Research Article

Bone Marrow Concentrate in the Treatment of Aneurysmal Bone Cysts: A Case Series Study

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Introduction. A recent attractive option regarding mesenchymal stem cells (MSC) application is the treatment of bone cystic lesions and in particular aneurysmal bone cysts (ABC), in order to stimulate intrinsic healing. We performed a retrospective evaluation of the results obtained at our institution. Methods. The study group consisted of 46 cases with an average follow-up of 33 months. Forty-two patients underwent percutaneous treatment as the first approach; four patients had curettage as first treatment. In all cases, autologous bone marrow concentrate (BMC) was associated too. The healing status was followed up through a plain radiograph 45 days and 2 months after the procedure. Results and Conclusions. At the final follow-up, thirty-six patients healed with a Neer type II aspect, nine healed with a type I aspect, and one patient was not classified having total hip arthroplasty. Bone marrow concentrate is easy to obtain and to manipulate and can be immediately available in a clinical setting. We can assert that the use of BMC must be encouraged being harmless and having an unquestionable high osteogenic and healing potential in bone defects.

1. Introduction

In the past 30 years, many studies have confirmed the potentials and plasticity of the so-called mesenchymal stem cells (MSC): they have been shown to reside within the connective tissues of most organs and can differentiate into osteogenic, adipogenic, and chondrogenic lineages under appropriate conditions [1–3]. These features have led to an increasing application of MSC in the orthopaedic field, especially when a strong regenerative capacity applied through a minimally invasive approaches is required. A simple method to have MSC is the bone marrow concentrate (BMC) obtained through autologous bone marrow aspiration and centrifugation. Local application of BMC is one of the current available treatments of bone defects and in particular of cystic lesions [4, 5]. Among them aneurysmal bone cysts (ABC) are uncommon osteolytic lesions, usually eccentric, with a hyperplastic behaviour often arising in the long bones of young people, being rare after 30 years of age [6]. The treatment approach to ABC has evolved in the past years ranging from radiotherapy to resection. More recently, less invasive procedures such as complete or partial curettage, and various substance injections seemed to be promising [7, 8]. We performed a retrospective evaluation of the results obtained at our institution after aneurysmal bone cyst percutaneous treatment with application of BMC in order to understand if the use of bone marrow stem cells actually gives benefits.

2. Material and Methods

We present a retrospective study involving 57 patients with diagnosis of aneurysmal bone cyst, treated at our institution between January 2013 and June 2019. The following exclusion criteria were applied: secondary ABC, initial treatment in other institution, and incomplete radiographic evaluation. Eight patients were excluded according to the following criteria: 2 ABC associated to chondroblastoma, 3 patients who had initial treatment in another hospital, and 6 patients for the absence of complete radiographic evaluation available. The study group consisted of 46 patients with an average
under formed using sedation and local anaesthesia or under general collected intraoperatively. All of the procedures were per-...ed initially and subsequently, the chosen drugs were injected into the cyst was then aspirated and sent for histopathologic eval-

Table 1: ABC anatomical location.

<table>
<thead>
<tr>
<th>Location</th>
<th>Number</th>
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<tbody>
<tr>
<td>Proximal humerus</td>
<td>14</td>
</tr>
<tr>
<td>Humeral diaphysis</td>
<td>8</td>
</tr>
<tr>
<td>Pelvis</td>
<td>3</td>
</tr>
<tr>
<td>Femur diaphysis</td>
<td>6</td>
</tr>
<tr>
<td>Proximal femur</td>
<td>13</td>
</tr>
<tr>
<td>Calcaneus</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 2: Enneking classification.

<table>
<thead>
<tr>
<th>Status</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>Inactive</td>
<td>Intact, well-defined margins</td>
</tr>
<tr>
<td>Active</td>
<td>Incomplete margins but well-defined lesion</td>
</tr>
<tr>
<td>Aggressive</td>
<td>Poorly defined margins with reactive bone formation</td>
</tr>
</tbody>
</table>

follow-up of 33 months. Forty-two patients underwent per-
cutaneous treatment as first approach; four patients had
curette as first treatment. The patients enrolled performed
a plain radiograph before intervention, and the following
radiographic variables were assessed: affected bone, staging
according to the Enneking system [9], and location according
to the Capanna classification [10]. In all cases, the diagnosis
was obtained through a histopathological study of specimens
collected intraoperatively. All of the procedures were per-
formed using sedation and local anaesthesia or under general
anaesthesia with an aseptic technique. The percutaneous
injections were performed introducing a Jamshidi needle,
under fluoroscopic guide, into the lesion. The content of
the cyst was then aspirated and sent for histopathologic eval-
uation; subsequently, the chosen drugs were injected into the
lesion. The injected substances were: vitamin C, atossisclerol
(0, 25%), methylprednisolone acetate, and autologous bone
marrow concentrate (BMC). The two lesions treated with
filled with bone chips enriched with the same
substances aforementioned. The BMC was obtained through
aspiration of bone marrow from the ipsilateral iliac crest and
centrifugation in a dedicated RegenKit® device. The healing
status was followed up through a plain radiograph 45 days
after the procedure and then 2 months after. According to
the modified Neer classification [11], the procedure was
repeated if no satisfactory healing of the lesion occurred after
2 months, i.e. if the radiolucent area was ≥50% of the lesion
diameter or in case of relapse.

3. Results

The mean age at diagnosis was 13.8 with a male prevalence
(31 males, 15 females). The anatomical location, collected
in Table 1, shows a predominant distribution in the proximal
metaphysis of long bones and in the pelvis. The cysts were
classified in inactive, active, and aggressive according to the
Enneking staging of musculoskeletal tumours as shown in
Table 2: they were all active, except for one that was an
aggressive lesion. According to the Capanna staging
(Table 3), all patients had type II lesions, i.e., central and
affecting the entire diameter of the bone, except for two cases
having eccentric lesion, defined as type III. Thirty-six
patients healed after the first treatment; among them, four
had an open curettage and the cavity was filled with bone
chips and autologous BMC. Of the remaining ten patients,
seven healed with 2 percutaneous injections; of the remaining
two, 3 had percutaneous injection and one had a resection
with total hip replacement. Healing was assessed using the
modified Neer classification (Table 4) used for unicameral
bone cyst treatment; at the final follow-up, thirty-six patients
healed with a type II aspect, nine healed with a type I aspect,
and one patient was not classified having total hip
arthroplasty.

4. Discussion

The application of bone marrow concentrate (BMC) in the
treatment of aneurysmal bone cysts (ABC) is a quite new
procedure. The use of BMC to fill bony defects is well known,
with a success rate that seems to be related to the number of
progenitors in the graft [12]. ABC are reactive and locally
aggressive lesions having osteolytic, hyperplastic, hyperemic,
and hemorrhagic features; they are uncommon and rarely
present after 30 years of age. Aneurysmal bone cyst-like
modifications can be observed also in other pathological con-
ditions, in malignant tumours such as telangiectatic osteosar-
coma, and this eventuality must be ruled out through the
histological study of specimens [6]. The aim of ABC treat-
ment is to arrest their potentially high destructive capability.
In the past years, different approaches have been proposed
for ABC treatment ranging from resection to mini-invasive
percutaneous procedures, and still today, there is no consen-
sus on the best treatment [13–15]. However, the analysis of
ABC pathogenesis and natural history, although not
completely understood, can be helpful to chose the most
appropriate treatment. It was long thought that ABC’s cause
was a vascular impairment due to abnormal venous circula-
tion with osteoclast activation and local bone resorption; a
more recent clonal theory overtook the vascular theory: the
origin of the lesion seems to be associated with a transloca-
tion of USP6 oncogene on chromosome 17 [16, 17]. This
finding confirms the oncological nature of ABC and there-
fore their high evolutivity: as for other musculoskeletal
tumors, ABC can be classified as inactive, active, and aggres-
sive and their evolution proceeds in phases. The initial osteo-
lysis can evolve to cortical destruction and periosteoal reaction
creating a bulky bone; the appearance of septa attests a stabi-
ization and remodelling attempt that in a few cases can lead
to spontaneous resolution. In other cases, ABC assume an
aggressive and destructive behaviour; however, the reason

Table 3: Capanna classification.

<table>
<thead>
<tr>
<th>Type</th>
<th>Morphological features</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Central lesion</td>
</tr>
<tr>
<td>II</td>
<td>Central lesion involving the entire bone diameter</td>
</tr>
<tr>
<td>III</td>
<td>Eccentric lesion</td>
</tr>
<tr>
<td>IV</td>
<td>Subperiosteal lesion</td>
</tr>
<tr>
<td>V</td>
<td>Subperiosteal lesion extending to soft tissues</td>
</tr>
</tbody>
</table>
that shifts to a stabilizing or a destructive pattern is still unknown [7, 18]. Delloye et al. were among the first to report two cases of ABC treated with BMC: the rationale underlying this treatment was in the inductive properties of mesenchymal stems cells [19]. Many studies have already confirmed that BMC, particularly, if obtained through iliac crest aspiration, is rich in mesenchymal cells that seem to represent the source of osteoblastic elements during growth, remodelling, and bone reparative processes [20–22]. Moreover, ABCs are subject to continuous reparative processes in a cavity filled with blood that provides an ideal environment for mesenchymal cells to express their inductive capacities. Therefore, the aim of our treatment was to induce spontaneous ossification of ABC through a minimally invasive procedure. Currently, there is no consensus on the ideal treatment of ABC. For eccentric and aggressive lesions, located in expendable bones like the proximal fibula or pubic ramus, many authors have advocate resection as treatment of choice, reporting very low recurrence rates [23, 24]. According to other authors, curettage with or without bone grafting seems to be the best choice, reporting acceptable recurrence rates with a much better functional outcome than resection [25, 26]. More recently, in consideration of patients’ young age and with better understanding of ABC pathogenesis, less-invasive procedures are gaining more success: percutaneous embolization, isolated intracystic injection of demineralized bone powder, bone marrow, calcitonin and Ethibloc are some examples [27–29]. Docquier and Delloye reported good results inducing ABCs’ healing with intralesional implantation, through a mini-invasive access, of a bone paste made of autogenic bone marrow and allogenic bone powder: the goal of this treatment was to interrupt the destructive osteoclastic process and promote spontaneous bone regeneration [7]. In our series, with the technique described, we obtained a full recovery after only one treatment in more than 50% of our cases; the remaining had a maximum of two other procedures except for one patient, affected by a lesion involving the femoral head in contact with the articular cartilage that eventually underwent prosthetic replacement. Only four patients received curettage as first treatment since they had wide lesions; they both reported a Neer II grade at follow-up. As regards percutaneous approach, we believe that, given the age of patients affected by this condition, the proposed treatment avoids extensive surgery and blood loss and can be repeatable with minor discomfort for the patient. Moreover, we did not report any complication, including superficial or deep infection, fracture, or other adverse reactions, both at the harvest site and at the application site: this confirmed the safety of the procedure used. Nevertheless, even if the results obtained are promising, the number of cases is exiguous and a larger group is necessary to confirm the validity of this procedure; perhaps with a greater number of patients a stratification based on anatomical location and cyst dimension would be feasible and would help in the choice of the best treatment.

5. Conclusions

Even if affected by the limitation of a relatively small number of patients, our case series proves that bone marrow concentrate is easy to obtain and to manipulate, and can be immediately available in a clinical setting: it offered good results with no complications. We believe that cavitary lesions like ABCs are ideal settings for using mesenchymal cells since they act as a biological chamber where the healing processes can be potentiated by the presence of blood and growth factors that stimulate differentiation of an osteogenic lineage.

Data Availability

The data sets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Consent

Written consent was obtained from all patients included in this study (or their parents for underaged patients).

Conflicts of Interest

The authors declare that they have no competing interests.

References


