

CASE REPORT

Intraosseous epidermal cyst of the great toe that was difficult to distinguish from chronic osteomyelitis: A case report and literature review

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Abstract

Obtaining a correct intraosseous epidermal cyst diagnosis is difficult due to the extreme rarity of this cyst. Further, the clinical manifestations and radiographic findings are very similar to those of a malignancy or infection. Early histopathological analysis is required for accurate diagnosis and for avoiding unnecessary antibiotic administration and amputation.

KEYWORDS

diabetic foot, great toe, infection, interosseous epidermal cyst

1 | INTRODUCTION

Epidermal cyst (EpC), also called epidermoid inclusion cyst, epithelial cyst, sebaceous cyst, squamous cyst, or atheroma, does not require any treatment when it is asymptomatic, but may need surgically resection when it becomes inflamed and symptomatic. The mechanism of inflammation and the treatment of the inflamed EpCs by the administration of antibiotics remain controversial. Earlier, infection was considered as the underlying cause of inflammation. Since there were no apparent differences in the microbiological milieu of inflamed and uninfamed EpCs, inflammation was speculated to be caused by the immune response rather than the infection,¹ and intralesional steroids were recommended for the

treatment.² However, there is a need to develop alternatives to antibiotics for this kind of noninfectious condition to reduce the complications associated with antibiotic use.³

Intraosseous EpC (IEpC) is a rare form of EpC that has been reported primarily in middle-aged men, after trauma or surgery, and within the phalanges of the fingers.⁴ A congenital etiology with intraosseous inclusion of the embryonic epithelial tissue has been proposed, although post-traumatic or iatrogenic events remain the most prevalent hypotheses.⁵ The diagnosis of IEpC can be clinically and radiologically challenging. An accurate diagnosis of IEpC is rarely made before operation by radiologists or surgeons primarily because of the failure to recognize this entity. In addition, its clinical manifestations and radiographic findings are similar to those of the malignant tumors or infection, and histopathological

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examination is the only way to make a definitive diagnosis.⁶ Therefore, it is important to consider this lesion in the differential diagnosis to avoid unnecessary antibiotic administration and digital amputation.

Here, we report a unique case of IEpC of the great toe, which was treated as a chronic osteomyelitis with long-term antibiotics, unfortunately leading to mass excision of the distal phalanx.

2 | CASE PRESENTATION

An 82-year-old woman consulted a dermatologist in our hospital complaining of recently aggravated inflammation of her right great toe. She underwent right hallux valgus surgery with a second metatarsal shortening osteotomy at her local hospital several years earlier, but she did not have any history of overt trauma or surgery on her right great toe. She had been taking mizoribine and prednisolone for systemic lupus erythematosus and lupus nephritis for the past 20 years. She also had diabetes mellitus.

Her right great toe was moderately enlarged with tenderness and redness along with pustules on the dorsal interphalangeal joint. The administration of cefcapene pivoxil was started. Over the subsequent 6 months, levofloxacin, faropenem, amoxicillin/clavulanate, minocycline, meropenem, and metronidazole were administered. Despite wound irrigation and incisional drainage, these treatments only resulted in recurrence after temporal improvement (Figure 1). Since wound healing problem of the great toe was not completely cured by these treatments, she was referred to our department for further assessment.

An almost closed ulcer and brown pigmentation without heat or swelling were observed in the posterior nail fold (Figure 2). During the course of treatment in the dermatology department, she did not experience fever, and her white blood cell (WBC) count and C-reactive protein (CRP) levels

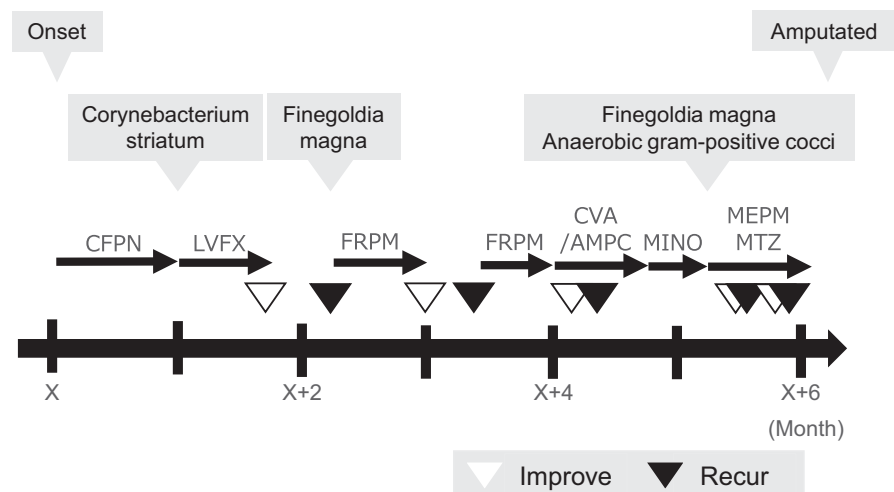
were normal. *Corynebacterium striatum*, *Finegoldia magna*, and anaerobic gram-positive bacillus were detected in the wound culture from the skin lesion on her right great toe. Both X-ray (Figure 3A) and computed tomography (CT) scan (Figure 3B) revealed an osteolytic lesion, which caused a pathological fracture, at the dorsal aspect of the distal phalanx of the right great toe. Except for soft tissue swelling, no apparent abscess was detected by the CT scan (Figure 3C). Based on these clinical findings and the course of treatment up to that point, it seemed most likely to be a case of diabetic foot infection with chronic osteomyelitis.

After obtaining informed consent, we performed the surgery with the intention of deciding whether to amputate her distal phalanx or not based on the intraoperative findings. Unexpectedly, during the irrigation and debridement, dirty creamy-brown material gushed out through lateral nail fold which was sent for cultures and histopathological examination. Then, the nail plate was easily extracted, and a fistulous connection from nail root to within the distal phalanx was found. Unfortunately, due to our preconceived notion, the tissue was not submitted for frozen section study and the great toe was ultimately amputated. The histopathological analysis revealed that the surgical specimen had the cyst wall lined with squamous epithelium with keratin debris (Figure 4A). There were no abnormal or cancerous cells, indicative of a benign tumor. There were gram-positive cocci outside the cyst, but not inside the cyst, indicating a noninfectious disease (Figure 4B). A diagnosis of IEpC was made based on these findings. After the operation, the pain had improved and the surgical wound had healed without infection during the 3 months' follow-up.

3 | DISCUSSION

Herein, we present a case where an 82-year-old woman suffered from IEpC. However, due to its difficult diagnosis and

FIGURE 1 Time course outlining the antibiotics treatment and culture results. Antibiotics treatments for 6 months resulted in the recurrence of the patient's symptoms after temporary improvement, and her phalanx was finally amputated. CFPN, Cefcapene pivoxil; CVA/AMPC, amoxicillin/clavulanate; FRPM, faropenem; Improve, temporary improvement; LVFX, levofloxacin; MEPM, meropenem; MINO, minocycline; MTZ, metronidazole; Recur, recurrence



lack of knowledge, the patient was kept on an unnecessary antibiotic treatment for 6 months. Early histopathological findings of such lesions may lead to early cure and avoid inappropriate treatment.



FIGURE 2 The right great toe of the patient. An almost closed ulcer and brown pigmentation with minimal redness and mild swelling are observed in the posterior nail fold

EpCs of the soft tissues were first reported by Masse in 1885⁷ and are commonly considered as the benign soft tissue tumors just underneath the skin. IEpC was initially documented in the digits by Harris in 1930.⁸ The lesion is mostly reported in adults, especially manual workers whose job involves potential traumatic injuries. Men are more frequently affected than women, and patients are mostly in their fourth or fifth decade of life.⁹ The distal phalanges of the hands are most affected, but rarely, the digits of the feet may be affected. The overall incidence or prevalence of IEpCs is unknown.

The etiology of IEpC remains enigmatic. One possible explanation is that the trauma may lead to the implantation of epithelial cells into the subcutaneous tissues. Surviving cells would subsequently proliferate and produce keratin.¹⁰ Another hypothesis is that IEpC may occur due to the proliferation of intraosseous inclusions of epithelial elements during embryogenesis.¹¹ The third iatrogenic possibility is that it may be related to a previous surgical procedure.¹² In the present case, there was no history of trauma or surgery that involved the patient's right distal phalanx of the great toe. However, the great toe may have been repeatedly rubbed by the second toe even the surgical correction of hallux valgus. Furthermore, given that she was taking steroids and she had diabetes, she may have sustained injury to her foot without her realizing it.

The diagnosis of IEpC can be difficult due to its extreme rarity, its clinical presentation mimicking that of a malignancy or infection, and the lack of diagnostic methods other than histopathology.⁶ In this case, the correct diagnosis of IEpC was made after 6-month antibiotics administration and

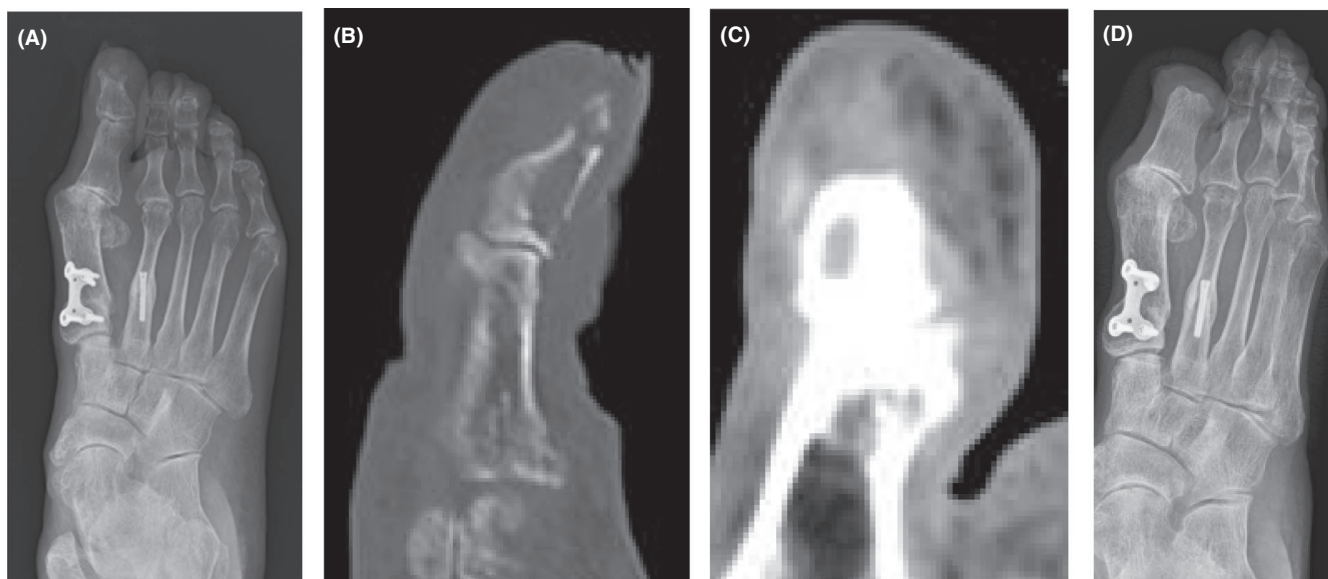
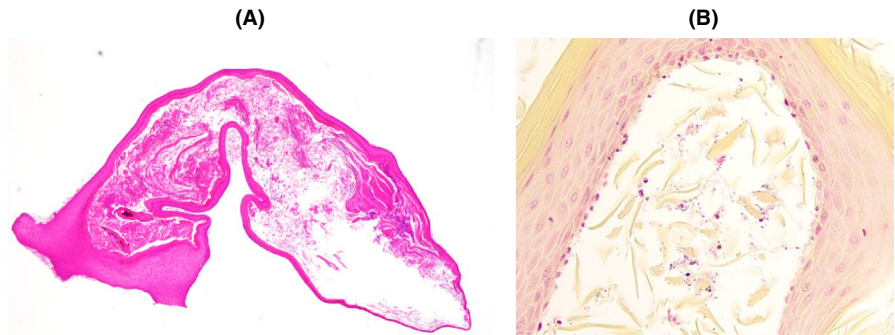


FIGURE 3 Imaging findings of the right great toe. Pre-operative (A) X-ray and (B) computed tomography (CT) scan revealed cortical erosion and bone destruction, and a pathological fracture in the distal phalanx. (C) No abscess is detected by the CT scan. (D) Postoperative X-ray shows no progression of bone erosion

FIGURE 4 Histopathological findings of the surgical specimen (Hematoxylin and Eosin staining (A) and Gram staining (B)). The cyst wall is lined with an epidermis-like tissue and the cyst contains keratin (A). No abnormal or cancerous cells are found. Bacteria are not detected inside the cyst (B)



surgery. WBC count and CRP levels were not elevated, and antibiotics treatment was not effective for a long time. Given the lack of fever and normal values for WBC and CRP, we should have explored the possibility that it was not an infection. However, spontaneous drainage and antibiotic treatment seemed to keep the response of WBC and CRP normal, making it difficult for us to make accurate decisions.

The typical radiologic presentation of IEPC is a well-defined, expanding radiolucent intraosseous lesion, often with an associated soft tissue swelling.¹³ IEPCs in the digits are commonly located at the distal aspect of the distal phalanx.⁵ In the present case, however, the lesion was located in the entire distal phalanx where severe bone destruction was observed (Figure 3A,B). These radiographic and CT findings presented the features similar to that of a diabetic foot infection with concomitant osteomyelitis. Unfortunately, we were unable to reach a definitive diagnosis of an IEPC until the histopathological confirmation, partly due to our lack of knowledge on IEPCs. The histopathological analysis revealed the gram-positive cocci outside the cyst. In cases of chronic osteomyelitis, epithelium growing from a skin fistula may

also result in nonmalignant malpighian epithelium growing in the bone.¹⁴ In addition, osteomyelitis has been reported to develop with IEPC in the literature.^{15,16} In the present case, the histopathological finding of gram-positive cocci outside the cyst alone might not be a sufficient evidence of a concomitant infection with IEPC.

It is challenging to decide not to prescribe antibiotics for this case despite an inflammatory condition,^{3,17} because most immune responses suggest the involvement of infection. Furthermore, it is unclear in which cases a biopsy should be considered. Regarding the inflamed EpC, the efficiency of antibiotics or intralesional triamcinolone has not been evaluated,¹⁷ leading to the increased use of antibiotics. In our case, there was a slight possibility that the patient had a concomitant infection with IEPC, and antibiotics had some positive influence. It was inevitable to prescribe antibiotics at the initial stage. However, in the present case, antibiotics alone did not cure the patient completely. An earlier biopsy followed by immediate curettage would have been the first option.

Previous reports have concluded that the history, biopsy, and intraoperative pathology are useful for the diagnosis of

TABLE 1 Previous cases of intraosseous epidermal cyst in toes

Age/sex	Causes	Diagnosis	Surgery	Antibiotics	Reference
41/M	Injury	Postoperation	Disarticulation	–	19
37/M	Injury	Postoperation	Amputation	–	5
54/M	Injury	Postoperation	Curettage/Disarticulation	–	14
33/F	Ingrowing nail/	Postoperation	Curettage	–	20
61/F	Surgery				
54/M	Injury	During surgery	Curettage	–	13
48/F	Operation	During surgery	Curettage	–	21
78/M	—	Postoperation	Amputation	+	12
71/F	—	Postoperation	Amputation	+	15
54/M	Injury	Biopsy before operation	Curettage	Postoperation	22
63/F	Operation	Biopsy before operation	Curettage/Amputation	–	18
57/M	After wart debridement	Postoperation	Curettage	Postoperation	16

IEpC^{5,12-16,18-22} (Table 1). A study reported that the fine needle aspiration of IEpC showed predominantly anucleated squames and few nucleated squamous cells, while that of the infected bones showed predominantly neutrophils, few macrophages, anucleated squames, nucleated squamous cells, and occasional multinucleated giant cells.²² However, it should be noted that, when conducting biopsies, the specimen must be wide and deep enough to show the characteristic epithelium.¹⁴ Furthermore, whether biopsies suggest malignant or benign tumors, the intraoperative pathology need to be assessed to confirm the diagnosis. MRI may also be useful for the diagnosis of IEpC. MRI is indicated as the best modality for the evaluation of soft tissue and bone marrow changes associated with the diabetic foot,²³ and MRI of the IEpC showed a low signal lesion on T1-WI, a high signal on T2-WI, with no gadolinium enhancement.⁴ However, given the rarity of IEpC and the lack of research on its imaging, MRI alone does not provide enough information for its accurate diagnosis²³ and further studies are warranted. Typically, IEpC develops in middle-aged individuals, often men, in their 40s or 50s.⁴ In this case, the patient was 82-year-old woman with no history of trauma or surgery. She developed ulcer due to poor wound healing, despite 6 months of antibiotic administration, partly due to diabetes mellitus. In this case of advanced foot problem, amputation would have been inevitable even if correctly diagnosed by intraoperative pathology. However, in the present case, earlier diagnosis through biopsy would have avoided unnecessary antibiotic treatment and amputation and would have led to an earlier cure.

4 | CONCLUSIONS

Intraosseous EpC is rarely diagnosed as it mimics the findings of malignancy and infection. It is important to perform a biopsy if the clinical findings are somewhat atypical of infection, and an accurate early diagnosis with histopathological analysis may avoid unnecessary administration of antibiotics and surgery. It should also be noted that IEpC can develop in elderly women with diabetes even in the absence of a history of overt trauma. Further studies exploring the diagnosis, treatment, and etiology of IEpC are warranted.

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CONFLICT OF INTEREST

The authors have declared that no conflict of interest exists.

AUTHOR CONTRIBUTION

All authors: made substantial contribution to the preparation of this manuscript. Hikaru Sugimoto and Kensuke Yasue:

wrote the preliminary manuscript and contributed equally to this work. Shoichiro Takakuma, Wako Yumura, and Tomio Arai: provided the histopathological image. Misako Kato, Kentaro Hayakawa, and Fumiaki Tokimura: completed the literature search and found the relevant articles for the discussion. Tsuyoshi Miyazaki: supervised the work.

ETHICAL APPROVAL

Written consent was taken from the patient for the publication of the case report and the images.

DATA AVAILABILITY STATEMENT

Data sharing was not applicable to this article as no datasets were generated or analyzed during the current study.

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