Treatment of Aplastic Anemia with Nandrolone Decanoate

By A. Daiber, L. Hernandez, I. Con and A. Donoso

Highly satisfactory results obtained with 50 mg./week nandrolone decanoate (Deca-Durabolin) for 3–16 months are reported in 10 cases of aplastic anemia. In the series thus treated there were only two deaths, occurring after only a few months of treatment. All other cases benefited to a large degree: in six, normalization was achieved, and a distinct improvement was seen in two still under treatment. Once therapy had been commenced, there was a period of latency which fluctuated between 1 and 9 months. Except for one patient with Fanconi's anemia, the other normalized cases have not relapsed after suspension of the drug.

Since Shahidi and Diamond reported their experience with androgen therapy in aplastic anemia, numerous papers have been published, all corroborating to a greater or lesser degree the myelostimulant effect of these hormones. Preparations employed during these 10 years include an extensive list: methyltestosterone, testosterone propionate, testosterone enanthate, fluoxymesterone, norethandrolone, methandrostenolone, oxymetholone, nandrolone phenylpropionate, ethylestrenol, stanozolol. Nevertheless, up to the present time there is great diversity of opinion with regard to the effectiveness of any one of these preparations, the suitable dosage, duration of treatment, and the results both immediate and long-term, in the different types of aplastic anemia.

The lack of high-concentration oral preparations in our country means that patients have to take a large number of tablets daily over periods of many months, resulting in frequent interruption of the treatment. This consideration led us to use an injectable preparation sufficiently potent to be administered once weekly. In view of the secondary effects of androgens and anabolics when given in high dosage, such as virilization, voice change, amenorrhea, hypertrichosis, alopecia, acne, fluid retention, premature epiphyseal closure and cholestatic jaundice, we have exclusively employed nandrolone decanoate (Deca-Durabolin) over the past 2 years because it is considered to be one of the least virilizing preparations.

Materials and Methods

The therapeutic scheme which we have applied for the past 2 years in our patients with aplastic anemia is prednisone 1 mg./kg./day for 15 days, nandrolone decanoate 1–1.5 mg./week for 1–16 months.
TREATMENT OF APLASTIC ANEMIA

Table 1.—Ten Cases of Aplastic Anemia Treated With Nandrolone Decanoate

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Etiology</th>
<th>Marrow Cellularity</th>
<th>Months of Treatment</th>
<th>Total Dose (mg)</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>L.H.H.</td>
<td>43</td>
<td>M</td>
<td>Benzol</td>
<td>1-1</td>
<td>4.5</td>
<td>800</td>
<td>Normalization</td>
</tr>
<tr>
<td>E.O.N.</td>
<td>64</td>
<td>F</td>
<td>Idiopathic</td>
<td>2-1</td>
<td>6</td>
<td>1000</td>
<td>Normalization</td>
</tr>
<tr>
<td>O.S.S.</td>
<td>42</td>
<td>F</td>
<td>Idiopathic</td>
<td>1-1-1</td>
<td>16</td>
<td>2550</td>
<td>Normalization</td>
</tr>
<tr>
<td>O.V.S.</td>
<td>39</td>
<td>M</td>
<td>Benzol</td>
<td>1-1</td>
<td>5</td>
<td>850</td>
<td>Normalization</td>
</tr>
<tr>
<td>M.B.V.</td>
<td>15</td>
<td>F</td>
<td>Idiopathic</td>
<td>1-0-1</td>
<td>3</td>
<td>450</td>
<td>Death</td>
</tr>
<tr>
<td>C.O.Q.</td>
<td>39</td>
<td>F</td>
<td>Chloramphenicol</td>
<td>1-1</td>
<td>5</td>
<td>1000</td>
<td>Normalization</td>
</tr>
<tr>
<td>M.G.R.</td>
<td>25</td>
<td>F</td>
<td>Idiopathic</td>
<td>1-1</td>
<td>4</td>
<td>700</td>
<td>Death</td>
</tr>
<tr>
<td>R.V.G.</td>
<td>8</td>
<td>M</td>
<td>Fanconi</td>
<td>2-1-2</td>
<td>12</td>
<td>1000</td>
<td>Normalization</td>
</tr>
<tr>
<td>M.A.R.</td>
<td>13</td>
<td>M</td>
<td>Idiopathic</td>
<td>1-1</td>
<td>4</td>
<td>800</td>
<td>Improvement</td>
</tr>
<tr>
<td>J.C.R.</td>
<td>43</td>
<td>F</td>
<td>Phenylbutazone</td>
<td>2-2</td>
<td>3</td>
<td>600</td>
<td>Improvement</td>
</tr>
</tbody>
</table>

mg./Kg./week intramuscularly without interruption for no less than 4 months and, as required, antibiotics and transfusions. The diagnosis was confirmed in 11 cases during this period, one of which we disregarded because of death due to cerebral hemorrhage 10 days after commencement of therapy. For each of the 10 remaining patients (Table 1), several myelograms, serial hemograms, serum iron determinations and routine examinations were made first and, as required, special examinations. Ambulatory controls were carried out monthly. In those cases where treatment was suspended because of hematologic normalizations, monthly follow-ups have been performed up to the present time. (Tables 1 and 3, Figs. 1 and 2).

To evaluate the results obtained with nandrolone decanoate we reviewed all patients with aplastic anemia observed over the 3 preceding years, disregarding those cases of doubtful diagnosis, discrete hypoplasia, and those in which an acute leukemia began as a pseudopenia, or those who developed a terminal leukemia. A total of 12 patients were treated with various androgens in medium or low dosage, the patients interrupting treatment on their own initiative for one reason or another; also, corticoids, vitamins, antibiotics and frequent transfusions were given. Details and therapeutic results for this group of aplastics are shown in Table 2.

The myelograms of all patients treated with and without nandrolone decanoate were reviewed by the same observer, and classified as: aplasia, 0; severe hypoplasia, 1; moderate hypoplasia, 2; normal cellularity, 3; and hyperplasia, 4. With regard to the peripheral blood,

Fig. 1.—Blood picture in patient O.S.S. before and during treatment with nandrolone decanoate. Cases 5 and 7 died within 3–4 months; all others improved or normalized.
Fig. 2.—Effect of nandrolone decanoate in aplastic anemia: latency period and subsequent reglobulization. Patient O.S.S.: improvement was noted after 9 months and normalization after 16 months of treatment with nandrolone.

we considered normalization to have occurred when erythrocyte counts rose above $4 \times 10^6$/cu. mm., leukocytes above 3500 cu. mm. and platelets above 100,000/cu. mm.

RESULTS

10 cases of aplastic anemia were treated with 50 mg./week nandrolone decanoate. Five of these were idiopathic, of which two died, two became normal, and one who is still under treatment improved notably. Four cases were drug induced, (two through benzol, one by chloramphenicol and one by phenylbutazone). Of these, three became normalized. The tenth case had a Fanconi-type anemia and had become normalized after 10 months of treatment (Table 1). Total dosage of nandrolone decanoate required to achieve normalization varied between 800 and 2250 mg. over a period of 4-16 months. The two patients who died had received 450 and 700 mg. for 3 and 4 months,

Table 2.—Twelve Cases of Aplastic Anemia Not Treated With Nandrolone Decanoate

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Etiology</th>
<th>Marrow Cellularity</th>
<th>Months of Treatment</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>C.R.</td>
<td>46</td>
<td>F</td>
<td>Benzol</td>
<td>2–3–3</td>
<td>24</td>
<td>Normalization</td>
</tr>
<tr>
<td>M.C.</td>
<td>48</td>
<td>F</td>
<td>Anilin</td>
<td>1–1</td>
<td>20</td>
<td>No improvement</td>
</tr>
<tr>
<td>A.L.</td>
<td>30</td>
<td>M</td>
<td>Chloramphenicol</td>
<td>3–3–3</td>
<td>8</td>
<td>Normalization</td>
</tr>
<tr>
<td>F.R.</td>
<td>18</td>
<td>M</td>
<td>Tuberculose</td>
<td>4–1–1–2</td>
<td>5</td>
<td>Death</td>
</tr>
<tr>
<td>F.V.</td>
<td>23</td>
<td>M</td>
<td>Benzol</td>
<td>1–1</td>
<td>5</td>
<td>Death</td>
</tr>
<tr>
<td>H.C.</td>
<td>11</td>
<td>F</td>
<td>Idiopathic</td>
<td>3–2</td>
<td>2</td>
<td>Death</td>
</tr>
<tr>
<td>A.M.</td>
<td>21</td>
<td>F</td>
<td>Idiopathic</td>
<td>1–1</td>
<td>3</td>
<td>Death</td>
</tr>
<tr>
<td>J.R.</td>
<td>71</td>
<td>M</td>
<td>Idiopathic</td>
<td>1–1</td>
<td>2</td>
<td>Death</td>
</tr>
<tr>
<td>L.L.</td>
<td>52</td>
<td>F</td>
<td>Varso</td>
<td>1–1–2</td>
<td>9</td>
<td>Death</td>
</tr>
<tr>
<td>O.S.</td>
<td>47</td>
<td>F</td>
<td>Idiopathic</td>
<td>1–0–1</td>
<td>27</td>
<td>No improvement</td>
</tr>
<tr>
<td>R.V.G.</td>
<td>43</td>
<td>M</td>
<td>Fanconi</td>
<td>1–2–2–1</td>
<td>48</td>
<td>Partial improvement</td>
</tr>
<tr>
<td>C.O.</td>
<td>39</td>
<td>F</td>
<td>Chloramphenicol</td>
<td>1–1</td>
<td>14</td>
<td>Partial improvement</td>
</tr>
</tbody>
</table>
TREATMENT OF APLASTIC ANEMIA

Table 3.—Survey of 22 Cases of Aplastic Anemia Treated With or Without Nandrolone Decanoate

<table>
<thead>
<tr>
<th></th>
<th>Without Nandrolone Decanoate (12 cases)</th>
<th>With Nandrolone Decanoate (10 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Idiopathic Secondary Fanconi Total</td>
<td>Idiopathic Secondary Fanconi Total</td>
</tr>
<tr>
<td>Normalization</td>
<td>— 2</td>
<td>2 3 1 6</td>
</tr>
<tr>
<td>Partial improvement</td>
<td>— 1</td>
<td>1* 1* — — 2</td>
</tr>
<tr>
<td>No improvement</td>
<td>1 1</td>
<td>— — — — — — — 2</td>
</tr>
<tr>
<td>Death</td>
<td>3 3</td>
<td>2 — — 2</td>
</tr>
</tbody>
</table>

* Cases now under 3 and 4 months of treatment in which marked improvement has been observed.

respectively. Both developed severe infections during the last weeks of life.

In those patients with very intense anemia requiring frequent blood transfusions, the first sign of a favorable response was the reduced transfusion requirement. In most cases, signs of improvement became clear only after 2–3 months of uninterrupted anabolic treatment (Fig. 2). One case responded in 1 month; in another improvement was noted after 9 months of treatment (Fig. 1). Improvement in leukopenia began after 2–3 months treatment and was less striking than the erythroid response. In several cases a marked lymphocytosis (45 to 55%) persisted. Thrombocytopenia improved more slowly and only in one case was a return to normal observed. In the others, the final figures fluctuated between 60,000 and 180,000/cu. mm.

All patients had bone marrow hypoplasia and in most it was marked. (Table 1) Post-treatment bone marrow examination in four patients in whom the peripheral blood had returned to normal showed marked repopulation, with a variable degree of erythroid hyperplasia.

Tolerance of weekly injections of nandrolone was excellent. Secondary effects consisted of virilization, a tendency to subclinical jaundice. Signs of virilization appeared only after 3–4 months of therapy. We noted hoarseness and deepening of the voice, swelling of the skin, slight loss of hair and amenorrhea, signs which were very moderate in female patients over 30 years of age, but more pronounced in the younger women, as were early signs of virilization in the only male child in the series.

After therapy was discontinued there were no signs of relapse in any of the normalized idiopathic or secondary aplastics; one of these has been under observation for 16 months. On the other hand, the only patient in the series with Fanconi’s anemia relapsed 2 months after being taken off the drug.

The results obtained in the series treated in this way were strikingly different from those of the immediately preceding series, in which treatment did not include a long-term high dose anabolic agent (Table 2). Mortality in the anabolic group was 20 per cent as compared to 50 per cent in the other. Of the six surviving patients in the group treated without an anabolic, there were two whose condition remained unchanged. Every one of the eight surviving patients in the anabolic series improved (Table 3).

DISCUSSION

Our experience confirms results obtained by other authors in the last 10 years.
Virilizing androgens or the less virilizing anabolic agents, administered in high dosage for a number of months, succeed in fundamentally changing the terrify-
ing prognosis of aplastic anemia. Although our series treated with nandrolone
decanoate 1 to 1.5 mg./Kg./week consisted of only 10 patients, the results
obtained are heartening when compared to a group of 12 patients who had not
received an anabolic agent or sustained and sufficiently high daily doses of an
androgen.

The favorable response achieved with this treatment began some 2 or more
months after initiation of treatment. Initially, transfusion requirements de-
creased. Thereafter there was a gradual hematologic improvement first noticed
in the erythroid series. This delayed effect was also described by Sanchez-
Medal'3 and others'11,16 and could be interpreted as the result of an indirect
action of the anabolic agent. Nevertheless, the fact that the less severe cases
responded earlier suggests a direct effect on the marrow. This period latency
implies the need of medical vigilance, an adequate supply of blood and
meticulous avoidance of complications due to infections.

The appearance of a mixed type
subicterus in those cases requiring prolonged
treatment, together with a reticulocytosis in excess of the rise in hemoglobin
leads us to suspect a shortened red cell life span during the recuperation phase.

Bernard et al.2 have described a form of acute aplasia in young adults that
would have a more sombre prognosis. On the other hand, authors such as
Nejean10,11 and others17 consider the idiopathic form as more severe than the
secondary. In our series, the two fatal cases occurred in young women without
a history of myelotoxic exposure, in whom progress of the disease was explosive,
without any evidence of a hematologic response at the end of 3–4 months treat-
ment. Splenectomy in one of these patients did not modify the disease but, on
the contrary, appeared to favor infections.

Of the six cases which normalized, five have been under observation for
between 2 and 16 months without signs of relapse. These include cases of both
the primary and the secondary form. These results are in contrast with those
published by Najean et al.10 who reported a high percentage of relapses in
idiopathic and secondary aplastic anemia. A more prolonged observation of our
recovered patients will be necessary before drawing any final conclusions. The
only patient with a Fanconi anemia in our series showed signs of relapse 30
days after discontinuing therapy. This is similar to observations described by
several authors.

Initial treatment with prednisone carried out in nine of the 10 patients showed
no benefit whatsoever. Its employment in this disease, therefore, seems un-
profitable. We nevertheless believe that it serves a purpose as a means of
differentiating between aplastic leukemia and “aleukemic” leukemia. In the
latter case the corticoid may, after an initial decrease of the leukocytes, nor-
malize their number and, afterwards, also the number of thrombocytes.

ACKNOWLEDGMENT

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REFERENCES


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