Ribbing disease – A Rare cause for Common Shin Pain

Roy S. Horowitz, M.D.¹ ; Rivka Drezner Pollak², M.D. ; Meir Liebergall¹, M.D. ; Omer Or¹, M.D.
¹Department of Orthopedic Surgery, Hebrew University Hadassah Medical Centers, Jerusalem, Israel
²Department of Endocrinology, Hebrew University Hadassah Medical Centers, Jerusalem, Israel

Abstract

Introduction: Ribbing Disease is an extremely rare bone dysplasia. It is difficult to diagnose and treat without published treatment guidelines. The common presenting symptom is usually shin pain with intramedullary sclerosis of the tibia.

Case report: A 46-years-old woman presented with a debilitating long-standing bilateral shin pain and intramedullary sclerosis of the tibial bones. Pathology test did not show a definite diagnosis and genetic testing was positive for TGFβ1 gene. Medical treatment including anti-TGFβ, Calcitonin and Bisphosphonate did not alleviate her symptoms. The patient underwent sequential surgery of intramedullary reaming of both her tibias. Following surgery her symptoms resolved completely.

Conclusion: We review Ribbing disease pathology, differential diagnosis and treatment options. A rare disease with a very common symptom which should be considered in any shin pain with bone sclerosis.

Introduction

Ribbing Disease is a rare yet probably under-reported etiology for severe pain of the long bones, especially of the tibiae. Only few reported cases were published without any clear guidelines for diagnosis and treatment. Patients often go unnoticed for years until diagnosis is made, assuming diagnosis is made at all. There are few treatment options which can alleviate the patient symptoms, albeit none directly address the disease's etiology.

Case report

A healthy 46 years old female patient reported to the orthopedic clinic in 2017 due to severe bilateral shin pain for several years, mostly at night, requiring narcotics. The left side was most dominant. The patient's physical examination was unremarkable aside local tenderness over the left tibial bone. X-Rays Imagining study showed hyperostotic sclerosis, cortical thickening and medullary obliteration of both tibiae more dominant on the left side. Mild sclerosis was also noted in both femura and left humerus without any clinical symptoms. Bone scan showed high uptake in both tibiae, femur and left humerus. Magnetic resonance Imaging (MRI) showed diffuse bone marrow edema without a defined bone lesion. Biopsies done at another institution demonstrated dense, cortical type lamellar bone mixed with bone dust, without inflammation or neoplasia. Laboratory values including serum levels of: vitamin D, calcium, potassium, alkaline phosphotase and parathyroid hormone were unremarkable. Genetic testing were done and revealed mutation in the TGFβ1 gene. Once, other possible etiologies were ruled out Ribbing disease was diagnosed. Conservative treatment was tried first. Following non-steroidal anti inflammatory medications (NSAID) failure to alleviate pain, Calcitonin nasal spray of 200 units per day for 12 weeks was given, without any improvement
either. Losaratn, an anti TGFβ1 medication, was used without success. Seen the failure of the conservative measures and considering the patient's immense pain, the patient was referred for surgery. In 2017 the patient underwent intramedullary reaming of the left tibia. Due to the diffuse diaphyseal involvement reaming was preferred to fenestration of the cortex. Technical difficulties arised during surgery due to the obliteration of intramedullary canal. manual reamers were used cautiously before power reaming. Bone cultures samples were negative and pathology showed normal bone trabeculae. Following the first intervention, the patient received 5mg Zoledronic acid intravenously and was monitored for calcium and vitamin D3 levels. The patient suffered post operatively of patellar tendon bursitis for several months until final resolution. Following few weeks from surgery the tibia bone pain resolved completely. Two years later the patient suffered from increased right side shin pain. A similar procedure was done without post-operative complications. A rapid resolution of pain was noted and all narcotics were discontinued. In 3 years follow up no recurrence of symptoms were noted and further interventions were not required.

**Discussion**

Ribbing Disease, also known as Hereditary Multiple Diaphyseal Sclerosis, manifests itself around the 3rd-4th decade of life through extremity pain, predominantly of the shins. Its etiology is considered as an uncontrolled diaphysary growth of the endosteum and periosteum of the long bones, guided by tilting the coupled bone formation and resorption towards bone formation[1]. Ribbing disease does not seem to be weakening the structural integrity of the bone. Nonetheless, there is a slow progressive obliteration of the cancellous bone and the Haversian system, and its replacement by a dense cortical bone[3]. Genomic studies have suggested the involvement of the TGFβ1 gene, which takes part of the TGF-BMP pathway, responsible for the

---

**Table 1: Differential Diagnosis of Long Bones' Diaphysis Endosteal and Periosteal Dysplasia – Rare Monogenic Diseases**

<table>
<thead>
<tr>
<th>Name</th>
<th>Radiologic Findings</th>
<th>Location</th>
<th>Genomics</th>
<th>Manifestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hereditary Multiple Diaphyseal Sclerosis (&quot;Ribbing Disease&quot;)</td>
<td>Endosteal and periosteal fusiform thickening of the diaphyseal cortices</td>
<td>Long bones, mostly the tibiae</td>
<td>TGFβ mutations</td>
<td>Asynchronous Bone Pain, onsets at middle age</td>
</tr>
<tr>
<td>Progressive Diaphyseal Dysplasia (&quot;Engelmann-Camurati Disease&quot;)</td>
<td>Endosteal and periosteal fusiform thickening of the diaphyseal cortices</td>
<td>Long bones, as well as the base of skull, the mandible and the facial bones.</td>
<td>TGFβ mutations</td>
<td>Bilateral Bone Pain, onsets at childhood-adolescence, Muscle Weakness</td>
</tr>
<tr>
<td>Melorheostosis (&quot;Leri Disease&quot;)</td>
<td>Periosteal and usually endostial ondulating thickening ridges of bone (&quot;Candle Wax&quot;)</td>
<td>Long and short bones in a sclerotome distribution</td>
<td>MAP2K1 mutations</td>
<td>Bone Pain, Progressive Joint Contractures</td>
</tr>
<tr>
<td>Ghosal Hematodiaphyseal Dysplasia</td>
<td>Diaphyseal and Metaphyseal endosteal and periosteal thickening of the cortices</td>
<td>Long bones</td>
<td>TBXAS1 mutations</td>
<td>Bone Pain, Refractory Anemia/Thrombocytopenia/Leukopenia</td>
</tr>
<tr>
<td>Hyperostosis Corticalis Generalisata (&quot;Van Bochem Disease&quot;)</td>
<td>Diaphyseal thickening of the cortices</td>
<td>Long bones, Cranium, Mandible</td>
<td>SOST deletion</td>
<td>Skeletal hyperostosis and sclerosis, mainly of the cranium and mandible.</td>
</tr>
</tbody>
</table>

---

**Figure 1:** X-Rays of a patient whom underwent intramedullary reaming in our institution for Ribbing Disease in 2019 (A - Before, B - After).

**Figure 2:** A CT Scan of a patient in our institution with Ribbing Disease (Coronal, Sagittal and Axial views).
osteoblast differentiation and osteogenesis. This rare disease is transmitted through an Autosomal Recessive pattern, with reports surmounting up to only few world wide. There are many etiologies that can lead to the presentation of cortical thickening, with differential diagnosis being Infection (chronic osteomyelitis), Endocrinology abnormalities, Stress Fracture, Paget’s Disease and Neoplasias (mainly Osteoid Osteoma and Osteosarcoma)[2]. Diagnosis of Ribbing Disease is done by means of clinical interview, physical examination and radiology. To date there is only a nosologic classification system for bone dysplasias[3], where Ribbing Disease partake the group of “other bone dysplasias” (Table 1). X-rays facilitates the diagnosis, delineating the fusiform thickening of the cortices at the expense of the medullary cavity. Computer Tomography is not mandatory, however it assists with the biopsy of the affected bone (figure 2). Bone Scan are useful for the detection of different foci of the disease at the systemic level. The serum levels of calcium, vitamin D3 and the Parathyroid hormone can help identifying endocrinology abnormalities, whereas Alkaline Phosphate and Lactate Hydrogenase indicate the intensity of activity of the Osteoblasts and Osteoclasts, respectively. Herein, MRI can be used primarily in order to rule out an alternative etiology, especially neoplasia. In the case of Ribbing disease, it will demarcate in the T2 phase the bone edema[4], resembling an intramedullary high pressure, which is thought to be the cause of pain. Conservative measures is the first line of treatment of Ribbing Disease, and it includes the use of anti-inflammatory such as NSAIDs[5] and steroids to lower the edematous pain. Bone anti-resorption medications, especially bisphosphonates, may be used in order to alternate the coupled bone remodeling process. It is use is controversial, as it targets the osteoclasts instead of the osteoblasts, which are the protagonists of this disease. The success rate of these medications is undetermined, with conflicting results[5-8], and attempts to correlate genomics with a good-to-excellent response to treatment did not succeed[9]. Our attempt to apply Salmon Calcitonin, yet another Osteoclast inhibitor, seeing an anecdotal success with another bone dysplasia[10], did not work. There has been no use of anti-TGFβ antibodies to counter the disease to date. The use of TGFβ pathway inhibitors, such as Angiotensin Converting Enzyme Inhibitors (ACEI) and Angiotensin Receptor Blockers (ARBs) has not been described in the literature for Ribbing Disease, however there are reports about good outcomes in a similar TGFβ-driven disease, Englemann-Camurati disease[11]. We have tried Losartan with our patient, to in a similar TFGβ-driven disease, Englemann-Camurati Disease, however there are reports about good outcomes (chronic osteomyelitis), Endocrinology abnormalities, Stress Fracture, Paget’s Disease and Neoplasias (mainly Osteoid Osteoma and Osteosarcoma)[2]. Diagnosis of Ribbing Disease is done by means of clinical interview, physical examination and radiology. To date there is only a nosologic classification system for bone dysplasias[3], where Ribbing Disease partake the group of “other bone dysplasias” (Table 1). X-rays facilitates the diagnosis, delineating the fusiform thickening of the cortices at the expense of the medullary cavity. Computer Tomography is not mandatory, however it assists with the biopsy of the affected bone (figure 2). Bone Scan are useful for the detection of different foci of the disease at the systemic level. The serum levels of calcium, vitamin D3 and the Parathyroid hormone can help identifying endocrinology abnormalities, whereas Alkaline Phosphate and Lactate Hydrogenase indicate the intensity of activity of the Osteoblasts and Osteoclasts, respectively. Herein, MRI can be used primarily in order to rule out an alternative etiology, especially neoplasia. In the case of Ribbing disease, it will demarcate in the T2 phase the bone edema[4], resembling an intramedullary high pressure, which is thought to be the cause of pain. Conservative measures is the first line of treatment of Ribbing Disease, and it includes the use of anti-inflammatory such as NSAIDs[5] and steroids to lower the edematous pain. Bone anti-resorption medications, especially bisphosphonates, may be used in order to alternate the coupled bone remodeling process. It is use is controversial, as it targets the osteoclasts instead of the osteoblasts, which are the protagonists of this disease. The success rate of these medications is undetermined, with conflicting results[5-8], and attempts to correlate genomics with a good-to-excellent response to treatment did not succeed[9]. Our attempt to apply Salmon Calcitonin, yet another Osteoclast inhibitor, seeing an anecdotal success with another bone dysplasia[10], did not work. There has been no use of anti-TGFβ antibodies to counter the disease to date. The use of TGFβ pathway inhibitors, such as Angiotensin Converting Enzyme Inhibitors (ACEI) and Angiotensin Receptor Blockers (ARBs) has not been described in the literature for Ribbing Disease, however there are reports about good outcomes in a similar TGFβ-driven disease, Englemann-Camurati disease[11]. We have tried Losartan with our patient, to no avail. It is possible that its effectiveness in Englemann-Camurati is derived from its elevated osteogenic activity, in respect to the latency of Ribbing Disease. The second line of treatment is surgical intervention which will reduce the intramedullary pressure. Intramedullary reaming, without the use of instrumentation or Polymethylmethacrylate (PMMA), as the bone is already stable. The reaming is believed to decompresses the intramedullary cavity, thereby dramatically decreasing the pain level, albeit not necessarily abutting it[12]. With the obliteration of the medullary cavity by the endosteal bone, breaching the canal is not expected to be smooth, and may require the use of hammers and manual reamers. Intraoperative fluoroscopy must be performed to rule out an unintended cortical breach and fracture. Cortical fenestration is also reported however it may not be as effective as reaming due to its limited decompression.

Conclusion

Ribbing Disease constitutes a rare yet probably under-reported cause for severe pain in the shins. Diagnosis is made by clinical interview, physical examination and a typical appearance of fusiform thickening of the cortices of long bones on X-Rays. Treatment constitutes the use of NSAIDs and anti-Resorptive medications with variable results as a first line. Surgery as a second line via intramedullary drilling demonstrates consistently good outcomes by means of decompression.

Conflict of interest statement: The authors declare that they have no conflict of interest in the publication of this case report.

Funding: This case report was not funded by a grant or public or non-profit sources.

Prior Publication/Presentation: This case report has not been previously published or presented in any form.

IRB: IRB approval was not required for this case report.

Data Availability: Data from this case report may be made available upon reasonable request.

References


