Ozaena and Iron Deficiency*

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The origin and pathogenesis of ozaena are unknown. On the basis of a study of 136 patients with ozaena, extensive epidemiological studies, and animal experiments Bernát (1966) concluded that this disease is a special manifestation of iron deficiency. This conclusion is interesting in that it implies that ozaena might be cured simply by iron therapy.

Iron deficiency is a common disease in Norway (Nattrig and Vellar, 1967), but ozaena is rare. This suggests that Bernát's conclusion may not be applicable to all areas. Therefore we made a study of a small series of ozaena patients from the point of view of iron deficiency.

Materials and Methods

Patients seen in the ear, nose, and throat department of Rikshospitalet, Oslo, are referred from all parts of Norway and represent a broad geographical selection. A review of the files of the department (both inpatients and outpatients) for the last 10 years has yielded only 11 patients with ozaena. The total number of patients during the same period was 24,176. We were able to examine nine of the 11 (see Table). All had suffered from ozaena for many years and showed the typical clinical picture of the disease. Bacterial examination of the nasal crusts usually revealed a mixed flora of Klebsiella ozaenae, Corynebacterium diphtheriae, staphylococci, pneumococci, and proteus.

The patients were questioned about symptoms and examined for signs of iron deficiency. Blood specimens and bone-marrow aspirates were taken three to four hours after a light breakfast. None of the patients were taking iron medications at the time of this study.

Venous blood was drawn into a plastic tube containing edetic acid as an anticoagulant. Haemoglobin and haematocrit were measured and red cells were counted with standard techniques (Dacie and Lewis, 1963). Blood smears were stained with May–Grünewald–Giemsa's stain. Blood for iron studies was drawn into iron-free tubes. Serum iron and total iron-binding capacity were measured in a Technicon AutoAnalyzer by standard technique. The normal range for serum iron in our laboratory is 90–150 μg/100 ml for men and 75–125 μg/100 ml for women. For total iron-binding capacity the normal range is 224–437 μg/100 ml serum.

Bone-marrow smears were stained with May–Grünwald–Giemsa's stain and also with Prussian blue iron staining (Dacie and Lewis, 1963).

Results

The clinical investigation revealed no signs of iron deficiency in eight patients. One patient (Case 1) had fissures in the corner of the mouth, but showed no alterations of the oral

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex</th>
<th>Age</th>
<th>Hb (g/100 ml)</th>
<th>Est. (%)</th>
<th>Red Cell (mill. multi.)</th>
<th>M.C.H. (μg.)</th>
<th>M.C.H.C. (%)</th>
<th>Serum Iron (μg./100 ml)</th>
<th>T.T.B. (μg./100 ml)</th>
<th>Iron in Bone Marrow</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>70</td>
<td>15±6</td>
<td>46</td>
<td>5·25</td>
<td>30</td>
<td>33</td>
<td>80</td>
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<td></td>
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<tr>
<td>2</td>
<td>F</td>
<td>68</td>
<td>17±7</td>
<td>30</td>
<td>4·90</td>
<td>30</td>
<td>35</td>
<td>105</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>59</td>
<td>14±1</td>
<td>40</td>
<td>4·40</td>
<td>32</td>
<td>36</td>
<td>105</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>58</td>
<td>15±0</td>
<td>44</td>
<td>4·96</td>
<td>34</td>
<td>34</td>
<td>115</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>47</td>
<td>15±0</td>
<td>40</td>
<td>4·89</td>
<td>31</td>
<td>38</td>
<td>105</td>
<td></td>
<td></td>
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<tr>
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<tr>
<td>7</td>
<td>M</td>
<td>45</td>
<td>16±0</td>
<td>41</td>
<td>5·31</td>
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<td>F</td>
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<td>4·81</td>
<td>36</td>
<td>95</td>
<td>330</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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mucosa or of the nails. Four women had taken iron tablets for long periods, but not for the six months previous to this investigation. During this time they had not observed any change in the ozaena.

The Table contains the results of the haematological investigations. All patients had haemoglobin, haematocrit, and red cell count within normal limits. Serum iron was normal in eight patients, and all had normal total iron-binding capacity. One male patient (Case 8) had a serum iron of 75 µg/100 ml and a total iron-binding capacity of 280 µg/100 ml, with a saturation index of 27, but with high values for haemoglobin and red cells. The iron content of his marrow was low, but iron was definitely present. Therefore, in spite of the reduced serum iron, we conclude that he was not iron-deficient.

Comments

In our small series of ozaena patients iron deficiency could not be demonstrated. We have no explanation for the discrepancy between our findings and those of Bernát (1966). However, ozaena may possibly result from several disease mechanisms, and iron deficiency may be a predisposing factor which leads to ozaena only in the presence of one or more other factors, which may be uncommon in this country. While general conclusions should not be drawn, we can only state that iron deficiency does not appear to be important in the pathogenesis of ozaena in our series of patients.

Summary

It has previously been suggested that ozaena is a special manifestation of iron deficiency (Bernát, 1966). However, iron deficiency is common in Norway, but ozaena is rare. Among 24,176 patients we found nine with ozaena. None of these had evidence of iron deficiency.

Improved Control of Long-term Anticoagulant Therapy

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Though anticoagulant therapy reduces the incidence of additional thrombosis and pulmonary embolism during the first few weeks after myocardial infarction, further attacks of thrombosis at various sites can occur subsequently during long-term oral anticoagulant treatment. Control of such treatment is not entirely satisfactory, and attempts have been made both to improve such control and to enable laboratories to report comparable results (Biggs and Denson, 1967; Poller, 1964).

By means of an activated partial thromboplastin clotting test in-vitro evidence of plasma hypercoagulability was found after acute haemorrhage and also in association with carcinoma; at the same time a rough direct relation between this clotting test and the corresponding prothrombin ratio during oral anticoagulant treatment was recorded (Eastham and Morgan, 1964). During 1967 both tests were performed on all inpatients and outpatients treated with oral anticoagulants. Examination of the results obtained suggests that the activated partial thromboplastin clotting-time is more useful than the prothrombin clotting-time as an indicator either of inadequate treatment or of overtreatment with consequent bleeding.

Patients and Methods

Blood samples were received from inpatients treated with oral anticoagulants. In addition regular samples of blood were obtained from a total of 103 outpatients during 1967, collected on Tuesdays between 9 and 11.30 a.m. and tested within five hours of collection. These patients were placed in three groups.

"Arterial Lesions."—(1) Nineteen men (aged 40–79 years) without angina of effort after myocardial infarction: one was a diabetic and two had suffered two attacks of infarction. (2) Twenty-two men and four women (38–73 years) with angina of effort after myocardial infarction: five men and one woman after two attacks of infarction and one male diabetic aged 52 after three attacks of infarction. (3) Five men and one woman (47–66 years) after carotid artery thrombosis. (4) One man and one woman (45–47 years) after cerebrovascular accidents. Of these 53 patients 42 were treated with phenindione, 11 with warfarin sodium, and one with a course of each drug.

"Venous Lesions."—(1) Six men and 12 women (26–69 years) after deep vein thrombosis or thrombophlebitis which developed in two of the women after surgical operations and in one woman after myocardial infarction. (2) Thirteen men and eight women (24–69 years) after attacks of pulmonary embolism, which occurred after surgical operations in two men, and with clinical evidence of deep leg vein thrombosis or thrombophlebitis in five men and one woman; two men developed pulmonary embolism after myocardial infarction. Thirty of these patients were treated with phenindione and nine with warfarin sodium.

"Mitral Valve Lesions."—Of the six women (44–56 years) and five men (39–55 years) in this group, three women and five men had suffered from embolic attacks, one woman was in congestive cardiac failure, one woman had developed thrombo-phlebitis, and one woman was given prophylactic anticoagulant following the development of auricular fibrillation. Nine of these patients received phenindione, and two received warfarin sodium.

A total of 913 results from these patients were examined. No results were included in the series until oral anticoagulants had been continued for at least 14 days, though some tests were taken during "tailing-off" of treatment.

Blood Samples.—Plastic disposable syringes were used to obtain samples of venous blood with minimal stasis, 1.8 ml. of blood being added to 0.2 ml. of 3.8% sodium citrate solution in polystyrene containers. These were centrifuged to produce platelet-poor plasma.

One-stage Prothrombin Ratio.—An EEL Prothrombinometer, rabbit-brain thromboplastin (Diagen from Diagnostic Reagents

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