Clinical Case Report

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Treatment of cryotherapy and orthotopic transplantation following chondromyxoid fibroma of zygomatic bone

A case report

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Abstract

Introduction: Chondromyxoid fibrotherma (CMF) is a rare benign cartilage tumor that occurs more frequently in young males at the age of 20 to 30. It occurs more frequently on long bones, but rarely involves craniofacial bones.

Case presentation: This study mainly introduced a 30-year-old male with CMF of zygomatic bone. Single tumor excochleation was conducted initially. However, CMF reoccurred, and then the following steps were adopted: firstly, the tumor was extensively excised; secondly, in vitro tumor excochleation was conducted; thirdly, the excised tumor bone was placed in liquid nitrogen for 3 cycles of cryoablation; finally, the orthotopic transplantation was performed to reconstruct the zygomatic appearance, with satisfactory follow-up efficacy obtained.

Conclusions: Orthotopic transplantation after tumorectomy and cryopreservation of tumor bone in liquid nitrogen could lead to excellent therapeutic efficacy and deserves to be widely applied in clinical practice in the treatment of a male patient with CMF of zygomatic bone, because it not only radically eliminates the tumor and kills tumor cells, but also provides bony skeleton for the growth of new bone, thus greatly promoting postoperative aesthetic degree and reducing the occurrence rates of complications.

Abbreviations: CMF = chondromyxoid fibrotherma, CT = computed tomography, ECG = electrocardiogram.

Keywords: chondromyxoid fibroma, freezing, liquid nitrogen, zygomatic bone

1. Introduction

Chondromyxoid fibrotherma (CMF) is a benign cartilage tumor rarely seen in clinical practice. X-ray of CMF is manifested by local osteolytic damage, with slow clinical disease course and mild symptoms observed. Its morbidity accounts for 0.5% of all bone tumors,[1] and for 1.6% in all benign bone tumors. In 1948, this disease was initially described and named on the basis of 8 cases by Jaffe and Lichenstein,[2,3] who found that this tumor, although was similar to chondrosarcoma, showed benign clinical characters.[4] CMF occurs more frequently in males at the age of 20 to 30 years.[5] It often involves long bones, flat bones, and craniofacial bones,[3,5] with higher morbidity in long bones, especially in paroxysmal tibia and distal femur. However, CMF in craniofacial region has been rarely reported, about 2%.[5,6] According to the report of Won et al,[7] the morbidity of CMF in craniofacial region was near to 5.4%; it often involved maxilla and mandible, but the morbidity in mandible was 76%, evidently higher than the 24% in maxilla, and there was no significant difference in sex.[4] This tumor can be cured after local excochleation, but the recurrence rate is high if the surgical treatment is improper. Therefore, the selection of surgical protocol is of great clinical significance. This study mainly introduced the CMF in zygomatic region, a rare part, in a 30-year-old male, and reviewed relevant literature.

2. Case report

A 30-year-old male has been engaged in accountancy in a real estate company. On April 27, 2015, he visited Department of Stomatology in our hospital due to pain in zygomatic region on left side for 1 year. In the hospital, excochleation of lesion of zygomatic bone on left side was conducted under general anesthesia on day 3 after routine examinations were completed and surgical contraindications were excluded, and postoperative pathological results indicated CMF. The patient was discharged from the hospital after the surgical wound healed. At postoperative month 6, the patient complained of swelling pain on surgical field, but he did not receive any special treatment. However, the local swelling pain lasted and was accompanied by dull pain, and visual examination showed mild protrusion on

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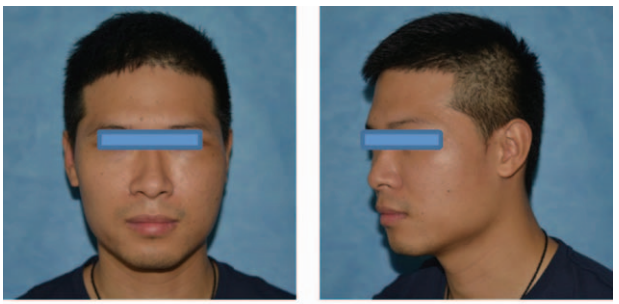
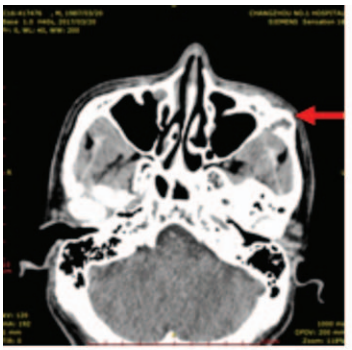


Figure 1. Preoperative photograph of the patient.

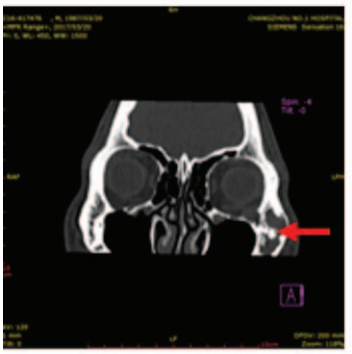
left-sided zygomatic region (Fig. 1). Therefore, on May 31, 2017, the patient re-visited our department, where computed tomography (CT) scan (Fig. 2) showed bone destruction region which protruded and was uneven in density and clear in border, with size of 2.3cm × 1.5 cm, and the bone cortex was discrete. Therefore, the patient was diagnosed with recurrence of CMF on left-sided zygomatic bone and was admitted in our hospital for surgery on selective day. He had been healthy at usual, and denied history of systematic system diseases like nerve system, cardiovascular system, respiratory system, digestive system, urinary system, or hematological system. He denied of infectious diseases like hepatitis B virus (HBV) or tuberculosis, or allergies to drugs or food, or contact with toxic and harmful chemical substances or radioactive substances. He also denied of history of smoking, alcohol consumption, contact with infected water, living in an epidemic region, drug abuse, feculent sexual intercourse, or family infectious diseases. After admission, examinations were conducted, including hematology test, liver function test, biochemical test, blood lipid test, coagulation function test, infectious marker test, and tumor marker test, which were all revealed to be in normal range. Electrocardiogram (ECG) showed sinus rhythm, and x-ray of the whole chest did not indicate any significant abnormalities in either lung. Preoperative examinations indicated that there were no significant surgical contraindications. Therefore, extensive tumorectomy of left-sided zygomatic bone + cryopreservation using liquid nitrogen + autologous tumor bone replantation for reconstruction of zygomatic bone was conducted under general anesthesia on June 2, 2017.

2.1. Process of surgery

The patient was placed in supine position. After general anesthesia acted, an incision about 8 cm was made from tragus to lateral left canthus and inferior margin of lower eyelid along the running line of zygomatic arch (Fig. 3), after which the skin subcutaneous tissues, orbicularis oculi muscle, and periosteum of infraorbital margin were exposed in succession. Flap was unfolded, and soft tissue was dissected from periosteum, after which multilacunal apiary-like lesion with size of 3.0cm ×



A Plain scan: Damage and invasion of zygomatic cancellous bone on left side



B Coronary scan: Room-assigning changes with uneven density in zygomatic cancellous bone on left side

Figure 2. Preoprative CT of the patient. CT = computed tomography.

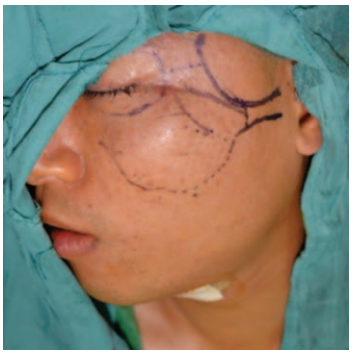
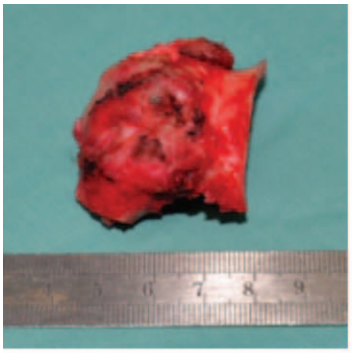
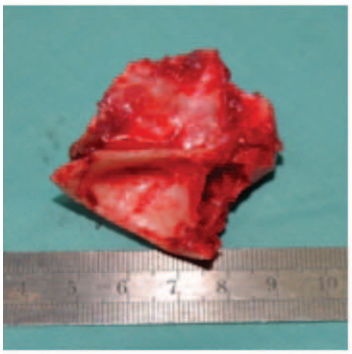


Figure 3. Blueprint for surgery.

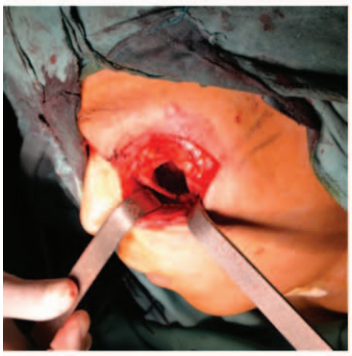
3.0cm × 2.5 cm was found in zygomatic bone. Affected zygomatic bone (Fig. 4) was removed by truncating the normal sclerotin around, and tumor tissues were completely scraped in vitro (Fig. 5). Several holes were made on the removed bone to prevent the occurrence of cracks on tumor bone due to alternation of contraction and expansion induced by sudden temperature change. Meanwhile, these holes were also beneficial to the neoangiogenesis after implantation. And then, the affected zygomatic bone was put into a small drug cup full of liquid nitrogen to be cryopreserved for 15 minutes, and then thawed at room temperature for 10 minutes (Fig. 6). The bone was replanted to the original focal region after 3 cycles of cryoablation, in which the bone was aligned with the lacerated ends of the dissected bone, and 3 titanium plates were applied for fixation (Fig. 7). A negative-pressure drainage tube was placed in surgical wound, which was then sutured layer by layer.



A Lateral view outside of the tumor: Cartilaginous bone tumor with size of 3.0cm×3.0cm×2.5cm



B Lateral view inside of the tumor: Cancellous bone damaged and showed multi-lacunal apiary-like changes



C Post-tumorectomy wound

Figure 4. Zygomatic bone tumor.

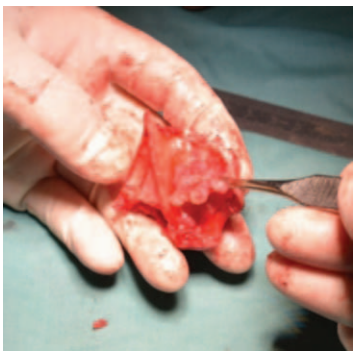


Figure 5. Tumor excochleation.

Postoperative pathological report demonstrated CMF of zygomatic bone on left side (Fig. 8). Drugs were intravenously injected for anti-inflammation, detumescence, and fluid transfusion after operation. The negative-pressure drainage tube was removed, followed by removal of suture, after which the patient was discharged from our hospital on postoperative day 9. The patient revisited our hospital for re-examination at postoperative month 6, and CT (Fig. 9) showed that there was no evidence of tumor recurrence, and the bone density of autogenous bone was reduced and absorbed slightly. As to the appearance, the reconstructed zygomatic bone was basically symmetric to the healthy one, the malformation was insignificant, and the aesthetic efficacy was excellent (Fig. 10) and satisfactory. No infection or immunological rejection response had been observed since postoperative day 1. The patient signed the informed consent form for surgery before treatment, and this study had received the approval of Ethics Committee of our hospital. It should be mentioned that the 3 titanium plates used had not been removed from the patient to date. At last, the patient had provided informed consent for publication of the case.

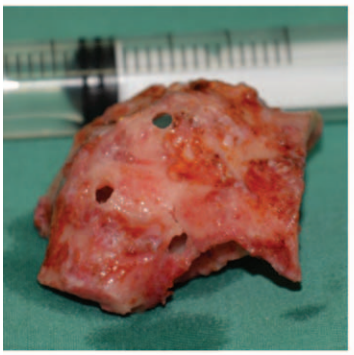
3. Discussion

3.1. Brief introduction of CMF

Chondromyxoid fibrotherma is a rare benign primary cartilage bone tumor. In 1948, it was initially reported and named by Jaffe and Linchtenstein, who believed that it was originated from cartilage connective tissue and occurred in immature myxoid mesenchymal cells, and that it was myxoid component dominated in early stage, followed by cartilage-like transformation or fibrosis of the myxoid components, and cartilage matrix calcification or ossification could be found in advanced stage.[2,3] CMF rarely involves craniofacial bones in which mandible is frequently reported as a site for the occurrence of CMF, and only 4 cases involving zygomatic bone have been reported.[8–11]

Chondromyxoid fibrotherma was chronic in attack, mild in symptoms, and long in disease course, without systematic symptoms. Generally, it is locally manifested by protrusion

A The removed bone is placed in liquid nitrogen for cryotherapy



B The removed bone is melted at room temperature, and holes are made to avoid cracks on involved bone

Figure 6. Cryoablation of involved bone.

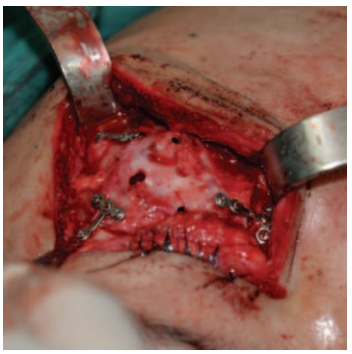


Figure 7. Replantation of treated autograft, and fixation of the broken end using titanium plate and screws.

and deformation complicated with mild pain and edema in the affected site,[6] and soft-tissue mass that is touchable in superficial or extensive lesions, with local pain aggravates, which may inhibit joint function in patients whose joints have been involved, consequently leading to limitation of motion (LOM). However, the occurrence of pathological bone fracture is rarely seen.[12] The case in this study visited our hospital with compliant of local swelling pain.

The imageological manifestations of CMF are usually marked by the characteristic changes of a benign lesion, which lack of certain specificity. X-ray examination results often show osteolytic bone defect with clear border which is marked by circular or oval transmission unicapsular or multicapsular changes, or scallop-like changes sometimes. The lesions often invade or protrude towards outside from cortex, and are frequently complicated with buttress-like protrusions formed

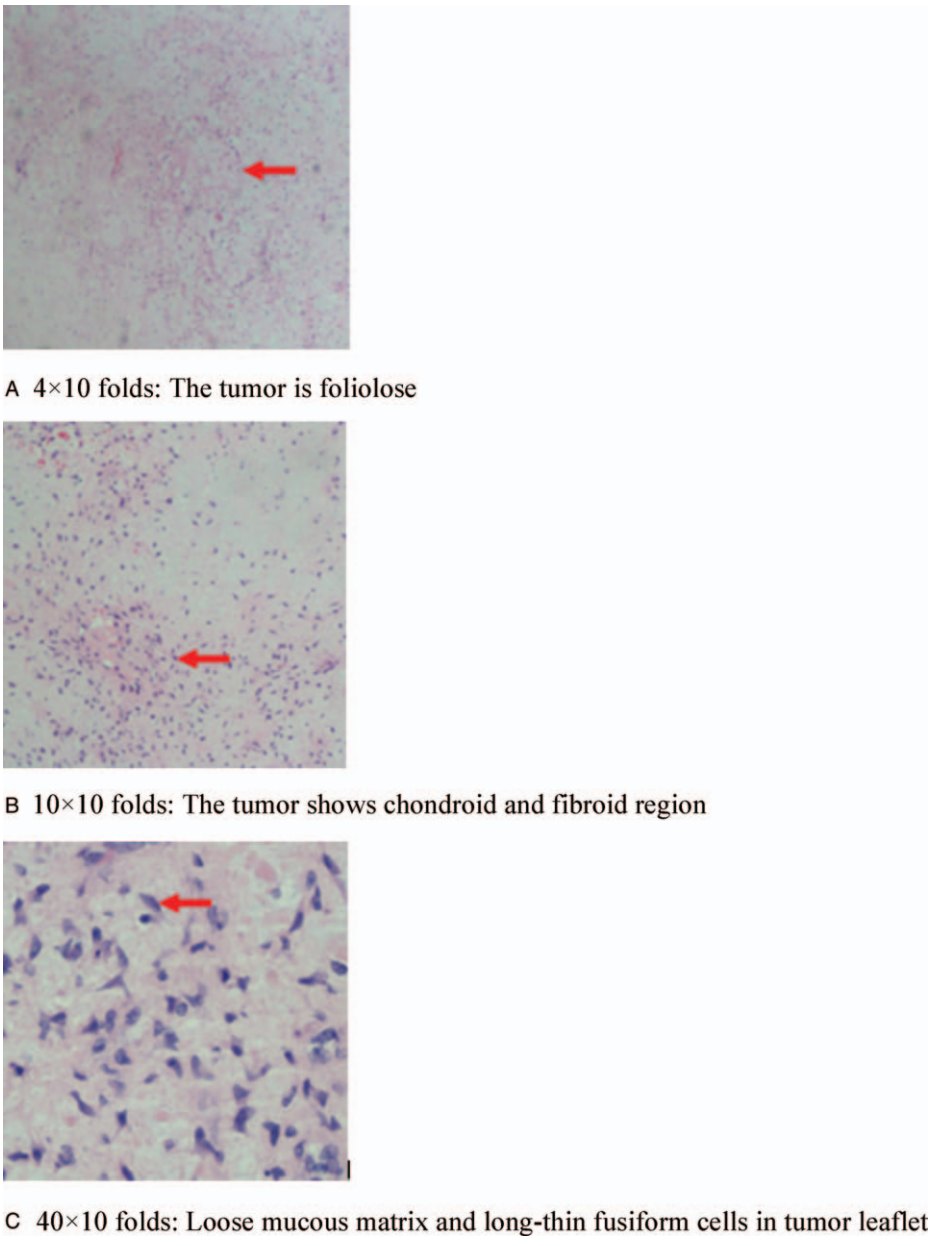
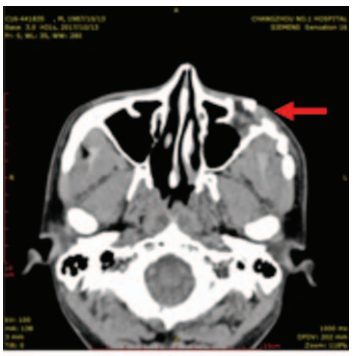
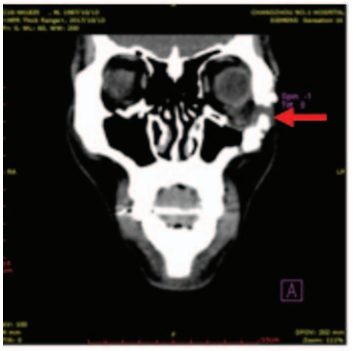


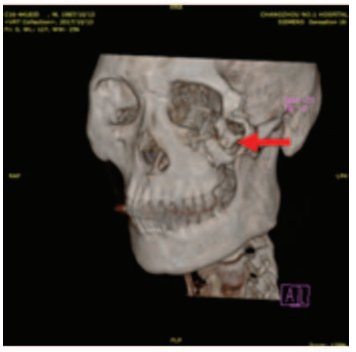
Figure 8. Hemooxylin and eosin (H&E)-stained pathological slice.



A Plain scan

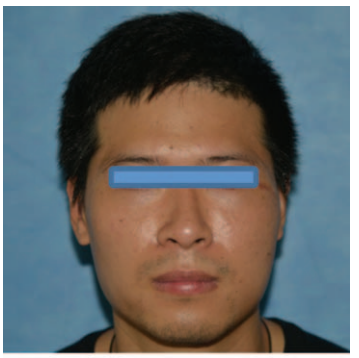


B Coronary scan

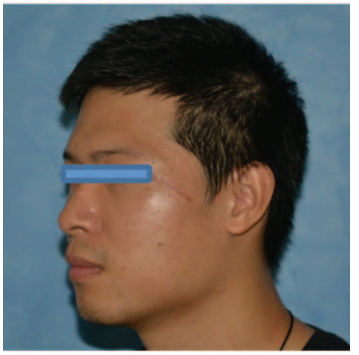


C 3D reconstruction

Figure 9. Patient's CT at postoperative 6: no tumor recurrence is found, and autograft is slightly low in bone density and is mildly absorbed. CT = computed tomography.



A Front view



B Lateral view

Figure 10. Patient's photograph at postoperative month 6: less changes than preoperative photographs, with favorable aesthetic degree.

by new bones on periosteum.[13] CT images usually reveal that the appearance is lobulated with sharp and sclerous margin, bone cortex is often thinned or expanded, that about 50% bone cortex are missing partially, and sporadic punctiform calcified lesions are found in about 13% tumors.[5]

Under microscope, chondroid, mucous, and fibrous regions vary in proportion in CMF. Typical CMF shows clear border or confertus lobular lesions. Loose mucous matrix and stellate long-thin fusiform cells are found in the center of the lobular lesions, cells at the margin of the lobular lesions are dense, the lobular lesions are separated by thin-layer fibrous vascular bundles, and multinuclear osteoclast-like giant cells, hemosiderin, and chondrocytes are found between the lobular lesions.[14,15] Frank hyaline cartilage center is rarely seen, and only 19% of patients with CMF have hyaline cartilage.[9,16] Meanwhile, local calcified lesions are also rare. CMF needs to be distinguished with chondroma using immunohistochemical test in which CMF is marked by epithelial membrane antigen and positive S100 proteins and cytokeratins, whereas chondroma is only manifested by positive S100 proteins.[6]

Generally, CMF needs to be distinguished with chondrosarcoma as 22% to 28% of patients with CMF may be misdiagnosed.[9] Imageologically, chondrosarcoma is marked by mouse-bite or insect-bite osteolytic bone lesions with invasive bone destruction, lobulated lesion, and unclear border, which often showed invasive growth to surrounding tissues. Histologically, chondrosarcoma lesions reveal fine calcified lesions, are atypical lobular in structure, and may be separated by fillet or saturate into trabecula. Generally, it varies with CMF in that it is not characterized by significantly few central cells and right peripheral cells, but is active in heteromorphosis and proliferation of chondrocytes.[16] In this study, the case should also be distinguished with osteoclastoma, abnormal fibrous dysplasia of bone, and bone cyst.

3.2. Treatment for CMF

Therapeutic treatment for CMF that have been reported include single excochleation, excochleation combined with cauterization of affected bone using phenol,[17] excochleation combined with phase I bone transplantation, and resection of the whole bone combined with phase I bone transplantation.[18] It is reported that application of single excochleation may reserve tumor cells, thus leading to 80% of tumor recurrence rate.[17] Soni et al[19]

believed that CMF should be treated with a more radical method named local resection as they noticed a biological behavior of local invasion in CMF in young patients. The recurrence rate of CMF can be reduced to 7% when excochleation combined with cauterization using phenol or osteotomy combined with bone transplantation is performed.[17,20] However, the recurrence rate needs to be further observed and followed up when resection of the whole bone is performed.[18] Radiotherapy is recommended to patients whose lesions cannot be excised by surgery.[18] However, radiotherapy will trigger chronic osteomyelitis, radioactive osteonecrosis, and malignant transformation.[20] Nevertheless, the patients who are reported to have recurrence and are clinically marked by malignancies are believed to be initially misdiagnosed by some scholars.[20]

Zygomatic bone is 1 of the most important constituent parts of lateral part of mid-face, and an important structure for reserving the width and forward protrusion of mid-face, whose morphology and protrusion has great influence on the coordination and aesthetics of face. Therefore, surgical resection of zygomatic bone, which is involved by tumors or trauma, may lead to bad influence on the aesthetics of face if there is no proper reconstruction method. In this study, different selections for the reconstruction of zygomatic bone, including rib graft, ilium graft, and cranial parietal bone graft,[21] are introduced, but the aesthetic efficacy after reconstruction is not satisfactory. In this study, the patient was a young male whose facial bone was involved by CMF, with aesthetic issue concerned, but CMF reoccurred not long after the primary surgery with single excochleation. Therefore, secondary surgery for the recurrent CMF had great difficulty as it not only needed to excise the whole lesion, but also achieve satisfactory aesthetic efficacy by repair and reconstruction. New surgical region was needed if ribs, ilium, or cranial parietal bone was selected for repair and reconstruction, which could result in great pain to the patient. Additionally, the above 3 bones were difficult to form zygomatic bone, which might bring about difficulty in recovering the lateral contour of mid-face, thereby impacting the postoperative anesthetic efficacy. Therefore, resection of tumor bone + excochleation of tumor tissue + cryoablation of involved bone using liquid nitrogen was performed after consideration to remove the residual tumor cells, and replant the tumor bone, which not only removed the lesion, but also had little influence on patient's facial appearance. However, this surgical method for CMF has not been reported so far.

3.3. Feasibility of cryotherapy

3.3.1. History of cryotherapy. Cryotherapy can be traced back to 19th century. In 1683, Boyle initially proved that condensation could kill living tissues. In 1851, Arnott attempted to treat breast cancer using −24°C salt-ice mixture to relieve patients' pain. Till 20th century, Gage[22] verified through experiments that liquid nitrogen cryotherapy could lead to necrosis to bone tissues from perimyelis to periosteum in 1966. In 1969, Marcove et al initially applied cryosurgery for the treatment of bone tumor, in which liquid nitrogen was directly placed to the residual cavities of bone tumors in order to directly kill the tumor cells, with success achieved. And then, after continuous exploration and study of applying liquid nitrogen cryotherapy for the treatment of multiple diseases comprising bone metastases, primary benign bone tumors, lowly-differentiated malignancies, and highly-differentiated malignancies in succession, Marcove group[23] concluded that liquid nitrogen cryotherapy, as a therapy for tumor cryoablation of after intracystic excochleation or resection of margins of tumors, could lead to necrosis of residual tumor tissues, and maximally kill tumor cells, consequently achieving the target of resection or expanded resection of tumor margin, and that as an auxiliary surgical treatment, it was more advisable for the treatment of primary benign, lowly-differentiated and metastatic bone tumors. Many clinical reports[24,25] revealed that this method had satisfactory efficacy in the treatment of benign invasive and lowly-differentiated bone tumors.

3.3.2. Influencing factors for cryotherapy. Cryogenic temperature, cooling velocity, cryogenic time, rewarming velocity, and cryoablation cycle frequencies have been considered as the influencing factors for cryotherapy currently. Kuylenstierna[26] proved through an animal experiment that the temperature from −40°C to −50°C was fatal to tissues. Rerte[27] found that ice crystals would be formed in histological and intercellular substances if the temperature was cooled down slowly, and they could absorb water from cells, which, in turn, inhibited the formation of crystals in cells, thus protecting cells away from cryoinjury. Only when the temperature decreases sharply can ice crystals be frozen and formed simultaneously inside and outside of cells, and fast cooling is an important factor to insure the cryotherapy efficacy as the damage caused by ice crystals formed inside of cells is the maximum. Rewarming process after the end of cryotherapy is another critical step that can induce damage to cells. Salt[28] believed that rewarming process could redamage residual cells, and shearing action induced by early recrystallization of small ice crystals and cells in hyposmosis environment when ablated might lead to rupture of cells due to expansion. Contrary to cooling process, slow ablation is greater in destructive power and can cause embolization to tissue microvessels, which may further aggravate hypoxia, thus triggering cell apoptosis. Woolley et al[29] used dogs' kidneys to observe the difference between different rewarming processes, and the results revealed no significant difference between natural rewarming and fast rewarming in damage to tissues. Therefore, in this study, the involved bone was immersed in liquid nitrogen to achieve the target of fast cooling, and the bone was ablated at room temperature, which, as a process of slow rewarming process, could better eliminate residual tumor cells.

Experiment proved that repeated freezing could increase the cooling rate. Mala et al[30] used magnetic resonance to measure the sizes of ice hockey in different cryoablation cycles during cryosurgery for liver metastases, and the results demonstrated that the mean size of ice hockey after the end of cycle 2 cryotherapy was larger than the mean size after the end of cycle 1 cryotherapy by 42%. Therefore, it is believed that repeated freezing can enhance the inactivation efficacy to tumor cells. In this study, 3 cryoablation cycles in total were performed so as to maximally inactivate tumor cells.

3.3.3. Advantages of liquid nitrogen cryotherapy. Using liquid nitrogen for cryotherapy has certain advantages as it is low in medical cost, can maintain osteoinductivity and osteoconduction, is sufficient in biomechanical intensity, is absent in risks of infectious diseases or immunological rejection reactions, can reserve mesochondrium, makes tendons and ligaments more easy to attach bones, is absent in harmful denaturized substances, and is characterized by early ababiosis and exertion of cryoimmunological action.[31] Tanzawa et al[32] reported the histological examinations of frozen autograft removed at postoperative year 6, and the results revealed that tissues in most cortex and medulla regions had been rebuilt and had vitality. As the bone morphogenetic proteins (BMPs) have not been damaged during freezing process, and osteoinductivity has been reserved, some

scholars believe that the long-term excellent therapeutic efficacy due to reconstruction using autograft after cryoalation is closely associated with the reserved osteoinductivity.

3.3.4. Disadvantages of liquid nitrogen cryotherapy. However, this method also has some disadvantages. After treatment with this method, in situ sequestrum forms, which has similar to allograft in complications like infection, bone un-union and bone absorption, etc.[31] The sequestrum cannot bear compression or weight locally in that it will take a long time to be completely replaced by new bone, before which it is easy to develop pathological bone fracture. Marcove et al[33] found that repeated cryotherapy might easily lead to pathological bone fracture due to pathological changes to normal bones around tumor, damage to blood circulation in frozen bone shell, and prolonged repair time of necrotic tissues. Therefore, it was believed that although repeated cryotherapy could enhance the inactivation efficacy on tumor cells, it also had negative factors on bone healing. In our case report, although patient's allograft had mild bone resorption, its bony supporting structure did not change, which had caused no influence on facial aesthetics.

3.4. Advantages of orthoptic transplantation in this study

In this study, orthoptic transplantation was applied for the patient instead of alloplastic materials because autograft could be more accepted by human body more easily with less rejection reactions than alloplastic materials, and it could unite with surrounding bones favorably after surgery. The case included in this study suffered recurrence of chondromyxoid fibroma and received orthoptic transplantation, after which he was completely cured, his tumor was radically removed and the tumor cells were completely eliminated. The technique used in this study was distinct with and superior to those used in other studied as it could also provide bony stent for the growth of new bone so that the appearance of zygomatic bone could be preserved. The patient had been followed up for half a year, but no evidence of tumor recurrence was found, only mild bone resorption was noticed, and patient was highly satisfactory to the surgical results.

4. Conclusions

In this study, excellent therapeutic efficacy was obtained by the male patient with CMF of zygomatic bone after receiving tumorectomy + in situ replantation, after liquid nitrogen cryotherapy of tumor bone, which not only radically cure the tumor and eliminate tumor cells, but also provide bony stent for the growth of new bone so that the appearance of zygomatic bone could be reserved basically, with mild influence on facial anesthetics and without occurrence of antigen-antibody rejection reactions or infection. The patient had been followed up for half a year, but no evidence of tumor recurrence was found, and only mild bone resorption was noticed, and the patient was highly satisfactory to the surgical results. The male patient will be followed up continuously to further understand the long-term efficacy of this therapeutic protocol in the treatment of CMF of zygomatic bone.

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Writing – original draft: Zhi-Chao Zhu.
Writing – review & editing: Wen-Jun Yang.

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