

ZOLENDRONATE
a case report

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Disclosures

- I have nothing to disclose related to this presentation

Objectives

- Present a case report on a patient that received Zolendronate
- Illicit discussion about the case
- Find out if others have had similar experiences

Zoledronic Acid

- Zoledronic acid slows down bone reabsorption (osteoclasts), allowing the bone-forming cells time to rebuild normal bone and allowing bone remodelling
- Zoledronate has shown significant benefits versus placebo over three years, with a reduced number of vertebral fractures and improved markers of bone density[1].

[1] Reid IR, et al (2002). "Intermittent zoledronic acid in postmenopausal women with low bone mineral density". *N. Engl. J. Med.* 346 (9): 872-80.

Zoledronic Acid

- Reclast, Zometa(Canada), Aclasta (Australia)
- From Monograph in >10% of patients
 - Bone pain (55%)
 - Nausea (29-46%)
 - Fever (32-44%)
 - Fatigue (39%)

Side Effects

- Side-effects can include fatigue, anemia, muscle aches, fever, and/or swelling in the feet or legs. Flu-like symptoms (myalgia, arthralgia, and headache) are commonly experienced after the first zoledronate infusion, although not subsequent infusions, and are thought to occur because of its potential to activate human $\gamma\delta$ T cell (gamma/delta T cells)
- Rare adverse effects include renal dysfunction, hypocalcemia, atrial fibrillation, and osteonecrosis of the jaw

Case Study

- Dec 2010
 - 6y6m old boy with hx of 7 fractures of lower limbs, all considered fragility fractures
 - 1- (R) tibia, at age 8mos, sitting down
 - 2- (R) tibia 22mos, getting off the bed
 - 3- (L) 5th metatarsal, 4yr, jumping off bottom stair
 - 4- (R) ankle, 5yr, running
 - 5- 4th metatarsal, 6yr, no clear mechanism
 - 6- (R) big toe while still in cast for 5th break
 - 7- previous week 2nd & 3rd metatarsals, piano bench

History cont'd

- Adopted, no family history available
- Parents and one younger sibling in the home
- No significant dental issues, no evidence of dentinogenesis imperfecta
- Blue sclera noted on exam
- Denies back pain, even with palpation
- MSK – hypermobility of the joints
- Grade 1, gifted program
- Umbilical hernia repair 2009, biopsy done at the time for OI
- No steroid, antiepileptic drug or heparin use

Plan

- Screening blood work (all normal)
- Pros and cons of bisphosphonate treatment was discussed with the parents including flu-like symptoms following the first injection as well as the remote risk of osteonecrosis of the jaw
- Parents opted to hold on the treatment

Bone Density Z scores

Date	Spine	Femoral Neck	Forearm	Total Body
Feb2010	1.9			-0.7
Jan2011	-0.8	-2.3		-2.6
Jan2012	-0.2	-3.6		
Feb2013	-1.6	-2.9		

Follow up

- From our initial visit in Dec 2010...
 - 2011 -2 further fractures, dx w/cold urticaria
 - Genetic testing results; neg for the COL1A1 and COL1A2 gene, skin fibroblast electrophoresis was normal
 - 2013 - No further fractures- therefore no tx recommended
 - Jan 2015 (no follow up for 2 years) 5 new fractures 2ribs, compression T7-8, in back brace, missing significant days of school, sclera now just faintly grey

Plan

- Due to an increase in fracture history, compression fractures and declining bone density scores bisphosphonate treatment was recommended
- Parents didn't want him missing school every 3-4 mos therefore Zolendronate versus Pamidronate was offered (once a year infusion). Parents elected to wait until summer holidays before starting
- July 2015 Zolendronate 4mg given

Aftermath of Treatment

- Major myalgia, nausea, vomiting and fever. Lasting 10 days. This was felt to be attributed to cytokine release
- Improved over the summer but with intermittent mild back pain remaining
- October 2015 – complaint of worsening back pain, worse in the morning, gets better for ½ day at school then starts worsening in the afternoon. Missing some days of school. Advil/Tylenol not working
- O/E – c/o pain when bending over and on palpation. Plan to start a trial of Naproxen and Prevacid

- Nov 2015 - Calls from Mom, at least twice a week.
- Now missing almost all of school
- Can't sit or lay in one position for any length of time
- Mom states this is affecting all of the family now
- Urgently seen in December by Endocrine for re-evaluation
 - o/e; walking with limp, holding spine in protected position. c/o local tenderness at L4-5, +Trendelenberg sign
- Pharmacy manufacturer contacted re; reporting a possible adverse reaction. Of note, none on record according to the company

- Urgent referral to Chronic Pain Clinic (Rheumatology, Anaesthesiology, Physio, Pharmacist)
- All possible inflammatory markers were normal
- Trial of Prednisone was initiated for 10 days
- Bone scan ordered – uptake appeared symmetric

- Diagnosed with: Right localized severe sacroiliac pain with a neuropathic component
- Rx oxcarbazepine to deal with the neuropathic component

Latest update

- End of Jan 2016 Mom feels that pain is improved with oxcarbazepine. Starting back at half days of school. With goal to increase to full days by end of Feb
- MRI Apr 6/16 for increase in severe back pain ? Nerve entrapment ? Inflammation ? Osteoid osteoma
- Normal – no abnormality of the lumbosacral spine and sacroiliac joints

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Feb2016	-1.0	-2.4	-0.5	

Questions for the Audience

- Are other centres using Zolendronate?
- Has anyone had a similar experience with Zolendronate?
- Any suggestions with the case study management?


