

Novel Practice Techniques: Percutaneous Doxycycline Injection for Aneurysmal Bone Cysts

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Summary:

Pros

1. Injection is minimally invasive
2. Material is easy to obtain and affordable
3. Appears to have similar or improved recurrence rates as compared to surgery

Cons

1. May need multiple injections to adequately treat tumor
2. Complications include skin necrosis and local recurrence

Background:

Aneurysmal bone cyst has a reported local recurrence rate after curettage of 10-70%. In the spine, it is particularly difficult to adequately treat.

What is new?

Doxycycline is commonly used as an antibiotic. It has also been found to heal lymphatic malformations that are associated with VEGF and MMPs. In cell culture, doxycycline has been shown to inhibit MMP, angiogenesis, and osteoclastic function. A doxycycline and albumin protein foam is an injectable substance that can be targeted to aneurysmal bone cysts.

What is the evidence for?

A search of PubMed online database was performed on October 11, 2022. The inclusion terms were "doxycycline" and "aneurysmal bone cyst." 14 citations were found, with the earliest documentation of this technique in 2013. One citation was a veterinary case report and was excluded; three were review articles; three were case reports, one of which was for treatment of giant cell tumor of bone. The remaining citations are summarized below.

All 7 studies were retrospective. All 7 studies documented percutaneous injection of doxycycline into aneurysmal bone cyst. Of these 7, one had a comparison cohort; the remaining 6 were case series. 3

studies specifically addressed the spine. The total number of cases treated with doxycycline in each series ranged from 7-21. The cumulative total number of doxycycline injections ranged from 1-15. The rate of recurrence varied between 0% and 14%. In the comparison study, 14 patients were treated with doxycycline alongside 11 patients who received surgery. There were no recurrences in the group treated with doxycycline compared to 2 in the group treated with surgery; however, this difference was not statistically significant ($p = 0.14$).

What is the evidence against?

The followup for these studies is varied and is as short as 6 months. While data is promising for decreased local recurrence rates, for the patients whose followup is less than 24 months, it is difficult to assess. Furthermore, the total number of cases involved is fewer than 25.

There are 2 reported incidences of skin necrosis from the injection. In addition, most patients are treated with a median of 3-5 treatments. For pediatric patients, this is likely 3-5 sedations.

Future directions

At this time, there is one case-control study and no prospective cohort studies. The evidence for doxycycline is promising but the total data is limited and even more limited in comparison to surgery. Furthermore, it is unclear how many treatments are needed for adequate control of disease. It would be nice to see a multicenter trial to determine safety and efficacy of doxycycline injections for aneurysmal bone cysts.

Citations:

Arleo TL, Hawkins CM, Fabregas JA, Gill AE, Percutaneous image-guided treatment of aneurysmal bone cysts: is there a superior treatment option? *Pediatr Radiol* [2022 Jul;52\(8\):1539-1549](#) PMID: 35325265 DOI: [10.1007/s00247-022-05326-6](#)

- 21 patients
- Mean age 13.5 (8-18)
- mean 3 treatments (1-6)
- Complications 7.7%
- mean 24 mo followup (4-68)
- 10% recurrence rate

Desai SB, O'Brien C, Shaikh R, Hedequist D, Proctor M, Orbach DB, Padua H, Multidisciplinary management of spinal aneurysmal bone cysts: A single-center experience. *Interv Neuroradiol* [2019 Oct;25\(5\):564-569](#) PMID: 31088242 DOI: [10.1177/1591019919848130](#)

- 7 patients
- Mean age 15 years (8-18)

- Mean 3 treatments (2-15)
- No complications within 30 days of intervention, 1 death 2 years post treatment secondary to spinal column collapse and progression of disease
- Mean 29 month followup (9-58)
- 2 patients underwent surgery following intervention secondary to progressive pain including 1 patient with progression of disease

Liu X, Han SB, Si G, Shao MY, Chang MW, Liang J, Wei F, Wu FL, Liu XG, Zhong JL, Percutaneous albumin/doxycycline injection versus open surgery for aneurysmal bone cysts in the mobile spine. *Eur Spine J* 2019 Jun;28(6):1529-1536 PMID: 30470879 DOI: [10.1007/s00586-018-5836-1](https://doi.org/10.1007/s00586-018-5836-1)

- 25 patients: 14 doxycycline injection, 11 surgery
- Mean age 25 years (14-26) doxy, mean age 18 years (6-36) surgery (p=0.19)
- Mean 3 treatments (2-4)
- No complications in doxy group, 3 complications in surgery group
- Mean 31 mo followup (24-50) doxy, mean 66 mo followup (51-96) surgery
- 0% recurrence doxy, 18.2% recurrence surgery, p=0.14

Shiels, WE, Beebe, AC, Mayerson JL, Percutaneous Doxycycline Treatment of Juxtaphyseal Aneurysmal Bone Cysts. *J Pediatr Orthop* 2016 Mar;36(2):205-12. PMID: 25985367 DOI: [10.1097/BPO.0000000000000413](https://doi.org/10.1097/BPO.0000000000000413)

- 16 patients
- Mean age 7.1 years (2-15)
- Total 102 treatments (mean 6, 2-14 per patient)
- 1 case focal skin necrosis (6.25%)
- mean 39 month followup (18-67)
- 6% recurrence rate

Shiels, WE, Mayerson JL, Percutaneous doxycycline treatment of aneurysmal bone cysts with low recurrence rate: a preliminary report. *Clin Orthop Relat Res* 2013 Aug;471(8):2675-83 PMID: 23670673 DOI: [10.1007/s11999-013-3043-2](https://doi.org/10.1007/s11999-013-3043-2)

- 20 patients
- Mean age 10 years (3-18)
- Mean 5 treatments (2-14)
- 1 case focal skin necrosis (5% complication)
- Mean 38 mo followup (24-63)
- 5% recurrence rate

Wong MN, Braswell LE, Murakami JW, Doxycycline sclerotherapy of cervical spine aneurysmal bone cysts: single-institution 13-year experience. *Pediatr Radiol* 2022 Jul;52(8):1528-1538 PMID: 35305122 DOI: [10.1007/s00247-022-05328-4](https://doi.org/10.1007/s00247-022-05328-4)

- 14 patients
- Mean age 14 years (3-24)

- Median 4 treatments (2-10)
- 1 complication (PICA spasm w cerebellar infarction)
- Mean 35 mo followup (6-71)
- 14% recurrence

Woon JT, Hood D, Graydon A, Flint M, Doyle AJ, Aneurysmal bone cyst treated with percutaneous doxycycline: is a single treatment sufficient? *Skeletal Radiol* 2019 May;48(5):765-771 PMID: 30809704 DOI: 10.1007/s00256-019-03188-y

- 7 patients
- Mean age 12 years (8-18)
- 4 patients - 1 treatment, 3 patients - 2 treatments
- No complications from doxycycline, 1 patient w AVN femoral head, 1 patient w LLD.
- Mean 25 mo followup (14-60)
- 14% recurrence