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Case report

Ultrasound evaluation of inflammation in patients with chronic recurrent multifocal osteomyelitis involving the mandible: report of three cases ☆,☆☆

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ABSTRACT

Chronic recurrent multifocal osteomyelitis (CRMO) is aseptic and can be diagnosed by excluding other diseases, such as bacterial osteomyelitis, scurvy, metabolic disorders, and malignant diseases; therefore, bone biopsy is usually performed to confirm the diagnosis. To prevent misdiagnosis, the appropriate timing and location for biopsy should be determined from an active phase of inflammation. We presented 3 cases of CRMO involving the mandible: Case 1: A 2-year-old girl diagnosed with CRMO in the chronic phase. A sonogram showed a slightly low echoic area adjacent to the bone cortex. Pathological examination revealed a slight accumulation of leukocytes and plasma cells, as well as predominant fibrous stroma. Case 2: A 9-year-old girl diagnosed with CRMO with massive new osteoid formation. A sonogram showed a massive inhomogeneous low echoic area adjacent to the bone cortex. Pathological examination revealed massive osteoid formation and scattered inflammatory cells infiltration. Case 3: A 3-year-old girl diagnosed with CRMO in the active phase. A sonogram showed a massive hypoechoic area adjacent to the bone cortex and hyperechogenicity associated with a muscular and subcutaneous edema. Pathological examination revealed massive bone destruction and neutrophils infiltration within damaged osteoid. Ultrasound was able to visualize the degree of inflammation in the mandible corresponding to that of the surrounding soft tissue in all 3 cases. Therefore, ultrasound would be useful in determining the appropriate timing and location for bone biopsy.

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Introduction

Chronic recurrent multifocal osteomyelitis (CRMO) is an autoinflammatory disorder and is referred to as chronic nonbacterial osteomyelitis or chronic aseptic osteomyelitis [1]. The diagnosis of CRMO is usually confirmed by bone biopsy after excluding other diseases, such as bacterial osteomyelitis, scurvy, metabolic disorders, and malignant diseases [1–3]. Imaging studies, such as radiography, computed tomography, magnetic resonance imaging (MRI), and bone scintigraphy, are useful for diagnosing CRMO and providing a roadmap for possible biopsy [1,2,4–6].

Until now, although there have been few reports focusing on imaging modalities for diagnosing CRMO, ultrasound has not been used for this purpose [1, 2,4–9]. Ultrasound is a useful imaging modality that offers high resolution and zero radiation exposure. In addition, previous studies using MRI have mentioned that the region of CRMO extends into the surrounding soft tissues [2, 3]; therefore, these findings may be detected by using ultrasound.

Herein, we present 3 cases of CRMO involving the mandible. Ultrasound demonstrated different findings around the mandible, corresponding to the pathological changes in the mandible.

Case report

This case report was approved by our institution's ethics committee, and informed consent was waived.

Case 1

A 2-year-old girl presented with neck and cheek swelling approximately 4 months before imaging. Although antibiotic therapy was administered, the symptoms persisted. CRMO was suspected, and further examination was performed. Imaging examination, including radiography, bone scintigraphy, MRI, and ultrasound, was performed. Although hyperostosis was not detected on radiography (Fig. 1A), bone scintigraphy showed increased uptake in the mandible, and there was no abnormal uptake in other locations (Fig. 1B). T2-weighted fat-suppression images showed high signal intensity in the bone marrow of the mandible and a slight periosteal reaction (Figs. 1C and D). An axial sonogram of the mandibular body showed a slightly low echoic area adjacent to the cortex (Figs. 1E and F). The mandible was selected as the biopsy location because it was the only location with abnormal findings in these examinations. A mandible biopsy was performed; pathological examination revealed a slight accumulation of leukocytes and plasma cells, as well as predominant fibrous stroma (Figs. 1G and H). Cultures for bacteria and malignant cells were negative. CRMO in the chronic phase, without an acute phase reaction, was diagnosed.

Case 2

A 9-year-old girl presented with fever and cervical pain, persisting for 3 months. Mandibular pain and swelling were also observed. CRMO was suspected, and further examination was performed. Hyperostosis was detected on radiography (Fig. 2A), and bone scintigraphy showed increased uptake in the mandible and right clavicle (Fig. 2B). Fat-suppressed T2-weighted images showed high signal intensity in the bone marrow of the mandible, thickening of the mandible, and a slightly high signal intensity adjacent to the mandible (Figs. 2C and D). An axial sonogram of the mandibular body showed a massive inhomogeneous low echoic area adjacent to the cortex (Figs. 2E and F). The selection of the mandible as the biopsy location was based on these image findings, and a mandibular biopsy was performed. Pathological examination revealed massive osteoid formation and scattered inflammatory cells infiltration (Figs. 2G and H). Cultures for bacteria and malignant cells were also negative for this case. CRMO with predominantly new osteoid formation was diagnosed.

Case 3

A 3-year-old girl presented with fever, persisting for approximately 8 months. Although antibiotic therapy was administered, the symptoms persisted. Cheek swelling was also observed. Imaging examination, including radiography, bone scintigraphy, MRI, and ultrasound, was performed. Hyperostosis was not detected on radiography (Fig. 3A), and bone scintigraphy showed increased uptake in the mandible, ribs, and maxilla (Fig. 3B). Fat-suppressed T2-weighted images showed high signal intensity in the bone marrow of the mandible and adjacent area (Figs. 3C and D). A mandibular sonogram showed a massive hypoechoic area adjacent to the cortex and hyperechogenicity associated with a muscular and subcutaneous edema (Figs. 3E and F). A mandibular biopsy was performed based on these examinations. Massive bone destruction was evident, and neutrophils infiltrated the damaged osteoid (Figs. 3G and H). Cultures for bacteria and malignant cells were negative. CRMO in the active phase was diagnosed.

Discussion

Here, we present 3 cases of CRMO of the mandible. The degree of inflammation in the bone corresponded to that of the surrounding soft tissue. This case report shows that ultrasound can be used to noninvasively visualize inflammatory changes in the mandible. It is important to accurately determine the timing and target location for biopsy for diagnosing CRMO. Bone scintigraphy and whole-body MRI are useful for detecting bone marrow edema or inflammation; however, it might be difficult to determine where the inflammatory change is most severe among these lesions. In the present case, ultrasound could predict the severity of inflammation by identifying inflammatory changes around the affected bone. Such high-resolution imaging of inflammation could prove beneficial to clinicians seeking to ascertain the appropriate timing and location for biopsy.

The degree of inflammatory change in CRMO is different in each location, and new lesions can appear in previously resolved sites or in sites with various phases of healing [7]. Although bone biopsy is usually performed to diagnose CRMO,

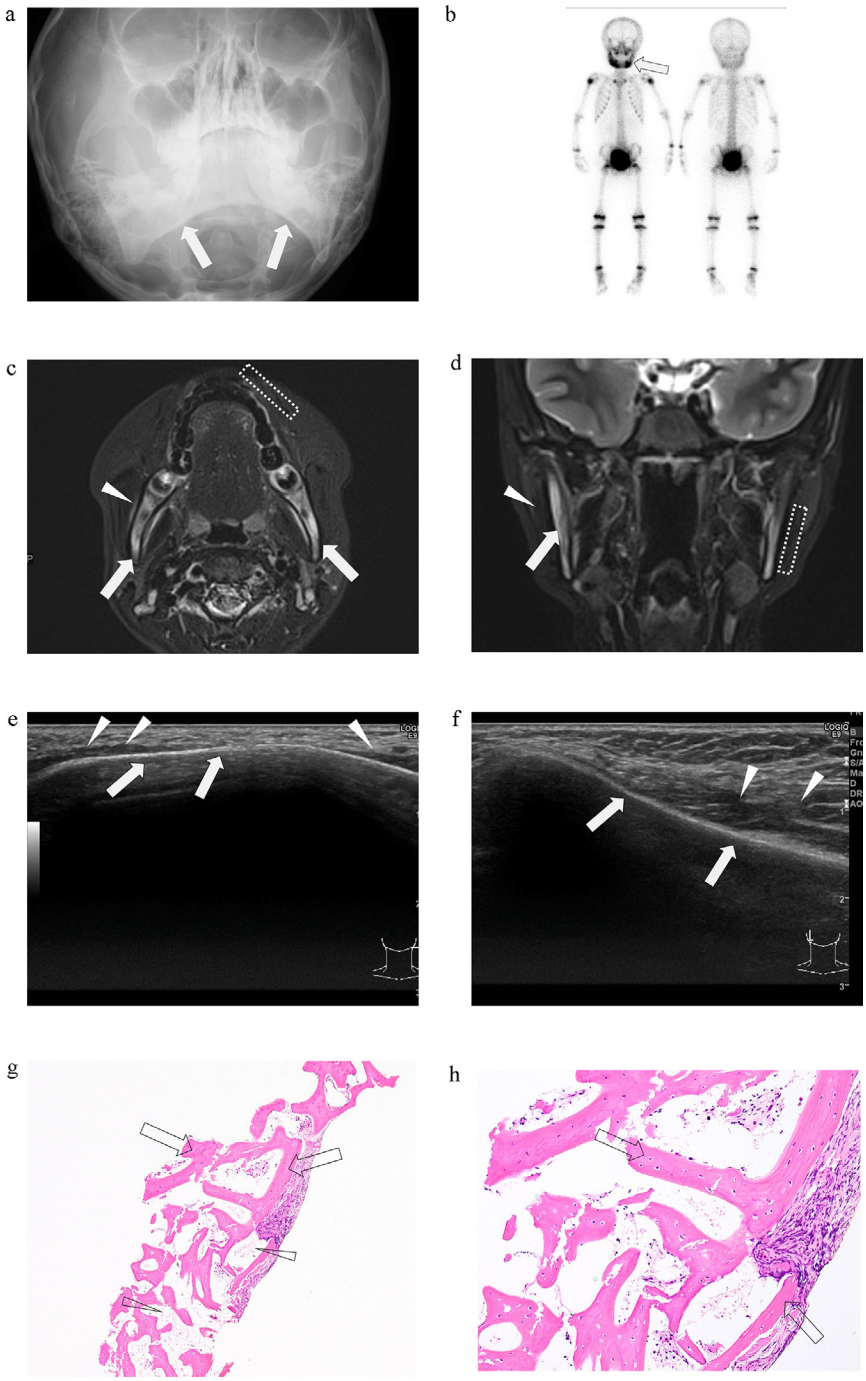

Fig. 1 – Case 1: A 2-year-old girl diagnosed with CRMO. (A) Radiograph of the mandible. Hyperostosis is not detected (arrows). (B) Bone scintigraphy showing increased uptake in the mandible (arrows), and abnormal uptake is not detected in other locations. (C) Axial fat-suppressed T2-weighted image. The bone marrow in the mandibular body shows high signal intensity (arrows). A slightly high signal intensity is seen adjacent to the mandible (arrowheads). The dotted square represents transducer placement, as seen in Fig. 2E. (D) Coronal fat-suppressed T2-weighted image. The ramus of the mandible (arrows) shows a high signal intensity. The masseter muscle shows low signal intensity (arrowheads). The dotted square represents transducer placement, as seen in Fig. 2F. (E) Axial sonogram of the mandibular body showing a slightly hypoechogenic area (arrowheads) along the surface of the mandibular cortex (arrows). (F) Sagittal sonogram of the right ramus of the mandible. The cortex shows a hyperechogenic line (arrows). The adjacent masseter muscle has normal echogenicity, and fluid effusion is not detected (arrowheads). (G) Pathological specimen showing few lymphocytes and plasma cells infiltration and a predominance of fibrous stroma (arrowheads) within the osteoid (arrows). The phase of inflammation is classified as a chronic phase. (H) Pathological specimen showing lymphocytes (black arrow) and osteoblasts (arrowheads) surrounding the osteoid (open arrow), and a massive new osteoid formation is absent.

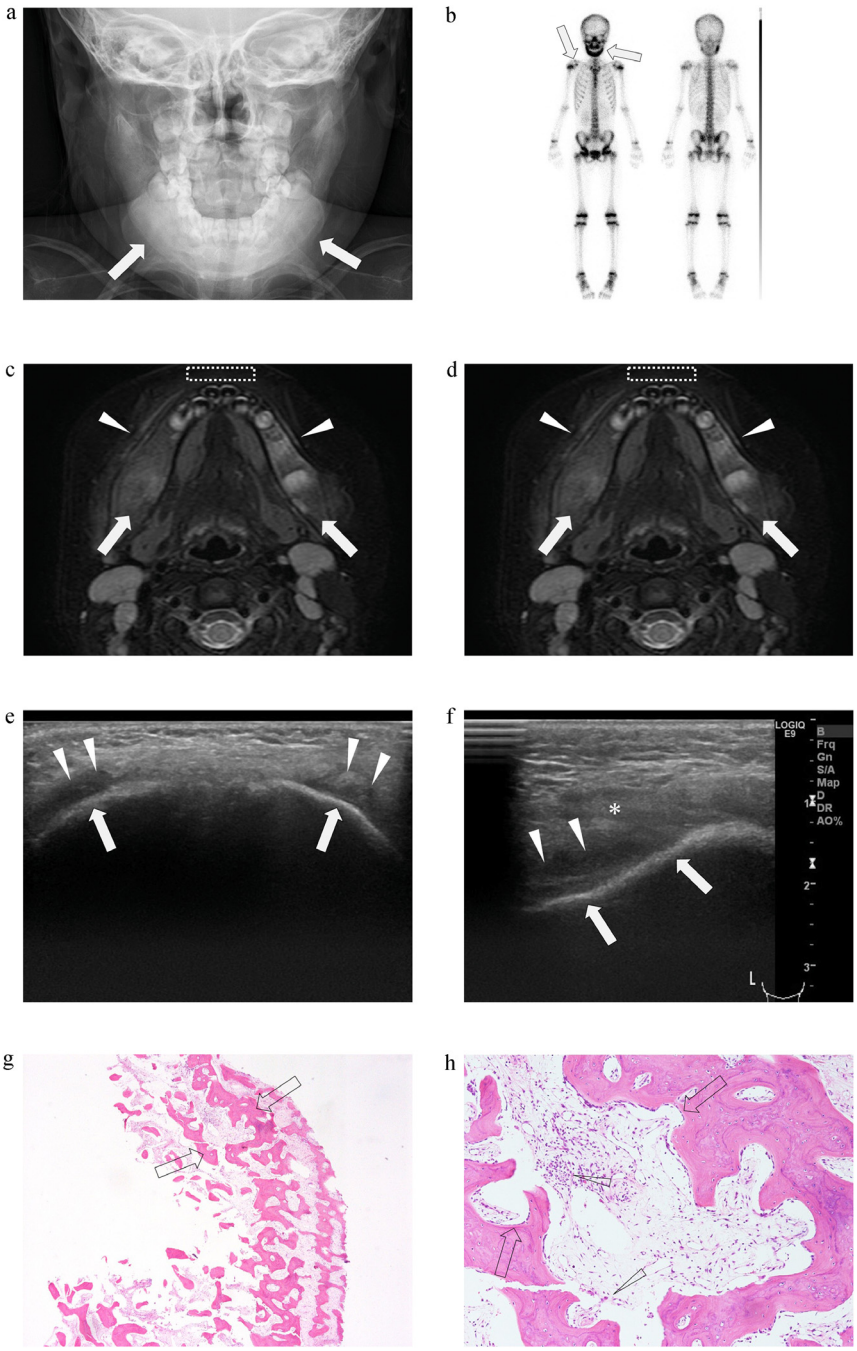

Fig. 2 – Case 2: A 9-year-old girl diagnosed with CRMO. (A) Hyperostosis is detected on the radiograph (arrows). (B) Bone scintigraphy showing increased uptake in the mandible and right clavicle (arrows). (C) Axial fat-suppressed T2-weighted image. The mandibular body shows high signal intensity in the bone marrow of the mandible and massive thickening of the mandible (arrows). A slightly high signal intensity is observed adjacent to the mandible (arrowheads). The dotted square represents transducer placement, as seen in Fig. 3E. (D) Coronal fat-suppressed T2-weighted image. The ramus of the mandible (arrows) shows a high signal intensity and swelling. The masseter muscle shows low signal intensity (arrowheads). The dotted square represents transducer placement, as seen in Fig. 3F. (E) Axial sonogram of the body of the mandible showing thickening of mixed hyper- and hypoechogenic areas (arrowheads) along the surface of the mandibular cortex (arrows). (F) Sagittal sonogram of the right ramus of the mandible. The cortex shows a hyperechogenic line (arrows). The adjacent masseter muscle is hyperechogenic, associated with muscle edema (asterisk) and massive homogenous echoic area due to periosteal reaction (arrowheads). (G) Pathological specimen showing massive new osteoid formation (arrows); leukocytes and fibrous stroma can be visualized within the osteoid. (H) Pathological specimen showing massive osteoblast and osteoid formation (arrow). Fibrous stroma and scattered inflammatory cells (arrowheads) are visualized between these osteoid formations.

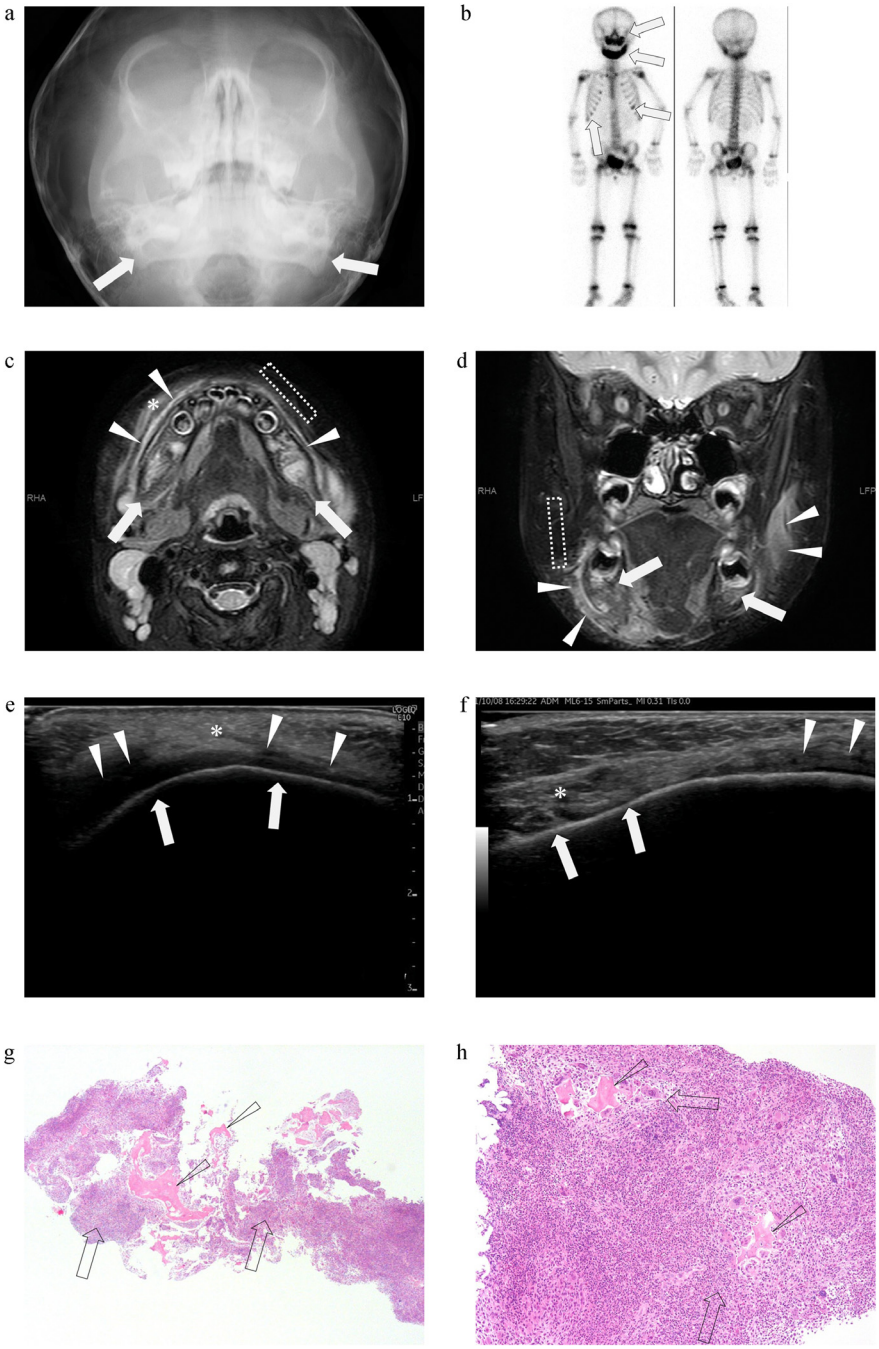

Fig. 3 – Case 3: A 3-year-old girl diagnosed with CRMO. (A) Hyperostosis is not detected on the radiograph (arrows). (B) Bone scintigraphy showing increased uptake in mandible, maxilla, and ribs (arrows). (C) Axial fat-suppressed T2-weighted image. The mandibular body shows high signal intensity in the bone marrow of the mandible (arrows). High signal intensity is revealed along the mandibular cortex (arrowheads). Subcutaneous tissue also shows high signal intensity (asterisk). The dotted square represents transducer placement, as seen in Fig 4E. (D) Coronal fat-suppressed T2-weighted image. The ramus of the mandible (arrows) shows high signal intensity. The masseter muscle shows high signal intensity (arrowheads). The dotted square represents transducer placement, as seen in Fig 4F. (E) Axial sonogram of the body of the mandible showing thickening of the hypoechogenic area (arrowheads) along the surface of the mandibular cortex (arrows). In addition, hyperechogenic subcutaneous fat tissue is evident (asterisk). (F) Sagittal sonogram of the right ramus of the mandible. The cortex shows hyperechogenic line (arrows). The adjacent masseter muscle shows hyperechogenicity associated with muscle edema (asterisk) and a massive hypoechoic area due to periosteal reaction (arrowheads). (G) Pathological specimen showing massive bone destruction (arrows), and neutrophils and multinucleated giant cells (arrowheads) are visualized within the osteoid. (H) Pathological specimen showing massive neutrophil infiltration (arrowheads) within the osteoid (arrows). The osteoid appears fragmented.

osteosarcoma and chronic bacterial osteomyelitis are important differential diagnoses due to the presence of osteoblasts or the possibility of negative culture from specimens [3, 8, 10–16]. Therefore, the appropriate timing and location for biopsy can be ascertained via a phase of active inflammation, not chronic. In our report, all 3 cases had uptake on bone scintigraphy; however, this imaging modality was unable to visualize differences in the degree of inflammation. On the other hand, ultrasound can show an inhomogeneous low echoic area adjacent to the mandible, indicating the degree of inflammation. In case 1, ultrasound demonstrated a slightly low echoic area adjacent to the cortex, and pathological findings showed a chronic phase of CRMO. In case 2, a large inhomogeneous low echoic area adjacent to the cortex was observed on ultrasound, and pathological findings confirmed the presence of a massive new osteoid formation. In case 3, massive fluid effusion and high echogenicity adjacent to the mandible were evident, and bone biopsy showed the active phase of CRMO. Therefore, ultrasound could be used to predict the activity of CRMO in each location, providing relevant information about the appropriate timing and location for biopsy.

In previous reports, a low echoic or heterogeneous echogenic area along the cortex on ultrasound has been shown to indicate the presence of osteomyelitis [17–20]. These findings represent periosteal abscess or periosteal reactions [17,18]. Notably, these findings were also observed in the current cases. In addition, destruction of the cortex is indicative of both CRMO and bacterial osteomyelitis [4,5,18]. Therefore, ultrasound cannot differentiate CRMO from bacterial osteomyelitis.

Despite the utility of ultrasound, there are some limitations to its efficacy in this case report. First, this case report included only 3 pediatric patients with inflammation of the mandible. Therefore, future studies involving more patients and various bone locations are required to confirm our preliminary findings. Second, the quality of ultrasound was dependent on the examiners' experience. Although some reports have focused on the use of ultrasound in evaluating bone, this technique for imaging bone may not be familiar to all sonographers.

In conclusion, this case report demonstrates that ultrasound could help predict the severity of inflammation in the bone marrow by showing inflammatory changes around the affected bone. Ultrasound is useful in determining the appropriate timing and location for bone biopsy and, ultimately, assisting in CRMO diagnosis.

Informed consent

Approval from the Institutional Review Board was obtained, and in keeping with the policies for a retrospective review, informed consent was not required.

REFERENCES

[1] Andronikou S, Kraft JK, Offiah AC, Jones J, Douis H, Thyagarajan M, et al. Whole-body MRI in the diagnosis of paediatric CNO/CRMO. Rheumatology 2020;59(10):2671–80 Oxford, England.
[2] Falip C, Alison M, Boutry N, Job-Deslandre C, Cotten A, Azoulay R, et al. Chronic recurrent multifocal osteomyelitis (CRMO): a longitudinal case series review. Pediatr Radiol 2013;43(3):355–75.
[3] Gaal A, Basiaga ML, Zhao Y, Egbert M. Pediatric chronic nonbacterial osteomyelitis of the mandible: Seattle Children's hospital 22-patient experience. Pediatr Rheumatol Online J 2020;18(1):4.
[4] Himuro H, Kurata S, Nagata S, Sumi A, Tsubaki F, Matsuda A, et al. Imaging features in patients with SAPHO/CRMO: a pictorial review. Japanese J Radiol 2020;38(7):622–9.
[5] Khanna G, Sato TS, Ferguson P. Imaging of chronic recurrent multifocal osteomyelitis. Radiographics. 2009;29(4):1159–77.
[6] Tiwari P, Bera RN, Kanojia S, Chauhan N, Hirani MS. Assessing the optimal imaging modality in the diagnosis of jaw osteomyelitis. A meta-analysis. Br J Oral Maxillofac Surg 2021;59(9):982–92.
[7] Mandell GA, Contreras SJ, Conard K, Harcke HT, Maas KW. Bone scintigraphy in the detection of chronic recurrent multifocal osteomyelitis. J Nucl Med 1998;39(10):1778–83.
[8] Taddio A, Ferrara G, Insalaco A, Pardeo M, Gregori M, Finetti M, et al. Dealing with chronic non-bacterial osteomyelitis: a practical approach. Pediatr Rheumatol Online J 2017;15(1):87.
[9] Nuruzzaman F, Zhao Y, Ferguson PJ. Chronic nonbacterial osteomyelitis: insights into pathogenesis, assessment, and treatment. Rheum Dis Clin North Am 2021;47(4):691–705.
[10] Bracamonte JD, Roberts CC. Chronic recurrent multifocal osteomyelitis mimicking osteosarcoma. Radiol Case Rep 2006;1(2):42–6.
[11] Shenoy PA, Vishwanath S, Bhat SN, Mukhopadhyay C, Chawla K. Microbiological profile of chronic osteomyelitis with special reference to anaerobic osteomyelitis in a tertiary care hospital of coastal Karnataka. Tropical Doctor 2020;50(3):198–202.
[12] Yu D, Kim SW, Jeon I. Antimicrobial therapy and assessing therapeutic response in culture-negative pyogenic vertebral osteomyelitis: a retrospective comparative study with culture-positive pyogenic vertebral osteomyelitis. BMC Infect Dis 2020;20(1):939.
[13] Wobma H, Jaramillo D, Imundo L. When local bone pain is just the tip of the iceberg-a case report of three patients with chronic multifocal recurrent osteomyelitis and some red flags to help make the diagnosis. Front Pediatr 2019;7:407.
[14] Demharter J, Bohndorf K, Michl W, Vogt H. Chronic recurrent multifocal osteomyelitis: a radiological and clinical investigation of five cases. Skelet Radiol 1997;26(10):579–88.
[15] Jurik AG, Klicman RF, Simoni P, Robinson P, Teh JSAPHO. The value of imaging. Semin Musculoskelet Radiol 2018;22(2):207–24.
[16] Earwaker JW, Cotten A. SAPHO: syndrome or concept? Imaging findings. Skelet Radiol 2003;32(6):311–27.
[17] Hoffer FA, Emans J. Percutaneous drainage of subperiosteal abscess: a potential treatment for osteomyelitis. Pediatr Radiol 1996;26(12):879–81.
[18] Riebel TW, Nasir R, Nazarenko O. The value of sonography in the detection of osteomyelitis. Pediatr Radiol 1996;26(4):291–7.
[19] Schleifer J, Liteplo AS, Kharasch S. Point-of-care ultrasound in a child with chest wall pain and rib osteomyelitis. J Emerg Med 2019;57(4):550–3.
[20] Shahid M, Holton C, O'Riordan S, Kraft JK. Sonography of musculoskeletal infection in children. Ultrasound (Leeds, England). 2020;28(2):103–17.