usually presenting in childhood as a result of a deficiency in glyoxylate metabolism, leading to increased synthesis and excretion of oxalic acid. Two different types are described [5]; in the first, an autosomal recessive trait, there is a deficiency of 2-oxoglutarate glyoxylate carboxylase leading to overproduction of glyoxylate and oxalate; in the second type a deficient activity of D-glycerine dehydrogenase exists, characterised by excretion of large amounts of oxalate and L-glyceric acid. Because of the rarity of the latter its mode of inheritance is not known. A third type of oxalosis in which the manifestations become manifest in adult life may exist [6].

Secondary oxalosis may occur either as a result of excessive ingestion of oxalate or its precursors or by a deficiency of pyridoxine or thiamine. Oxalate deposits

![Diagram of oxalate metabolism and excretion](image)

Figure 2. Endogenous and exogenous formation of oxalate (simplified)
are seen in kidneys of patients after methoxyflurane anaesthesia [7], after intestinal bypass [8] and after ethylene glycol poisoning [9]. Excessive ingestion of ascorbic acid is only a theoretical possibility, because of the low capacity for its conversion to oxalate [10]. Decreased excretion, as in terminal renal failure, may also cause secondary oxalosis (Figure 2).

In recent studies [11,12] oxalosis has been described as a complication of chronic renal failure, the severity appearing to be related to the duration.

**Patients and methods**

In three patients we observed a clinical syndrome, characterised by multiple fistula complications, peripheral ulceration and unexplained muscle weakness. Hyperparathyroidism was excluded by exploration or normal PTH values; in one case a hyperplastic parathyroid was found. Two patients died, one underwent nephrectomy because of pyelonephritis.

At autopsy, extensive oxalate deposition was observed by studying routinely stained haematoxylin-azofloxine sections of kidneys, myocardium and peripheral vessels. In the nephrectomised kidney severe oxalate deposition was also present.

Primary oxalosis was only excluded by history. This prompted us to review the autopsy files of 43 patients. Twenty-three were previously on chronic haemodialysis (CHD).

This group of 23 patients with an average age of 45.9 years, ranging from 22 to 83 years. The duration of terminal renal failure varied from 5 months to 5 years with an average of 29 months. Haemodialysis therapy lasted from 3 months to 4 years with an average of 14.6 months.

Ten patients had acute renal failure treated with haemodialysis (AHD). They had an average age of 57 years, range 29–75 years, and a mean duration of renal failure of 9 days, ranging from 5 to 29 days and were on haemodialysis therapy for the same period.

Ten patients had terminal renal failure not treated with haemodialysis (NHD). In this group the average age was 68 years with a range of 51 to 82 years; the average duration of renal failure was 22 months.

A group of 30 patients suffering from renal stones was used as a control (C). Renal failure was defined as a creatinine clearance less than 5ml/min. Clinical information was obtained from hospital records, primary oxalosis could only be excluded by family history and absence of urinary tract calculi, since no information about urine or plasma oxalate levels was available.

The pathological findings in haematoxylin-azofloxine stained histological slides of kidneys, myocardium, peripheral vessels and thyroid were studied. The severity of oxalate deposition was graded subjectively from 0 to 3+.

**Results**

In the CHD group no oxalate deposition was found in 7 cases, in 4 it was mild (1+), in 5 moderate (2+) and in 7 severe (3+).

When patients underwent nephrectomy before death, the severity of deposits
TABLE I. Degree of oxalosis at nephrectomy compared with autopsy in five chronic haemodialysis patients

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Degree of oxalosis at nephrectomy</th>
<th>Degree of oxalosis at autopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>11</td>
<td>+</td>
<td>2+</td>
</tr>
<tr>
<td>13</td>
<td>+</td>
<td>2+</td>
</tr>
<tr>
<td>16</td>
<td>+</td>
<td>2+</td>
</tr>
<tr>
<td>20</td>
<td>3+</td>
<td>3+</td>
</tr>
</tbody>
</table>

was increased at autopsy when compared with material obtained at operation, in 3 cases out of 5 (Table I). In the AHD group, severe and moderate deposits were found in one patient, mild in two. No deposits were observed in six patients.

In the NHD group no oxalate deposition was observed in 5 cases, mild in 3, moderate in one and severe in one.

A group of 30 patients, suffering from renal stones, was used as a control. We found no oxalate deposits in this group. In all other groups moderate to severe oxalate deposits were present in the thyroid. These data are summarised in Table II.

TABLE II. Severity of oxalosis in 73 patients

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of patients</th>
<th>Average duration of renal failure</th>
<th>Average duration of haemodialysis</th>
<th>Degree of oxalosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>CHD</td>
<td>23</td>
<td>29 months</td>
<td>14.5 months</td>
<td>7</td>
</tr>
<tr>
<td>AHD</td>
<td>10</td>
<td>9 days</td>
<td>9 days</td>
<td>6</td>
</tr>
<tr>
<td>NHD</td>
<td>10</td>
<td>22 months</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>C</td>
<td>30</td>
<td></td>
<td></td>
<td>30</td>
</tr>
</tbody>
</table>

Discussion

Oxalate deposits occur frequently in chronic renal failure. There is evidence that the incidence and severity of these deposits are related to the duration of renal failure or the duration of haemodialysis therapy. The pathogenesis of this secondary type of oxalosis remains uncertain. Since the only way to clear oxalate is renal excretion, it seems reasonable to assume that impairment of renal function leads to elevated serum levels. Zarembski et al [13] demonstrated these elevated concentrations in 11 out of 15 patients with terminal renal failure. Crystallisation occurs when the solubility product of calcium oxalate in plasma is exceeded.

In our study no statement can be made about the relation between duration of renal failure and the degree of oxalosis, because no statistical analysis was
possible in this material. There is an indication that with increasing duration of renal failure the degree of oxalosis increases. In 3 out of 5 unilaterally nephrectomised patients, we observed an increase in oxalate deposition in the autopsy material compared with material obtained at surgery; the time interval between operation and death in all cases being several years.

Mechanisms other than impairment of renal function are suggested. In our group of patients no evidence existed of methoxyxylfluorane anaesthesia, or of intestinal bypass.

Primary oxalosis, only excluded by family history and absence of urinary tract calculi, is in our opinion only a theoretical possibility in this study because of its rarity.

No information about plasma oxalate levels or urinary excretion was available. In one patient there was a history of urinary stones.

The syndrome we describe in three patients was at first interpreted as a result of secondary hyperparathyroidism, but this was excluded in two patients by exploration, although in one patient a hyperplastic parathyroid was found. In this patient however no other signs of hyperparathyroidism, such as elevated PTH levels or renal osteodystrophy, were established. Because of the very extensive deposition of oxalate in the media of peripheral vessels at autopsy in two of the patients and the extensive oxalosis in the nephrectomised kidney of the third patient, we think that these deposits cause an oblitative vasculitis, responsible for the syndrome described.

In the literature, peripheral vascular damage has been reported only in primary oxalosis [14].

Cardiac complications of oxalate deposition are well recognised [15]. Whether or not these deposits and the associated fibrosis are the cause of conduction disturbances such as heartblock cannot be established, because haemodialysis patients are also predisposed to accelerated atherosclerosis.

Conclusion

Oxalosis, frequently observed in haemodialysis patients may be the cause of a syndrome characterised by multiple shunt complications, peripheral ulceration and muscle weakness.

Hyperparathyroidism and primary oxalosis need to be excluded.

References

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